PRESCRIPTION MEDICINES
CODE OF PRACTICE AUTHORITY

CODE OF PRACTICE REVIEW

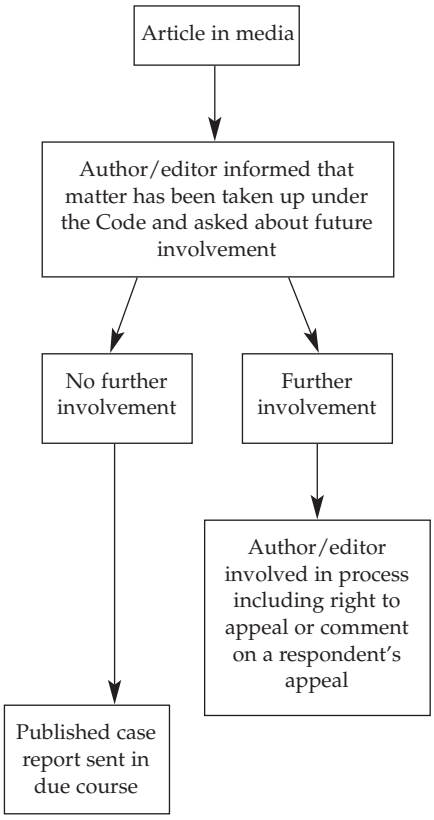
NUMBER 54 NOVEMBER 2006

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.

Cases arising from media criticism

Following consideration of recent cases which arose from articles in the media, the Code of Practice Appeal Board decided that it would be helpful to look at the established procedure for dealing with such cases. Media information from which it appears that a company might have breached the Code can come from, *inter alia*, letters or articles published in the professional or lay press.

The Appeal Board considers it is very important for the reputation of the industry and the continued effectiveness of self-regulation that articles etc in the media, from which it appeared that a company might have breached the Code, are taken up and dealt with as complaints under the Code. This has been established practice for a number of years.



The existing procedure – whereby the Director instigates the complaints procedure when it appears from something published in the press that a company might have contravened the Code, with the rights of the complainant being given to the author of the article – will continue.

If no author is named, the editor of the publication will be given the rights of the complainant. However, the author, or editor, will now be asked if they want to be involved in the case and whether they have any additional information to submit; the consequences of not being involved (no right of appeal and no right to comment on a respondent's appeal) will be explained in writing. If the author or editor declines involvement, this will now be stated in the case report.

The ABPI Board of Management has agreed this procedure and considers it is important for self-regulation that articles, and the like, criticising the activities of pharmaceutical companies are taken up and dealt with under the Code irrespective of whether the author or editor wants to be involved.

Public reprimand and suspension for Merck Sharp & Dohme

Merck Sharp & Dohme Limited has been publicly reprimanded by the Code of Practice Appeal Board for breaches of the Code in relation to a nurse audit programme. The Appeal Board considered it to be an extremely serious matter.

Merck Sharp & Dohme was subsequently suspended from membership of the ABPI for a minimum of three months by the ABPI Board of Management.

The ABPI Board noted that Merck Sharp & Dohme had fully accepted responsibility for the matters giving rise to the complaint and that current management, including the new managing director, was taking action to ensure that there was no repeat, action which ranged from training through to changes in culture. The suspension took effect from 2 October 2006. Merck Sharp & Dohme will be required to comply with the Code during the period of suspension.

Full details can be found at page 13 of this issue of the Review in the report for Case AUTH/1814/3/06.

Serious breaches of the Code are advertised

Paragraph 13.7 of the Constitution and Procedure requires brief details of cases in which companies were ruled in breach of Clause 2 of the Code, were required to issue a corrective statement or were the subject of a public reprimand, to be advertised.

An advertisement has been published in the BMJ and the Pharmaceutical Journal concerning Case AUTH/1827/4/06 (published in the August 2006 Review) where Merck Sharp & Dohme had been ruled in breach of Clause 2 of the Code.

CODE OF PRACTICE TRAINING

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

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

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

Friday, 23 March

Friday, 4 May

Further seminar dates for 2007 will be arranged in due course.

Short training sessions on the Code or full all day seminars can be arranged for individual companies, including advertising and public relations agencies and member and non member companies of the ABPI. Training sessions can be tailored to the requirements of the individual company.

For further information regarding any of the above, please contact Jean Rollingson for details (020 7747 1443).

How to contact the Authority

Our address is:

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Code of Practice Authority
12 Whitehall
London SW1A 2DY

www.pmcpa.org.uk

Telephone: 020 7930 9677
Facsimile: 020 7930 4554

Copies of the Code of Practice for the Pharmaceutical Industry and of this Review can be obtained from Lisa Matthews (020 7747 8883).

Direct lines can be used to contact members of the Authority.

Heather Simmonds:	020 7747 1438
Etta Logan:	020 7747 1405
Jane Landles:	020 7747 1415

The above are available to give informal advice on the application of the Code of Practice.

The Authority rather than the ABPI is the contact point for information on the application of the Code.

Representatives' call rates

The Authority has received a number of complaints from representatives alleging that the call rates they are set are excessive, in breach of the Code.

Companies are reminded that the number of calls made on a doctor or other prescriber by a representative each year should not normally exceed three on average. This does not include the following which may be in addition to those three visits:

- attendance at group meetings, including audio-visual presentations and the like
- a visit which is requested by a doctor or other prescriber or a call which is made in order to respond to a specific enquiry
- a visit to follow up a report of an adverse reaction.

Thus although a representative may call on a doctor or other prescriber three times in a year the number of contacts with that health professional in the year may be more than that. Briefing material should clearly distinguish between expected call rates and expected contact rates. If representatives are bonused on contacts their targets must be realistic such that, in order to achieve them, representatives do not have to solicit opportunities to call back or use the delivery of an item as an inducement to gain an interview.

The Authority considers it helpful if all briefing material relating to call/contact rates either reminds representatives of the requirements of the Code in that regard or refers them to another relevant document.

Bye Jean

Jean Rollingson, who has been with the Authority since 1999 as its Administrator and Personal Assistant to the Director, will retire early in January. The Authority thanks Jean for all her hard work on its behalf and wishes her a long and happy retirement.

The basis of case reports

Reports of completed cases published in the Review generally consist of the complaint, the response from the company concerned and the ruling of the Code of Practice Panel. Some also have details of an appeal to the Code of Practice Appeal Board and a few include the outcome of consideration by the ABPI Board of Management.

The complaint and the response from the company are published essentially as received, except for the omission of certain details, in particular the names of individuals and third party organisations. They are not corrected in any way and may therefore contain errors. The rulings of the Panel and the Appeal Board and the decisions of the ABPI Board are published in full, again except for the omission of certain details such as the names of individuals.

THE SUNDAY TIMES/DIRECTOR and a GENERAL PRACTITIONER v PFIZER

Sponsored nurses

An article entitled 'Nurses earn bonuses for use of latest drugs', which appeared in The Sunday Times, criticized the activities of, *inter alia*, Pfizer. In accordance with established practice the matter was taken up by the Director as a complaint under the Code (Case AUTH/1807/3/06).

The article stated that Pfizer had paid nurses through an agency to conduct free audits in GP surgeries to identify patients with conditions such as asthma or diabetes who might benefit from a new medicine. The nurses were paid a salary and usually a bonus; nurses were said to be rewarded for the number of surgeries they visited or the number of patients or records they saw. The article also stated that the nurses were described in promotional literature as being able to 'influence' new prescriptions for the benefit of their pharmaceutical companies. The nurses were routinely backed up by sales teams.

A general practitioner subsequently complained about the involvement of Pfizer in providing nursing advisors as detailed in The Sunday Times (Case AUTH/1810/3/06). The complainant was greatly concerned about the nurse advisors because they had a conflict of interest to promote a particular product. The Sunday Times had assured the complainant that the story was correct. The GP alleged that it was a clear admission that the nurse advisors were not independent but were involved in the marketing of medicines. A breach of the Code was alleged.

The Panel noted that Pfizer had sponsored nurses to enable a primary care trust (PCT) to perform a chronic obstructive pulmonary disease (COPD) audit. The provision of such nurses was not dependent upon the prescription of any Pfizer medicine. Any recommendations for management made by the nurse would be in accordance with the National Institute for Health and Clinical Excellence (NICE) COPD guidelines or from the relevant formulary. A draft protocol for the audit noted that four pharmaceutical companies would fund the work; the companies would have no involvement in the design of the audit or be able to influence its conduct. The Panel did not consider that the audit was an inducement to prescribe, supply, administer, recommend or buy any medicine. No breach of the Code was ruled.

With regard to a coronary heart disease (CHD) audit programme, the Panel noted that the agreement was to support a particular medical group with its project to implement nurse led CHD clinics. A document setting out the terms stated that for the avoidance of any doubt, the funding provided by Pfizer was a stand-alone arrangement and was not dependent on or related to any past, present or future commercial relationship with Pfizer nor any business decision that the practice might make relating to Pfizer or any of its products. The Panel thus did not consider that the audit was an inducement to prescribe, supply, administer, recommend or buy any medicine. No breach of the Code was ruled.

The Panel noted that a cardiovascular risk management programme was a national project provided by a team of nurse advisors. In a representatives' briefing the project was listed as one of four Lipitor value added programmes. Representatives were instructed that the first key consideration was to always sell Lipitor first and be confident that the practice supported the use of Lipitor in appropriate patients. The representatives should ensure that they had discussed, agreed and understood the practice patient management protocols and that these correctly positioned Lipitor as statin of choice for 'defined' patients groups. Representatives should understand how each of the value added programmes could support them and their customers. The representatives were reminded that the use of the programme should not be an inducement to prescribe and selected practices should continue to prescribe as they chose. A 2005 Outcomes Summary showed that in 109 completed practices, of 3,524 patients not treated to target, 2,756 (78%) were initiated or titrated on Lipitor. The summary slide informed representatives that targeting was critical so as to maximise benefit to them and their customer. Although the official contract between the practice and Pfizer contained the same statement as described above with regard to the nurse led CHD clinics, ie the funding provided by Pfizer was a stand-alone arrangement etc, the Panel nonetheless considered that the instructions to representatives, that the service should only be offered where they were confident that Lipitor would be used as the statin of choice in appropriate patients, were unacceptable. Similar instructions were included in the relevant service agreement between the nurse agency and Pfizer. The Panel thus ruled breaches of the Code including Clause 2.

The Panel noted that it had previously considered an outcomes guarantee study (Case AUTH/1109/11/00) wherein it had considered that the scheme, which at that time was a pilot study, was not in breach of the Code. The documents provided in respect of the case now at hand described an outcomes guarantee programme as being when a pharmaceutical company guaranteed that its medicine would achieve certain targets in a given patient group. The project aimed to ensure that those patients who would benefit from LDL cholesterol lowering medicines received them. Within the programme Pfizer had provided an outcomes guarantee for Lipitor although participating doctors were not obliged to prescribe it. Any rebate due under the terms of the guarantee was paid to a PCT for the general purpose of improving primary care services and not to individual general practices. The company submitted that this ensured that there was no financial inducement for prescribers to choose one

lipid-lowering medicine over another. It was stated that the programme and the support provided by Pfizer was not conditional upon or related to any commitment on the part of the PCT to purchase, prescribe, administer or recommend any Pfizer product. The Panel thus ruled no breach of the Code.

The COPD Response programme was also a nationally run project to identify primary care patients with COPD, or a component thereof, and ensure that they were optimally treated according to recognised national guidelines. Although representatives identified suitable practices the criteria they worked on did not include any reference to particular medicines. Pfizer hoped that provision of the service would foster closer relationships between the sales teams and the practices. There was, however, no obligation to use Pfizer products, although it was acknowledged that these were included in the national and European guidelines on the treatment of COPD. The Panel noted that the nurse advisor briefing document was for use by both the sales team and the nurse advisors. The selection of appropriate practices was by the sales team using a list of criteria, some or all of which were to be met. The criteria related to size, computerised notes, spirometer availability and an interest in respiratory medicine and COPD in particular. Sales representatives would attend the introductory meeting. The briefing document included objection handling. The response to maintenance of prescribing perogative was 'Whilst [a named pharmaceutical company] and Pfizer hope that you will consider the benefits of using their product for COPD patients there is no obligation to do so. The BTS COPD Guidelines and the European GOLD initiative both recommend treatment pathways that include [the named pharmaceutical company] products that are licensed for the management of COPD'. Overall the Panel did not consider that the COPD response programme was an inducement to prescribe, supply, administer, recommend or buy any medicine. No breach of the Code was ruled.

The Panel noted that Pfizer had provided some information about other similar programmes that it had run within the last three years. A standard letter relating to the payment of a nurse's overtime to allow her to conduct patient or medicine reviews stated that the funding provided by Pfizer was a stand-alone arrangement and was not dependent on or related to any past, present or future commercial relationship with Pfizer or any business or other decisions that the practice had or might make relating to Pfizer and its products. The Panel considered that the evidence before it was not such as to demonstrate that any of the programmes had been an inducement to prescribe, supply, administer, recommend or buy any medicine. No breach of the Code was ruled.

An article entitled 'Nurses earn bonuses for use of latest drugs', which appeared in The Sunday Times on 3 March 2006, criticized the activities of, *inter alia*, Pfizer Limited. In accordance with established practice the matter was taken up by the Director as a complaint under the Code (Case AUTH/1807/3/06).

A general practitioner subsequently complained about the involvement of Pfizer in providing nursing advisors as detailed in The Sunday Times (Case AUTH/1810/3/06).

COMPLAINT

The article stated that Pfizer had paid nurses through an agency to conduct free audits in GP surgeries to identify patients with conditions such as asthma or diabetes who might benefit from a new medicine. The nurses were paid a salary and usually a bonus linked to the number of patients or records they saw.

The article also stated that the nurses were described in promotional literature as being able to 'influence' new prescriptions for the benefit of their pharmaceutical companies. The nurses were routinely backed up by sales teams.

A recruitment consultant had told an undercover reporter that the job of the nurses was to identify patients with a specific condition '[it] opens the doors to a medical representative. They come in and close the business'.

The general practitioner was greatly concerned by the involvement of these nurse advisors because they had a conflict of interest to promote a particular company product. The complainant stated that he had contacted The Sunday Times which had transcripts of conversations between a reporter and an agency representative. The Sunday Times had assured the general practitioner that the story was correct. The general practitioner alleged that it was a clear admission that these nurse advisors were not independent but were involved in the marketing of medicines. The complainant alleged that this was in breach of the Code. The complainant requested that the Panel considered halting any current nurse advisor activity until this case had completed.

When writing to Pfizer, the Authority asked it to respond in relation to Clauses 2, 9.1 and 18.4 of the Code and, if the activities had not taken place in 2006, to respond in relation to the requirements of Clauses 2, 9.1 and 18.1 of the 2003 Code.

RESPONSE

Pfizer stated that it had ten programmes that it believed were relevant to this complaint. It had responded to this complaint on the basis of the 2003 Code, regardless of whether the programmes were current or not. In support of its submission, Pfizer provided the Authority with a large number of documents relating to the audit programmes.

With respect to the implied criticism of its nurse-led programmes in The Sunday Times article, Pfizer rejected the headline allegation that 'Nurses earn bonuses for use of latest drugs' and the implication that the objective of nurse-led programmes was to influence a switch of patients to 'costly new drug regimes'.

Pfizer's nurse-led primary care programmes benefited patients by giving them the time, attention and guidance which were not often available within the

average 7-minute GP consultation. This additional support helped GP practices improve the management of their patients' medical conditions in line with local and/or national NHS guidelines or targets.

The Sunday Times article alleged that 'there are no incentives to curb their [GPs'] drugs bills'. On the contrary, GPs were heavily incentivised locally and nationally to minimise their expenditure on medicines. It would not be in any practice's interest to participate in a programme that drove up costs without any economic or patient benefits.

GPs whose practices participated in Pfizer nurse programmes always retained freedom to choose which (if any) medicines to prescribe. Pfizer's medicines would not necessarily be chosen by participating practices and indeed, in some areas covered by these programmes, it did not make any of the relevant medicines.

Pfizer submitted that its nurse-led primary care programmes were ethical, legal, and complied with the Code and professional regulations. The benefit that Pfizer gained from these programmes was not a crude *quid pro quo*, whereby it provided a service in return for patients being switched to its medicines. Rather, by providing a specialist resource that might not otherwise be available, Pfizer supported GP practices in conducting a review of appropriate treatment in a particular patient population. Often this generated evidence that demonstrated the value of prescribing more effective medicines, in terms of reduced hospital admissions, fewer repeat patient visits, a reduction in complications arising from under-treatment, and therefore lower overall costs to the NHS. Clearly, where these more effective medicines were Pfizer medicines, there was a commercial benefit for the company.

Pfizer did not accept that this potential benefit rendered these programmes unacceptable – rather it represented an advantage for the NHS, for patients and for Pfizer. It was important to note that there was no direct or guaranteed return to Pfizer from these programmes.

The process by, and purpose for, which the nurse advisors were placed in GP practices was explained below in relation to each programme. In each case, access to patients' records was granted by GPs in order to see whether patients were being treated in accordance with relevant local and national prescribing guidance. Although recommendations might be given by nurse advisors (on the basis of the local or national NHS guidelines or targets or the practice's protocol), prescribing decisions were made by a GP.

The Sunday Times article also highlighted the number of nurses, the fact that their wages were effectively paid by pharmaceutical companies and certain bonus arrangements which were alleged to be linked to the number of patients or records that the nurses saw or the number of surgeries that they visited or the switch to 'costly new drug regimes' and thus act as an inappropriate incentive.

Pfizer submitted that the fundamental question was whether the nurses' activities were appropriate: if so, the number of nurses or the arrangements under which they were paid or incentivised was irrelevant. However, for the sake of completeness Pfizer's current programmes involved 14 nurse advisors. So far as it was aware, any bonuses paid under the programmes were based on legitimate criteria and did not exceed 10% of salary. The detail of any applicable bonus arrangements in relation to each individual programme was explained below. None of the programmes had a bonus scheme that was based on the number of patients or records seen or surgeries visited, the switch to costly new drug regimes or the sales or promotion of any product.

Specific issues relating to current programmes

1 Nurse Agency Primary Care COPD Audit – a local PCT

Pfizer submitted that it had funded a COPD programme together with a number of other pharmaceutical companies. Pfizer's involvement related to the hire of one full time equivalent nurse advisor and one project administrator from a nurse sales agency. The arrangement expired on 31 March.

As this was a very limited programme, the best documentation that Pfizer had to describe it was the related legal contract. The aim of the programme was, *inter alia*, to 'ensure optimal control of diagnosed, treated COPD patients in accordance with NICE and/or local guidelines'. Pfizer co-promoted Spiriva (tiotropium bromide) with another pharmaceutical company; the product was licensed for the treatment of COPD. The contract stated that:

> 'The Nurse's role is to provide a professional and ethical COPD review programme to Pfizer customers at Primary Care level. This COPD audit will assess the standards of care of approximately 2,500 COPD patients in general practices. The data will be used to quantify the effectiveness of current treatment and management protocols and highlight the areas requiring investment, development and improvement.'

The standard operating procedure to the contract made clear the sort of report that was produced for patients by the agency nurse. Attention was drawn particularly to the points highlighted below in italics:

'For the patient, the report will indicate disease severity from spirometry, *according to NICE guidelines*, their exacerbation status, their smoking status, and their questionnaire scores. Information leaflets will be provided as indicated by the LINQ scores. The report will also include *recommendations for management according to NICE COPD guidelines and from the relevant Formulary.* The recommendations will include:

> Drug treatment
> Non-drug management
> Referrals e.g. smoking cessation, pulmonary rehabilitation
> Suggested follow-up GP/practice nurse

This report will be reviewed by the Nurse who will be able to make appropriate modifications before giving

it to the patient. This report will not give specific details of drugs just that their treatment regime may need reconsidering in the light of current guidelines and requires further discussion with their GP.'

Pfizer submitted that this programme was not prohibited by Clause 18.1 of the Code. As required by the supplementary information to Clause 18.1 of the Code, Pfizer ensured that:

- The programme was delivered by an appropriately qualified nurse and a GP made the decision about whether and, if so, how to change the patients' treatment. Although the contract referred to the GP getting a report 'detailing the treatment recommendations', this clearly only referred to *recommendations* – it was up to the GP to decide whether to modify the patients' treatment.
- Pfizer avoided access to data/records that could identify particular patients.
- The remuneration of the agency staff was not linked to sales in any way. There were no bonus payments associated with this arrangement (see contract for the payment terms).
- Patient confidentiality was maintained and data protection laws complied with.
- A written protocol was provided for the recipients of the programme, which outlined the services to be provided and the role of the sponsoring pharmaceutical companies.

Pfizer also required that the agency staff (including the nurse):

- received proper training in respect of the Code, as amended from time to time; and
- complied with all applicable laws, codes, regulations including the Code and the Nursing & Midwifery Council (NMC) Code.

As recommended by the Code, Pfizer had also ensured that relevant parties were informed of the activities.

2 Nurse Agency Audit Programme in Coronary Heart Disease

Pfizer's programme was put in place in response to a request from the local PCTs in relation to their CHD management programme. This arrangement involved the hire of one nurse advisor and project administrator from the agency. The contract between Pfizer and a nurse agency stated that the aim of the programme was to 'identify, review and treat patients with long term conditions'. The support was to enable 'practices to deliver a high standard of care to patients with cardiovascular disease, and deliver recommendations from the National Service Framework for Coronary Heart Disease and British Hypertension Society Guidelines'.

The contract made clear the sort of report that was produced for the patient and the patient's GP. Attention was drawn particularly to the points highlighted in italics:

> '…patients will be given a treatment card where all advice and treatment that has been given in the clinic will be recorded…. The report to the Practice will also include recommendations for management *according to NICE CHD guidelines and from the relevant Formulary.* This report will be reviewed by the Nurse who will be able to make appropriate modifications before giving it to the patient. The recommendations will include:
>
> Non-drug management
> *Referrals* e.g. smoking cessation, cardiac rehabilitation; and exercise counselling
> Suggested follow-up GP/practices' nurse.
>
> This report *will not give specific details of drugs or treatments.* It may state that a patient's treatment regime may need reconsidering in the light of *current guidelines* and/or requires further discussion with their GP.'

The contract also set out strict parameters for the circumstances in which the patient's further management would be discussed with the GP:

- 'patients whose assessment indicated active exacerbation of disease who might benefit from a change in therapy
- patients whose assessment indicated symptom recurrence due to inappropriate preparation or form of medication
- patients with symptoms that warranted further investigations at secondary care level
- patients experiencing chest pain during clinic would be managed according to local protocols'.

Pfizer submitted that this programme was not prohibited by Clause 18.1 of the Code. As required by the supplementary information to Clause 18.1, Pfizer had ensured that:

- The audit services were delivered by an appropriately qualified nurse.
- The remuneration of the agency staff was not linked to sales in any way. There were no bonus payments associated with this arrangement.
- Patient confidentiality was maintained and data protection laws complied with.
- The recipients of the service (two GP practices) each had a written agreement for the arrangements, describing the services to be provided and Pfizer's role. The contracts with the GP practices made it clear that the arrangements were not dependent on or related to 'any business or other decision(s) that the practice had made or might make relating to Pfizer or any of its products'.
- As recommended by the Code, relevant parties were informed of the activities.

Pfizer also required that the agency staff (including the nurse):

- complied with all applicable laws, codes, regulations including the ABPI Code and the NMC Code of Professional Conduct; and
- provided the services only in accordance with the protocol agreed by the Trust and any relevant practices.

3 Nurse Agency Advisor Programme relating to Cardiovascular Risk Management

Pfizer submitted that the best description of this programme was provided by the two short booklets entitled 'Cardiovascular Risk Management programme' and '[a nurse agency] Cardiovascular Risk Management programme'. This programme involved 12 nurse advisors and was designed to support primary care practices in identifying and ensuring optimal management of patients with cardiovascular disease and diabetes by assessing cardiovascular risk and providing treatment recommendations in accordance with national and local guidelines. The programme re-assessed and reviewed patients with a history of CHD, diabetes, hypertension and stroke and captured practice information to meet the GMS quality and outcomes framework that GP practices were required to report on. The aims of the programme included 'to ensure patients with diagnosed CVD and diabetes achieve optimal management including cholesterol targets *in accordance with GMS and/or local guidelines*' and 'to help customers maximise GMS points in the field of CHD, stroke/TIA, hypertension and diabetes'.

Although the programme focused on the prescription of statins (which could include Lipitor), it also tested for medical conditions and carried out medical interventions that had no relevance to any medicines made by Pfizer (eg influenza inoculations). One of the slides provided showed the broad extent of the matters covered in clinics run under this programme.

Practices interested in entering the programme were identified by Pfizer's sales representatives and checked against certain listed criteria (including the practice having an interest and commitment to running statin management and CHD clinics, an agreed cholesterol and statin treatment protocol and being fully computerised – all these elements were necessary in order for the programme to work). Assuming that the practice met the criteria, Pfizer's District Leadership Team had to agree to the practice joining the programme, to ensure that the number of practices joining did not overstretch or exceed the available resource.

If the practice proceeded with the programme, Pfizer's sales representative would ensure that one of the GPs: (a) documented the practice's agreed cholesterol and statin treatment protocol on Pfizer's standard form 'Cardiovascular Risk Management and Review Protocol' and (b) completed a standard 'Referral Form'. The standard Protocol and Referral forms, together with some completed examples which showed the wide variation between different practices' protocols and the fact that not all completed protocols would favour Pfizer's medicine Lipitor, were provided. These forms were sent to the agency where they triggered the scheduling of a meeting between the nurse advisor and the practice (as described in the booklet under 'Initial Meeting') at which the nurse reconfirmed and/or clarified the work that the practice wished her to carry out. The nurse advisor then had to sign a contract with the practice, committing to confidentiality obligations so that she could access the practice's data and implement the Cardiovascular Risk Management and Review Protocol chosen by that practice.

Further details of the practical process involved in the referral and the various stages of the agency nurse advisor's role in the programme were explained in the '[Agency] Standard Operating Procedure Pfizer Cardiovascular Risk Management Programme' document. If the practice wished to proceed with the programme, a formal contract between Pfizer and the practice had to be signed.

Broadly speaking, the programme provided a screening service for patient groups identified via a record search, in accordance with the practice's requirements. Patients were sent an appointment to attend a clinic at which they received relevant screening according to the request of the practice and the target disease area. This might include assessment of BP, cholesterol, BMI, urinalysis, diabetic neuropathy assessment and random glucose. Nurses also provided lifestyle guidance, for example about the importance of exercise and diet.

If, following this assessment, the patient met any criteria for further management he/she would either be seen by, or have his/her case reviewed by the GP who would make any decision about the future management of the patient's health.

Pfizer submitted that this programme was not prohibited by Clause 18.1 of the Code. As required by the supplementary information to Clause 18.1, Pfizer had ensured that:

- The programme was delivered by an appropriately qualified nurse – the contract required the agency to ensure that the nurse advisors were appropriately qualified. In addition the '[Agency] Protocol of Confidentiality for an [Agency] Nurse Advisor Working in General Practice' confirmed that all agency nurse advisors were NMC registered.
- A GP decided whether and, if so, how to change the patients' treatment (by completing the 'Cardiovascular Risk Management and Review Protocol' and confirming or changing it during the initial meeting). In the '[Agency] Cardiovascular Risk Management programme' under the heading 'Can I feel confident in an Industry-sponsored programme?', it was clearly stated that 'all prescribing choices are made by the practice'. Similarly, the patient brochure stated 'if medical treatment is advisable for you, the Nurse Advisor will discuss this with your doctor and any treatment your doctor recommends will be explained to you'.
- Pfizer had no access to data/records that could identify particular patients. The sales representatives' involvement ceased before the initial meeting (ie before there was any access to patient data). The '[Agency] Protocol of Confidentiality for an [Agency] Nurse Advisor Working in General Practice' committed the nurse advisors to adhere to the Caldicott Principles of Good Practice and included assurances that:
  - the nurse advisors were NMC registered and therefore governed by the Code of Professional Conduct and Scope of Professional Practice;
  - no access to patient records could be sought by the nurse advisors unless they had the signed agreement of the patient or GP;

- all patient information would be coded: no identifiable patient information would be removed from practices (all 'keys' to patient data would be held at the practice); and
- any information given to Pfizer would be coded, anonymised and aggregated.

- Patient confidentiality was maintained and data protection laws complied with. The contract provided that '[Agency] will ensure the confidentiality of patients' medical records at all times and shall not share such records with Pfizer'. One whole clause of the contract was devoted to data protection obligations. In addition to the points made above, the '[Agency] Protocol of Confidentiality for an Agency Nurse Advisor Working in General Practice' also contained assurances that:
  - the nurse advisors complied with the Data Protection Act (relevant extracts from the Act and example patient consent forms were also provided); and
  - in addition to being bound by the NMC Code of conduct, the nurse advisors would ensure that patient data would be anonymised and, where necessary, patient consent obtained.
- The Agency Cardiovascular Risk Management Programme explained this programme to the recipient practices and this clearly identified both the service provider and Pfizer's role eg the section entitled 'Can I feel confident about an Industry-sponsored programme?'. In addition, the contract referred to the need for each participating practice to sign a letter in the form specified in the contract. The printed materials designed for use in connection with the programme were non-promotional and clearly identified Pfizer as the sponsoring company. None of the materials criticised competitor products.

Pfizer also required that:

- the agency nurses received proper training in respect of the ABPI Code, as amended from time to time; and
- all agency staff involved in delivering the programme complied with all applicable laws, codes, regulations including the ABPI Code and the NMC Code.

Pfizer submitted that because of the size of this programme, its sales representatives were specially briefed about it. The slides used made it clear to the field force that the programme should not be used as an inducement to prescribe and that practices should continue to prescribe as they saw fit.

In response to a request for further information Pfizer noted that the relevant briefing material contained the following guidance:

> 'In accordance with Clause 18.1 ABPI Code of Practice the Nurse Advisor programme must not be linked to the sales call. There must be a clear separation between the promotion of product/sales call and any discussion with practice personnel around offering the Nurse Advisor programme to assist with a surgery therapy review.'

To help maintain this separation and to enable each practice to evaluate the service in the absence of a representative, a general guide to the service was left with practices which stated 'the service is non-promotional – all prescribing choices are made by the Practice'.

In addition, the slides used to brief the representatives on this programme included one which set out 'ABPI Considerations'. This slide made it clear to the field force that the programme should not be used as an inducement to prescribe and that practices should continue to prescribe as they see fit.

Bonus payments

Pfizer explained that bonus payments might be earned by nurse advisors under this programme, but the remuneration was not linked to sales or promotion.

The nurse advisors' salary and bonus changed between 2005 and 2006. Pfizer provided details.

According to the agency documentation, from January to June 2006 this bonus was awarded on the basis of:

- completion of more than 2.5 audits per month (Pfizer noted that as nurse advisors could only visit a practice after it had been referred and had agreed to the initial meeting, this element of the bonus related to the efficiency of each audit, rather than to gaining access to additional practices);
- drive for patient attendance at clinics (to improve patient outcomes);
- communication, client and customer feedback (including feedback from the practices); and
- reporting/administration (25% of bonus might be lost for late or inaccurate reporting).

Before 30 January 2006 the bonus was awarded on the basis of four equally weighted 'key areas' briefly described as:

- timeliness in carrying out practice audits;
- reporting/administration;
- communication with client and customer; and
- value added services eg training and supporting colleagues.

Specific issues for programmes involving an agency and/or recruitment consultancy within the last three years

Pfizer submitted that it had not run any nurse advisor audit programmes through the recruitment consultant but it had had two programmes with the agency in the last three years and these were detailed below.

4 Nurse Agency Assistance with Outcomes Guarantee programme

Pfizer stated that this programme had ended in June 2005.

The Outcomes Guarantee programme differed significantly from the other nurse programmes described above, due to its reimbursement (or 'guarantee') element. The Outcomes Guarantee programme was the subject of an earlier complaint to

the Authority [Case AUTH/1109/11/00]; the Panel had ruled no breach of the Code.

The Outcomes Guarantee Project Summary (LIP 374) described the programme as follows:

> 'An Outcomes Guarantee programme is when a pharmaceutical company guarantees that its drug will achieve certain targets in a given patient group. If the drug does not reach these targets then the company will reimburse the healthcare team for the shortfall between the target and what the drug actually achieved. In this programme, Pfizer Ltd has provided an Outcomes Guarantee for its cholesterol-lowering drug, atorvastatin. A doctor who participates in this programme is under no obligation to prescribe the drug involved in the Outcomes Guarantee programme.'

The agency had provided nurse advisors to help implement the Outcomes Guarantee programme by assisting the PCTs in 'identifying through general practice audit those patients who were most at risk from cardiovascular disease, including patients with diabetes'.

Pfizer submitted that this programme was not prohibited by Clause 18.1 of the Code. As required by the supplementary information to Clause 18.1, Pfizer had ensured that:

- The programme was delivered by appropriately trained nurses and the GP decided which statin to prescribe.
- The support provided by Pfizer was a service to the NHS and the wider community and was 'not conditional upon nor related to any commitment on the part of the PCT to purchase, prescribe, administer or recommend any products of Pfizer'. In addition, in order to ensure that there were no financial inducements for prescribers to choose one lipid-lowering agent over another, 'any rebates due under the terms of the guarantee was paid to the PCT for the general purpose of improving primary care services and not to individual general practices'.
- Pfizer avoided access to data/records that could identify particular patients.
- The remuneration of the nurses was not linked to sales. There were no bonus payments associated with this arrangement.
- Patient confidentiality was maintained and data protection laws complied with.
- The recipients of the service were required to enter into a written agreement with Pfizer, which described the programme and Pfizer's role.
- As recommended by the Code, relevant parties were informed of the activities.

Pfizer also drew attention to the following:

- The programme was approved by the local Scientific Merit and Ethics Committee. Approval was only granted once the Committee 'had established that there was no directive to prescribe a particular lipid-lowering agent'.
- The agency was required to ensure that its personnel were familiar with and complied with the Code.
- The agency staff involved in delivering the programme were obliged to comply with the NMC Code.

5 Nurse Agency Advisor Programme relating to COPD

Pfizer submitted that this programme was sponsored by another pharmaceutical company for a considerable period of time before it became involved in it. The contract setting out Pfizer's involvement in the programme ran from January to June 2003. The programme involved the sponsorship of 40 nurses, four field managers, two team administrators and one project director from the agency to carry out the 'COPD Response Programme'.

The best description of the programme was provided by the booklets entitled 'COPD Response' and 'COPD Response Nurse Adviser Programme Briefing Document', which were provided by the sales representatives and the agency team. The programme was designed to provide COPD education and support to primary care teams with the aim of improving diagnosis, management and treatment of COPD. Because of the size of the programme, sales representatives were specially briefed about it and liaised with the agency nurses to select suitable practices, introduce the nurse and the programme to the practice and discuss the progress of the programme. The contract (which was provided) comprehensively described the programme the objectives of which were:

'To identify primary care patients with COPD or a component thereof leading to optimal therapeutic management according to recognised guidelines (British Thoracic Society/GOLD). A crucial element of the programme was the transfer of skills from the nurse to the practice. The programme is structured to allow the practice nurse to develop the necessary skills and confidence to continue to identify patients once the nurse has completed the clinic cycle in this document.'

Practices suitable for the programme were identified by representatives and checked against certain listed criteria. These included the practice having an interest in respiratory medicine and COPD in particular, its own or regular access to a spirometer, and computerised patient notes (all these elements were necessary in order for the programme to work) as well as being of a sufficient size to ensure that limited resources were used sensibly.

If the practices were interested in the programme, approval would be sought from Pfizer's district sales managers to ensure that the number of practices joining the programme did not overstretch or exceed the resource available for it and that the representative had correctly applied the criteria. In some cases the representative would attend an introductory meeting with the practice to introduce the nurse and the programme to the key decision makers in the practice. The representative would not promote any product at this meeting. At the introductory meeting the practice would sign a 'Practice Agreement' which confirmed that this programme was not conditional upon or related to any commitment on the practice's part to prescribe,

administer, purchase or recommend any particular product, and that patient confidentiality would be maintained at all times.

Once a practice had signed up to the programme, the patients were selected for clinical review on the basis of their respiratory history, smoking history, occupation, and whether they had had more than two antibiotic prescriptions for an upper or lower respiratory tract infection in the previous six months. Patients meeting the criteria would then be invited for clinical review with the COPD nurse and the practice nurse. If, following this assessment, the patient met any criteria for further management the patient would be referred to the GP who would make any decision about the future management of the patient's health. The agency nurse also provided an education workshop for the practice, monitored the programme and provided support to the practice nurse for a limited period once the programme was complete.

Pfizer submitted that this programme was not prohibited by Clause 18.1 of the Code. As required by the supplementary information to Clause 18.1 of the Code, Pfizer ensured that:

- The programme was delivered by appropriately qualified nurses as the contract required the agency to ensure that the nurse advisors were appropriately qualified and experienced.
- A GP made all prescribing decisions in relation to a patient's treatment, following the review by the nurse.
- Pfizer had no access to data/records that could identify particular patients.
- Patient confidentiality was maintained. The contract provided that '[the agency] shall ensure at all times that the confidentiality of patients' medical records were maintained, and the agency would not share such records with the companies'.
- The contract made it clear under the heading 'Roles and Responsibilities' that sales representatives 'must not promote Spiriva, in meetings arranged to discuss the Programme'; that the agency nurses 'will not promote any specific products (including Spiriva)', and that the work of the nurses 'does not entail any prescribing obligations on the part of the practice'.
- A whole clause of the contract was devoted to data protection obligations, including obligations to:
  - comply with the Data Protection Act; and
  - only process personal data in accordance with the approval of the relevant GP, the Act, the Code and for no other purpose than the necessary administration of the services agreed in the contract.
- The recipient of the service would have a written agreement of the arrangements explaining the service and Pfizer's role. The contract referred to the need for each participating practice to sign a letter.

Pfizer also required that:

- The nurses received proper training in respect of the Code, as amended from time to time; and
- The agency ensured that the nurses performed the services in compliance with all applicable laws, codes, regulations including the Code and the NMC Code of Professional Conduct.

The agency was paid a daily fee for each nurse working on the programme; details were provided. Elements that were included within the fee included national insurance contributions, sick pay, maternity pay, pension, vehicle costs and a daily allowance.

Bonus payments

An annual average nurse bonus payment was included in the fee paid to the agency. Neither this bonus nor the remuneration of the nurses or agency was linked to sales or promotion. Nurses were rewarded for meeting certain project-specific objectives which could be briefly described as: timely completion of audits; customer satisfaction and the revenue generated for the agency from Pfizer under the contract.

Other similar programmes within the last three years

Pfizer had conducted a number of programmes which had completed within the last three years, which were listed below.

- A six month nurse advisor programme with an agency relating to COPD which aimed to: accelerate the rate at which COPD patients were reviewed through patient clinics; transfer skills to nurses and enable ongoing review of patients and ensure optimal control of diagnosed, treated COPD patients in accordance with NICE and/or local guidelines.
- A six month nurse advisor programme with the agency which supported the implementation of the PCT statin guidelines in GP practices in relation to 'at risk' patients, as identified by the PCT.
- A nurse advisor programme with the agency relating to cholesterol management of patients at risk of coronary heart disease, which was the precursor to, and ran on similar lines to, programme 3 above.
- Various nurse advisor programmes with a nurse agency whereby the agency personnel reviewed primary care patients through COPD and CHD clinics, carried out system searches for practices and provided IT, spirometry and CPR training to practice staff. None of these programmes was ongoing but Pfizer provided for completeness a copy of the standard contract used with the agency.
- An osteoarthritis/rheumatoid arthritis patient review service with a nurse and IT consulting agency which ran from November 2002 to September 2003.
- Pfizer sometimes paid the costs of a practice nurse's overtime to allow her to conduct patient or medicines reviews as required by the practice.

Such payments were made directly to the GP practice concerned. Since no agency was involved, it considered that these arrangements fell outside the scope of this complaint but it had provided for completeness a copy of the standard form contract used in these circumstances.

Other issues

Pfizer submitted that it should be evident from the above that it and the agencies with which it worked had taken care to ensure that nurse programmes were run appropriately. In addition to the documentation relating to the programmes mentioned above, Pfizer provided various procedures, guidance and template agreements it had issued in order to ensure that its activities were properly run. The materials relating to the nurse programmes described above were approved in accordance with Pfizer's procedures, established to ensure compliance with the Code as well as with the law and Pfizer's own internal requirements. The nature and extent of the safeguards put in place demonstrated the lengths to which Pfizer had gone to ensure that its nurse programmes were run in an ethical manner and in compliance with legal and Code requirements.

Conclusion

Pfizer submitted that none of its programmes breached Clauses 18.1, 9.1 or 2 of the Code.

PANEL RULING

The Panel noted that some of the services were used in 2006. The article had appeared and the complaint had been received in March 2006. However the transition period for the 2006 Code stated that during the period 1 January 2006 to 30 April 2006 no promotional material or activity would be regarded as being in breach of the Code if it failed to comply with newly introduced requirements. Clause 18.4 of the 2006 Code was a newly introduced requirement. Most of the supplementary information to Clause 18.4 had been in the 2003 Code as supplementary information to Clause 18.1. These cases were considered in relation to the 2003 Code using the 2006 Constitution and Procedure.

Medical and educational goods and services had to enhance patient care or benefit the NHS under the supplementary information to Clause 18.1 of the 2003 Code. The change under Clause 18.4 of the 2006 Code was that such services had to either enhance patient care or benefit the NHS and maintain patient care.

With regard to therapy review services the supplementary information to Clause 18.4 of the 2006 Code provided helpful guidance. A therapeutic review which aimed to ensure that patients received optimal treatment following a clinical assessment was a legitimate activity for a pharmaceutical company to support and/or assist. The results of such clinical assessments might require, among other things, possible changes of treatment including changes of dose or medicine or cessation of treatment. A genuine therapeutic review should include a comprehensive range of relevant treatment choices, including non-medicinal choices, for the health professional and should not be limited to the medicines of the sponsoring pharmaceutical company. The arrangements for therapeutic review must enhance patient care, or benefit the NHS and maintain patient care. The decision to change or commence treatment must be made for each individual patient by the prescriber and every decision to change an individual patient's treatment must be documented with evidence that it was made on rational grounds.

The supplementary information to Clause 18.1 of the 2003 Code (and the supplementary information to Clause 18.4 of the 2006 Code) stated that sponsored health professionals should not be involved in the promotion of specific products. Nurses were required to comply with the Nursing & Midwifery Council Code of professional conduct which required that registration status was not used in the promotion of medicines.

The remuneration of service providers must not be linked to sales in any particular territory or place or to sales of a specific product or products. Bonus schemes linked to actual performance or to the level of service provided might be acceptable. The supplementary information to Clause 18.1 of the 2003 Code (and the supplementary information to Clause 18.4 of the 2006 Code) stated that companies must ensure that patient confidentiality was maintained and that data protection legislation was complied with.

The Panel noted that Pfizer had sponsored nurses at a PCT to perform a COPD audit. The provision of such nurses was not dependent upon the prescription of any Pfizer medicine. Any recommendations for management made by the nurse would be in accordance with NICE COPD guidelines or from the relevant formulary. A draft protocol for the audit noted that four pharmaceutical companies would fund the work; the companies would have no involvement in the design of the audit or be able to influence its conduct. The Panel did not consider that the audit was an inducement to prescribe, supply, administer, recommend or buy any medicine. No breach of Clause 18.1 of the 2003 Code was ruled. The Panel also ruled no breach of Clauses 9.1 and 2 of the 2003 Code.

With regard to the CHD audit programme, the Panel noted that the agreement was to support a particular medical group with its project to implement nurse led CHD clinics. A document setting out the terms stated that for the avoidance of any doubt, the funding provided by Pfizer was a stand-alone arrangement and was not dependent on or related to any past, present or future commercial relationship with Pfizer nor any business decision that the practice might make relating to Pfizer or any of its products. The Panel thus did not consider that the audit was an inducement to prescribe, supply, administer, recommend or buy any medicine. No breach of Clause 18.1 of the 2003 Code was ruled. The Panel also ruled no breach of Clauses 9.1 and 2 of the 2003 Code.

The Panel noted that the cardiovascular risk management programme was a national project provided by a team of nurse advisors. In a briefing to representatives the project was listed as one of four

Lipitor value added programmes. Representatives were instructed that the first key consideration was to always sell Lipitor first and be confident that the practice supported the use of Lipitor in appropriate patients. The representatives should ensure that they had discussed, agreed and understood the practice patient management protocols and that this correctly positioned Lipitor as statin of choice for 'defined' patients groups. Representatives should understand how each of the value added programmes could support them and their customers. The briefing to representatives included a reminder that the use of the programme should not be an inducement to prescribe and selected practices should continue to prescribe as they chose. A 2005 Outcomes Summary showed that in 109 completed practices, of 3,524 patients not treated to target, 2,756 (78%) were initiated or titrated on Lipitor. The summary slide informed representatives that targeting was critical so as to maximise benefit to them and their customer. Although the official contract between the practice and Pfizer contained the same statement as described above with regard to the nurse led CHD clinics, ie the funding provided by Pfizer was a stand-alone arrangement etc, the Panel nonetheless considered that the instructions to representatives that the service should only be offered to those practices where a representative was confident that Lipitor would be used as the statin of choice in appropriate patients were unacceptable. Similar instructions were included in the relevant service agreement between the agency and Pfizer. The Panel thus ruled a breach of Clause 18.1 of the 2003 Code. The Panel further ruled breaches of Clauses 2 and 9.1.

The Panel noted that it had previously considered the outcomes guarantee study (Case AUTH/1109/11/00) wherein it had considered that the scheme, which at that time was a pilot study, was not in breach of Clause 18.1 of the Code. The documents provided in respect of the case now at hand described an outcomes guarantee programme as being when a pharmaceutical company guarantees that its medicine will achieve certain targets in a given patient group. The project aimed to ensure that those patients who would benefit from LDL cholesterol lowering medicines received them. Within the programme Pfizer had provided an outcomes guarantee for Lipitor although a doctor participating in the project was not obliged to prescribe it. Any rebate due under the terms of the guarantee was paid to a PCT for the general purpose of improving primary care services and not to individual general practices. The company submitted that this was to ensure that there was no financial inducement for prescribers to choose one lipid-lowering medicine over another. It was stated that the programme and the support provided by Pfizer was not conditional upon or related to any commitment on the part of the PCT to purchase, prescribe, administer or recommend any Pfizer product. The Panel thus ruled no breach of Clause 18.1 of the 2003 Code. The Panel also ruled no breach of Clauses 2 and 9.1 of the 2003 Code.

The COPD Response programme was also a nationally run project to identify primary care patients with COPD, or a component thereof, and ensure that they were optimally treated according to recognised national guidelines. Although representatives identified suitable practices the criteria they worked on did not include any reference to particular medicines. Pfizer hoped that provision of the service would foster closer relationships between the sales teams and the practices. There was, however, no obligation to use Pfizer products although it was acknowledged that these were included in the national and European guidelines on the treatment of COPD. The Panel noted that the nurse adviser briefing document was for use by both the sales team and the nurse advisers. The selection of appropriate practices was by the sales team using a list of criteria, some or all of which were to be met. The criteria related to size, computerised notes, spirometer availability and an interest in respiratory medicine and COPD in particular. Sales representatives would attend the introductory meeting. The briefing document included objection handling. The response to maintenance of prescribing perogative was 'Whilst [a named pharmaceutical company] and Pfizer hope that you will consider the benefits of using their product for COPD patients there is no obligation to do so. The BTS COPD Guidelines and the European GOLD initiative both recommend treatment pathways that include [the named pharmaceutical company] products that are licensed for the management of COPD'. Overall the Panel did not consider that the COPD response programme was an inducement to prescribe, supply, administer, recommend or buy any medicine. No breach of Clause 18.1 of the 2003 Code was ruled. The Panel also ruled no breach of Clauses 9.1 and 2 of the 2003 Code.

The Panel noted that Pfizer had provided information about other similar programmes that it had run within the last three years. A standard letter relating to the payment of a nurse's overtime to allow her to conduct patient or medicine reviews stated that the funding provided by Pfizer was a stand-alone arrangement and was not dependent on or related to any past, present or future commercial relationship with Pfizer or any business or other decisions that the practice had or might make relating to Pfizer and its products. The Panel considered that the evidence before it was not such as to demonstrate that any of the programmes had been an inducement to prescribe, supply, administer, recommend or buy any medicine. No breach of Clause 18.1 of the 2003 Code was ruled. The Panel also ruled no breach of Clauses 9.1 and 2 of the 2003 Code.

Case AUTH/1807/3/06

Proceedings commenced **10 March 2006**

Case completed **3 July 2006**

Case AUTH/1810/3/06

Complaint received **13 March 2006**

Case completed **3 July 2006**

CASE AUTH/1814/3/06

FORMER EMPLOYEE v MERCK SHARP & DOHME

Nurse audit programme

A former sales representative, writing under a pseudonym, complained about a nurse audit disease management programme offered by Merck Sharp & Dohme and delivered by a service provider. The complainant referred to this as the Hypertension Review Programme Supportive of the GMS Contract (HRP-GMS).

The complainant stated that the HRP-GMS programme had been in operation from 2004 to the present day. Throughout this time, Merck Sharp & Dohme's representatives involved in the first-line promotion of Cozaar (losartan) had been given primary responsibility for identifying surgeries that were to be offered nurse advisors from the service provider to undertake audits relating to hypertension and Type 2 diabetes. The stated goals of the HRP-GMS were to improve patient management and support practices to achieve GMS contract targets in these disease areas.

The complainant was concerned about the way in which representatives and their managers had to select surgeries to be considered for placement of a nurse advisor. In this regard the complainant noted that the hypertension and Type 2 diabetes proformas explicitly referred to a number of sales and prescribing behaviour metrics to be fulfilled before a particular surgery was offered the service. The complainant understood that this was in breach of the Code as services to medicine and product promotion must not be linked in any way. An email from a senior manager in the Cozaar team, and a slide presentation entitled 'COZAAR Nurse Audit Programme', showed that representatives and their managers were required to complete the proformas in order to secure placements.

The complainant stated that he had raised his concerns with several superiors within Merck Sharp & Dohme but repeatedly failed to receive a substantive answer to questions.

The complainant also alleged that Merck Sharp & Dohme representatives were set annual objectives which required them to call on target doctors up to six times within a six month period. The complainant and other colleagues raised this issue with line managers to be told that call frequency must be elevated during a launch phase and that representatives must use their acumen to circumvent the restrictions imposed by the Code.

The Panel noted Merck Sharp & Dohme's submission that there were differences between the slides sent by the complainant and the Cozaar nurse audit programme briefing slides used by the company to train the representatives. The Panel noted that the training slides, as provided by Merck Sharp & Dohme, were branded with the Cozaar logo. The first slide referred to the 'COZAAR Nurse Audit Programme'. The service would thus be seen by representatives as being linked to the promotion of the product. No mention was made in the presentation of the need to separate the provision of medical and educational goods and services from the promotion of medicines. This was totally unacceptable.

The slides provided by Merck Sharp & Dohme included instructions that the audit service was only to be offered to practices that, *inter alia*, had 'Strong buy into LIFE and COZAAR messages'. Surgeries had to agree to Cozaar as the medicine of choice in relation to 'A' as set out in the British Hypertension Society (BHS) guidelines where A meant ACE inhibitor or angiotension antagonist. The practice also had to have a 'call rate of 6 prior to audit plus speaker meeting attendance'. The surgeries selected must have target doctors as project lead. The programme was referred to as a targeted resource to influence the environment.

The aim of the programme was to provide practices with an independent nurse advisor to review all uncontrolled hypertensive patients over 55 in order to improve blood pressure management in accordance with the ABCD goal (this was taken to be a reference to the BHS guidelines). The programme aims included the benefits of restoring blood pressure to normal or optimum levels, enhanced patient education through detailed lifestyle advice and the update of existing practice registers.

The slides headed 'The program guidance form' had 'Cozaar/Losartan' printed in a box beneath the heading 'Practice Policy – please complete'.

Another slide provided by Merck Sharp & Dohme was headed 'Implementation changes' and referred to a more focussed proforma for both programmes. This was shown on the following slide which made it clear that if the practice angiotensin antagonist of choice was not Cozaar then the practice was not suitable. If the practice had not agreed to Cozaar as the drug of choice for A in the BHS guidelines ABCD then it was not suitable. If the brick market share was not above 40% for Cozaar then the practice was not suitable. The proforma provided by the complainant was similar to that shown on the slides; it additionally included a section asking the representative for the rationale as to why it was important to nominate the surgery for the audit.

The medical/legal approved proformas provided by Merck Sharp & Dohme, however, were very different to those on the slides and those provided by the complainant; there were different questions to be completed and there were no criteria to be met for the practice to be deemed suitable for offering the service.

The HRP-GMS Protocol provided by the complainant referred to the BHS recommendations for combining blood pressure lowering medicines. It included the reference to A as 'angiotension receptor blocker or ACE inhibitor'; this matter was the subject of complaint in Case AUTH/1762/10/05 and the Panel considered that Merck Sharp & Dohme should have changed the protocol as a result of the ruling in that case.

The Panel noted that the practice had to agree each stage of the process. Hypertensive patients were invited for review by the nurse if they were over 55 and had not achieved national audit targets, ie blood pressure higher than 150/90, and had been on current treatment for at least six weeks prior to assessment. The nurse would then put patients into one of three registers: those appropriate for medication review according to the HRP-GMS as directed by the GP; those appropriate for medication review by the practice (ie not at target but less than 55 years old) and the third for those inappropriate for medication review as directed by the GP. The Panel queried how the second register would come about given that the inclusion criterion was for patients over 55.

The audit proposal form appeared to go beyond the inclusion and exclusion criteria. The practice prescribing policy had to be entered on a form which also reproduced the incorrect version of the BHS guidelines. The form was to be signed by some of the practice doctors.

The template letter for patients regarding the audit did not state that the audit was sponsored by Merck Sharp & Dohme.

The Panel considered that the Merck Sharp & Dohme training slides clearly associated the programme with the promotion of Cozaar by use of logos and the introductory slide. The amendments to the proformas clearly linked the nurse audit programme to the use of Cozaar. The Panel considered that the arrangements were unacceptable and ruled a breach of the Code.

The Panel considered that high standards had not been maintained and the circumstances brought discredit upon the pharmaceutical industry; breaches of the Code including Clause 2 were ruled.

The Panel decided to report Merck Sharp & Dohme to the Code of Practice Appeal Board in accordance with Paragraph 8.2 of the Constitution and Procedure.

With regard to the allegation about call rates, the Panel noted Merck Sharp & Dohme's submission that the two sales forces together were expected to have either seven or five contacts with target customers each year (depending on whether they were primary or secondary targets). In total this meant each representative would have either four or three contacts with primary target doctors or two or three contacts with secondary target doctors. Such contacts included all occasions on which a representative met a customer. The Panel noted that the annual objectives did not appear to be included in the sales incentive scheme 2005 documents. The Panel noted that there was a discrepancy between the complaint and the response in this regard. The Panel considered that there was no evidence to show that representatives were encouraged to make six calls in six months as alleged. No breach of the Code was ruled.

The Appeal Board was extremely concerned that the arrangements for the audit programme had highlighted very serious deficiencies in Merck Sharp & Dohme's procedures including the copy approval system. Given the significant investment that the audit represented the Appeal Board considered that it was inconceivable that it was not more tightly controlled; material had been used which had not been approved. The service had been clearly linked to the promotion of Cozaar and there appeared to be a serious lack of control by senior managers. The Appeal Board considered that the arrangements were totally unacceptable.

With regard to the Panel's ruling that the circumstances brought discredit upon the pharmaceutical industry, the Appeal Board was concerned that Merck Sharp & Dohme's actions had the potential to compromise patient safety by inappropriate prescribing. Further, Merck Sharp & Dohme's actions would undermine both prescribers' and patients' confidence in the provision of properly conducted services. The Appeal Board was extremely concerned that some Merck Sharp & Dohme staff had not realised that the amended proformas and the slides used as training material were totally unacceptable in relation to the requirements of the Code.

The Appeal Board considered that this was an extremely serious case.

The Appeal Board decided, in accordance with Paragraph 11.3 of the Constitution and Procedure, to require an immediate audit of Merck Sharp & Dohme's procedures. In addition, Merck Sharp & Dohme would be publicly reprimanded and required to issue a corrective statement. In accordance with Paragraph 12.1 of the Constitution and Procedure, the Appeal Board decided to report the company to the ABPI Board of Management with the recommendation that it be suspended from membership of the ABPI.

Upon receipt of the audit report and Merck Sharp & Dohme's comments upon it, the Appeal Board noted that the company had started to implement the recommendations and address the observations set out in the audit report. This would take some time given that the problems were institutional in nature and many changes were necessary.

The Appeal Board decided that Merck Sharp & Dohme should be reaudited later in the year.

The ABPI Board of Management noted the audit report and Merck Sharp & Dohme's comments upon it.

It was noted that the Appeal Board had recommended that Merck Sharp & Dohme be suspended from membership of the ABPI. It was further noted that Merck Sharp & Dohme was to undergo a second audit of its procedures, that the company was to be publicly reprimanded and that Merck Sharp & Dohme had issued a corrective statement. The ABPI Board noted that Merck Sharp & Dohme had fully accepted responsibility for the matters giving rise to the complaint and that current management, including the new managing director, was taking action to ensure that there was no repeat: action which ranged from training through to changes in culture.

Nevertheless, given the serious nature of the case, the ABPI Board decided to suspend Merck Sharp &

Dohme from membership of the ABPI for a minimum of three months, commencing 2 October 2006, after which time the situation would be reassessed. The ABPI Board requested it see a copy of the report for the second audit.

A former sales representative of Merck Sharp & Dohme Limited, writing under a pseudonym, complained about a nurse audit programme offered by Merck Sharp & Dohme and delivered by a service provider. The complainant referred to this as the Hypertension Review Programme Supportive of the GMS Contract (HRP-GMS).

COMPLAINT

The complainant stated that the HRP-GMS programme had been in operation and supported by Merck Sharp & Dohme from 2004 to the present day. Throughout this time, Merck Sharp & Dohme's representatives involved in the first-line promotion of Cozaar (losartan) had been given primary responsibility for identifying surgeries that were to be offered nurse advisors from a service provider to undertake audits relating to hypertension and Type 2 diabetes. The stated goals of the HRP-GMS were to improve patient management and support practices to achieve GMS contract targets in these disease areas.

The complainant understood from the previous and current editions of the Code that representatives could introduce general practices to company sponsored disease management programmes, as long as this was done in a non-promotional call. However, his concerns about the conduct of this programme related to the way in which representatives and their managers had to select those surgeries to be considered for placement of a nurse advisor. In this regard the complainant noted that the hypertension and Type 2 diabetes proformas explicitly referred to a number of sales and prescribing behaviour metrics to be fulfilled before a particular surgery was offered the service. The complainant understood that this was in breach of the letter and spirit of the Code which mandated that services to medicine and product promotion must not be linked in any way. An email from a senior manager in the Cozaar team, and the slide presentation entitled 'COZAAR Nurse Audit Programme' showed that representatives and their managers were required to complete the proformas in order to secure placements.

The complainant's motive for making the Authority aware of these issues was to establish the correctness, or not, of the conduct of this programme. Having taken the ABPI representatives examination, the complainant believed that he was individually accountable for adherence to the Code at all times and in the event that he observed behaviour that appeared to contravene the Code was duty bound to seek guidance from the Authority to rectify the matter. He had raised his concerns with several superiors within Merck Sharp & Dohme but repeatedly failed to receive a substantive answer to questions. In light of the company's avowed ethical stance the complainant felt frustrated and powerless to address this issue through internal company channels.

The complainant knew that Merck Sharp & Dohme was recently found in breach of the Code in relation to the inaccurate representation of the British Hypertension Society (BHS) guidelines. This, combined with another concern about representatives being set call frequency targets that appeared to be in breach of the Code, had left him no option but to raise these points directly with the Authority. Specifically, Merck Sharp & Dohme sales representatives were set annual objectives which required call frequencies on so-called target doctors up to six times within a six month period. The complainant stated that he and other colleagues raised this issue with line managers to be told that call frequency must be elevated during a launch phase and that representatives must use their acumen to circumvent the restrictions imposed by the Code.

When writing to Merck Sharp & Dohme, the Authority asked it to respond in relation to Clauses 2, 9.1, 15.4 and 18.4 if the 2006 edition of the Code applied or, if the 2003 edition applied, then Clauses 2, 9.1, 15.4 and 18.1, paying particular attention to the supplementary information to Clause 18.1.

RESPONSE

Merck Sharp & Dohme stated that as the relevant documents pre-dated September 2005, the 2003 edition of the Code applied.

Merck Sharp & Dohme dealt with the complaint in three elements.

1 The nurse audit

This was a nurse audit programme offered by Merck Sharp & Dohme and delivered by a service provider. Two audits were available; one in hypertension and one in Type 2 diabetes. GPs were offered the audit by a Merck Sharp & Dohme sales force. If the GP was interested in taking up the offer, the representative filled in a form, which was approved by their manager and by the Cozaar marketing team which authorized the service provider to offer the audit to that surgery. A nurse auditor from the service provider then contacted the practice directly and thereafter the Merck Sharp & Dohme representatives had no further involvement in the delivery of the audit itself. The audit was conducted by the nurse, working on behalf of the service provider, in conjunction with the practice and Merck Sharp & Dohme had no further involvement.

The nurse audit was originally offered in 2004 on a small pilot basis in hypertension, Type 2 diabetes and hypercholesterolaemia. The pilots proved successful and so, in 2005, they were rolled out nationally. The complainant had attached a number of documents relating to the audit:

a) Hypertension review programme protocol

This document was fully reviewed within Merck Sharp & Dohme which believed it complied with the Code, save that the BHS Guidelines on the Management of Hypertension contained the footnote 'A: Angiotensin receptor blocker or ACE Inhibitor' whereas the guidelines had these treatments options the other way round. This had been the subject of Case AUTH/1762/10/05.

b) Nurse booking form

So far as Merck Sharp & Dohme could tell, this was a document provided by the service provider to its nurse auditors. Accordingly, this document was not reviewed by Merck Sharp & Dohme. It nonetheless believed that it complied with the relevant provisions of the Code.

c) Email dated 28 July 2005 from a senior manager in the Cozaar team

This was a communication from the Cozaar marketing team to the relevant sales forces offering the audit to doctors. As noted by the complainant, this email referred to 'a good increase in the number of proformas coming through again this week' (please see below). Unsurprisingly given the nature of the document, it was not reviewed internally. Nonetheless, Merck Sharp & Dohme believed that in all other respects it complied with the Code.

d) Cozaar nurse audit programme briefing slides

Merck Sharp & Dohme was unable to identify the slide presentation. A slide presentation was used at the launch of the audit to the sales forces and whilst the slide set supplied by the complainant contained some of those slides it appeared to have a number of additional ones as well. As the complaint was anonymous, Merck Sharp & Dohme was unable to identify who created this precise presentation. It did, however, agree with the complainant that the slide presentation referred to the proformas and indicated that they should be completed by representatives and sent to the Cozaar marketing team.

e) Hypertension and Type 2 diabetes proformas

Merck Sharp & Dohme stated that these documents were created by the Cozaar marketing team and circulated to the relevant sales forces offering the nurse audit programme. [At the audit it became apparent that the proformas at issue had been used in the pilot project which was organised by another business unit before being handed to the cardiovascular business unit for rollout.] They were not reviewed internally and Merck Sharp & Dohme believed that they breached Clause 18.1 of the Code. Merck Sharp & Dohme apologised for this; once an internal investigation into the matter was complete, disciplinary action would be taken if appropriate.

For completeness sake, Merck Sharp & Dohme noted that some of the material relating to the nurse audit was re-approved in September 2005. At this stage, the relevant proformas were fully reviewed. Copies of the proformas currently being used by its representatives were provided.

2 Whistle-blowing

Merck Sharp & Dohme stated its policy was to take all allegations of breaches of the Code extremely seriously. It was thus surprised and disappointed to note that the complainant's attempt to raise his concerns with his superiors did not result in a thorough investigation of the matter.

As the complaint was anonymous, Merck Sharp & Dohme could not take this matter further. If the complainant was willing to identify himself and the superiors spoken to, Merck Sharp & Dohme would undertake a full investigation.

3 Annual call objectives

Merck Sharp & Dohme stated that as the complainant was anonymous it was unable to respond in detail to the particular allegations that had been made. However, it set out its general expectations of representatives in terms of frequency of contacts with GPs.

The 2005 Sales Incentive Scheme for the two sales forces offering the nurse audit (Chibret and Falcon) set out various targets and the level of bonus which they could expect to receive for various levels of achievement against those targets. The relevant information ('Quarterly Coverage') was set out in detail in each document. Each representative was assigned a number of target GPs on their territory who they were expected to see during the course of a year. Merck Sharp & Dohme provided details of the percentage of target customers to be seen in quarters 1, 2, 3 and 4 to achieve maximum bonus. In addition, they received a team bonus based on the percentage of target customers that the two representatives working on that territory (Chibret or Falcon, as appropriate) saw during the year between them, as a joint activity objective. The relevant figures for the entire teams were 70% in quarter one, 90% in quarter two and 80% in quarters three and four. It should be noted that 'see' included all occasions on which a representative met a customer ie not only pre-arranged visits but also group meetings or visits in response to a specific enquiry from the customer. All representatives had to pass the ABPI examination for medical representatives, as set out in their terms and conditions of employment. Merck Sharp & Dohme therefore expected its representatives to know the requirements of the supplementary information to Clause 15.4 when contacting customers, and indeed this was reinforced to them verbally by their managers.

The annual objectives for representatives in these two sales forces for 2005 required that between them they saw either seven or five target customers each year (depending on whether they were a primary or secondary target). Accordingly, a representative in either Chibret or Falcon would be expected to liaise with their counterpart on the same territory in the other field force to ensure that, between them, they saw at least seven or five target customers per year.

While Merck Sharp & Dohme believed this was clear to its representatives, in light of a number of Appeal Board decisions on this topic in 2005, the two 2006 Sales Force Incentive Schemes specifically reminded representatives of the requirements of the supplementary information to Clause 15.4.

Merck Sharp & Dohme believed that it was clear, therefore, that the annual objectives for each of its representatives required them to see either four or three primary target doctors (or see three or two secondary target doctors). In addition, these contacts

must be made in accordance with the supplementary information to Clause 15.4 of the Code. Merck Sharp & Dohme was, therefore, unable to understand why the complainant believed that they were required to visit target doctors 'up to six times within a six month period'. In addition, Merck Sharp & Dohme noted that under no circumstances should managers ever encourage representatives to 'use their acumen to circumvent the restriction imposed by the Code'. Again, if the complainant was willing to identify himself and the manager in question, Merck Sharp & Dohme would investigate the matter fully. It believed, however, that both the objective for its representatives and the Sales Force Incentive Schemes complied with the Code both in letter and spirit.

PANEL RULING

The Panel noted Merck Sharp & Dohme's submission that the relevant documents predated September 2005. Thus the 2003 edition of the Code applied; the supplementary information to Clause 18.1 of that Code stated that medical and educational goods and services had to enhance patient care or benefit the NHS. The change under Clause 18.4 of the 2006 Code was that such services had to either enhance patient care or benefit the NHS and maintain patient care.

With regard to therapy review services the supplementary information to Clause 18.4 of the 2006 Code provided helpful guidance. A therapeutic review which aimed to ensure that patients received optimal treatment following a clinical assessment was a legitimate activity for a pharmaceutical company to support and/or assist. The results of such clinical assessments might require, among other things, possible changes of treatment including changes of dose or medicine or cessation of treatment. A genuine therapeutic review should include a comprehensive range of relevant treatment choices, including non-medicinal choices, for the health professional and should not be limited to the medicines of the sponsoring pharmaceutical company. The arrangements for therapeutic review must enhance patient care, or benefit the NHS and maintain patient care. The decision to change or commence treatment must be made for each individual patient by the prescriber and every decision to change an individual patient's treatment must be documented with evidence that it was made on rational grounds.

The Panel noted Merck Sharp & Dohme's submission that there were differences between the slides sent by the complainant and the Cozaar nurse audit programme briefing slides used by the company to train the representatives. The Panel noted that the training slides for representatives, as provided by Merck Sharp & Dohme, were branded with the Cozaar logo. The first slide referred to the 'COZAAR Nurse Audit Programme'. The service would thus be seen by representatives as being linked to the promotion of the product. No mention was made in the presentation of the need to separate the provision of medical and educational goods and services from the promotion of medicines. This was totally unacceptable.

The slides provided by Merck Sharp & Dohme included instructions that the audit service was only to be offered to practices that, *inter alia*, had 'Strong buy into LIFE and COZAAR messages'. Surgeries had to agree to Cozaar as medicine of choice in relation to 'A' as set out in the British Hypertension Society (BHS) guidelines where A meant ACE inhibitor or angiotension antagonist. The practice also had to have a 'call rate of 6 prior to audit plus speaker meeting attendance'. The surgeries selected must have target doctors as project lead. The programme was referred to as a targeted resource to influence the environment.

The aim of the programme, as set out in the slides provided by Merck Sharp & Dohme, was to provide practices with an independent nurse advisor to review all uncontrolled hypertensive patients over 55 in order to improve blood pressure management in accordance with the ABCD goal (this was taken to be a reference to the BHS guidelines). The programme aims included the benefits of restoring blood pressure to normal or optimum levels, enhanced patient education through detailed lifestyle advice and the update of existing practice registers.

The slides headed 'The program guidance form' had 'Cozaar/Losartan' printed in a box beneath the heading 'Practice Policy – please complete'.

Another slide provided by Merck Sharp & Dohme was headed 'Implementation changes' and referred to a more focussed proforma for both programmes. This was shown on the following slide which made it clear that if the practice angiotensin antagonist of choice was not Cozaar then the practice was not suitable. If the practice had not agreed to Cozaar as (A) drug of choice in ABCD then it was not suitable. If the brick market share was not above 40% for Cozaar then the practice was not suitable. The proforma provided by the complainant was similar to that shown on the slides; it additionally included a section asking the representative for the rationale as to why it was important to nominate the surgery for the audit.

The medical/legal approved proformas provided by Merck Sharp & Dohme, however, were very different to those on the slides and those provided by the complainant; there were different questions to be completed and there were no criteria to be met for the practice to be deemed suitable for offering the service.

The HRP-GMS Protocol provided by the complainant referred to the BHS recommendations for combining blood pressure lowering medicines. It included the reference to A as 'angiotension receptor blocker or ACE inhibitor'; this matter was the subject of complaint in promotional material in a previous case, Case AUTH/1762/10/05. The Panel considered that Merck Sharp & Dohme should have changed the protocol as a result of the ruling in the previous case.

The Panel noted that the practice had to agree each stage of the process. Hypertensive patients were invited for review by the nurse if they were over 55 and had not achieved audit targets set in the nGMS (blood pressure higher than 150/90) and had been on current treatment for at least six weeks prior to assessment. The nurse would then create three registers: one for patients appropriate for medication review according to the HRP-GMS as directed by the GP; the second for patients appropriate for

medication review by the practice (ie not at target but less than 55 years old) and the third for patients inappropriate for medication review as directed by the GP. The Panel queried how the second register would come about given that the inclusion criterion was for patients over 55.

The audit proposal form appeared to go beyond the inclusion and exclusion criteria. The practice prescribing policy had to be entered on a form which also reproduced the incorrect version of the BHS guidelines. The form was to be signed by some of the practice doctors.

The template letter for patients regarding the audit did not state that the audit was sponsored by Merck Sharp & Dohme.

The Panel considered that the nurse audit programme did not meet the requirements of Clause 18.1 of the Code. The Merck Sharp & Dohme training slides clearly associated the programme with the promotion of Cozaar by use of logos and the introductory slide. The amendments to the proformas clearly linked the nurse audit programme to the use of Cozaar. The Panel considered that the arrangements were unacceptable in relation to Clause 18.1 and ruled accordingly.

The Panel considered that high standards had not been maintained and the circumstances brought discredit upon the pharmaceutical industry; breaches of Clauses 9.1 and 2 were ruled.

The Panel decided to report Merck Sharp & Dohme to the Code of Practice Appeal Board in accordance with Paragraph 8.2 of the Constitution and Procedure.

The Panel noted that the complainant had further alleged that Merck Sharp & Dohme required representatives to call upon target doctors up to six times within a six month period.

The Panel noted Merck Sharp & Dohme's response which stated that the two sales forces together were expected to see either seven or five target customers each year (depending on whether they were primary or secondary targets). In total this meant each representative would see either four or three primary target doctors or two or three secondary target doctors. Merck Sharp & Dohme had submitted that 'seeing' included all occasions on which a representative met a customer. The Panel noted that the annual objectives did not appear to be included in the sales incentive scheme 2005 documents.

The Panel noted that there was a discrepancy between the complaint and the response in this regard.

The supplementary information to Clause 15.4 of the 2003 Code referred in detail to calls on doctors stating that a representative should not normally call upon a doctor more than three times a year on average. This did not include attendance at group meetings, a visit requested by the doctor or a visit to follow up a report of an adverse reaction. The Panel noted that the representatives' personal performance grid did not refer to the requirements of Clause 15.4 of the Code but nonetheless considered that there was no evidence to show that representatives were encouraged to make six calls in six months as alleged. No breach of Clause 15.4 was ruled.

CONSIDERATION BY THE APPEAL BOARD

At the consideration of the report the Merck Sharp & Dohme representatives apologised on behalf of Merck Sharp & Dohme and stated that this matter was being taken extremely seriously by the company. The audit service was suspended in March 2006 in response to the complaint. The representatives submitted that this case had arisen as a result of a failure of its internal processes, including a breakdown in communication. The approval process had already been highlighted as a key priority for review following an internal review in October 2005 which was still ongoing. New standard operating procedures had been written and staff training had commenced. Internal disciplinary procedures were under way. The representatives submitted that the company was taking action to ensure that it never happened again.

The Appeal Board was extremely concerned that arrangements for the audit programme had highlighted very serious deficiencies in Merck Sharp & Dohme's procedures including the copy approval system. Given the significant investment that the audit represented the Appeal Board considered that it was inconceivable that it was not more tightly controlled; material had been used which had not been approved. The service had been clearly linked to the promotion of Cozaar and there appeared to be a serious lack of control by senior managers. The Appeal Board considered that the arrangements were totally unacceptable.

With regard to the Panel's ruling that the circumstances brought discredit upon the pharmaceutical industry, the Appeal Board was concerned that Merck Sharp & Dohme's actions had the potential to compromise patient safety by inappropriate prescribing. Further Merck Sharp & Dohme's actions would undermine both prescribers' and patients' confidence in the provision of properly conducted services. The Appeal Board was extremely concerned that some Merck Sharp & Dohme staff had not realised that the amended proformas and the slides used as training material were totally unacceptable in relation to the requirements of the Code.

The Appeal Board considered that this was an extremely serious case.

The Appeal Board decided in accordance with Paragraph 11.3 of the Constitution and Procedure to require an immediate audit of Merck Sharp & Dohme's procedures. In addition Merck Sharp & Dohme would be publicly reprimanded and required to issue a corrective statement. The corrective statement should be sent as soon as possible to all practices that had been identified and approached to take part in the audit. In accordance with Paragraph 12.1 of the Constitution and Procedure the Appeal Board decided to report Merck Sharp & Dohme to the ABPI Board of Management with the recommendation that it suspended Merck Sharp & Dohme from membership of the ABPI.

CONSIDERATION OF THE AUDIT REPORT BY THE APPEAL BOARD

Upon receipt of the report of the audit carried out in July 2006 and Merck Sharp & Dohme's comments on

it, the Appeal Board noted that the company had started to implement the recommendations and address the observations set out in the audit report. This would take some time given that the problems were institutional in nature and many changes were necessary. This audit report would be provided to the ABPI Board.

The Appeal Board decided that Merck Sharp & Dohme should be reaudited. It was later decided that this audit would take place in November 2006 and the report of this audit would be made available to the ABPI Board.

CONSIDERATION BY THE ABPI BOARD OF MANAGEMENT

The ABPI Board noted that Merck Sharp & Dohme had been ruled in breach of Clauses 2, 9.1 and 18.1 of the Code. It also noted the audit report and Merck Sharp & Dohme's comments upon it.

The ABPI Board noted that the Appeal Board had recommended that Merck Sharp & Dohme be suspended from membership of the ABPI. It was further noted that Merck Sharp & Dohme was to undergo a second audit of its procedures in accordance with Paragraph 11.3 of the Constitution and Procedure; that Merck Sharp & Dohme was to be publicly reprimanded; and that Merck Sharp & Dohme had issued a corrective statement. The ABPI Board noted that Merck Sharp & Dohme had fully accepted responsibility for the matters giving rise to the complaint and that current management, including the new managing director, was taking action to ensure that there was no repeat: action which ranged from training through to changes in culture.

Nevertheless, given the serious nature of the case, the ABPI Board decided that the appropriate course of action was to suspend Merck Sharp & Dohme from membership of the ABPI for a minimum of three months commencing 2 October 2006. The suspension would be reassessed after three months. The ABPI Board noted that Merck Sharp & Dohme was to undergo a further audit of its procedures and requested that it be provided with a copy of the report for this second audit.

CORRECTIVE STATEMENT

In accordance with Paragraph 11.3 of the Constitution and Procedure, details of the proposed content of the corrective statement and the mode and timing of its dissemination were provided to the Appeal Board for approval prior to use.

The corrective statement was mailed in July 2006 to all surgeries which either participated in, or had been approached to participate in, the nurse audit programme.

'Dear Dr X

Following a complaint to the Prescription Medicines Code of Practice Authority (PMCPA), Merck Sharp & Dohme has been ruled in breach of the Association of the British Pharmaceutical Industry (ABPI) Code of Practice for the Pharmaceutical Industry in relation to an audit service, 'Hypertension review programme supportive of the GMS contract' offered to practices to assess patients with hypertension. The service was suspended in March 2006 and has now been stopped.

Internal documents, which had not been through the company approval system, were provided to the representatives and clearly linked the provision of the service to the use of Cozaar. The audit service was only to be offered to practices that agreed to use Cozaar as the medicine of choice in respect of nationally agreed guidelines. In some documents those guidelines had been altered in favour of Cozaar. The arrangements were considered to be completely unacceptable. Breaches of the Code (Clauses 2, 9.1 and 18.1) were ruled including a failure to maintain high standards and bringing discredit upon the pharmaceutical industry. I thus apologise unreservedly for the way in which Merck Sharp & Dohme conducted the audit.

In addition to the issue of this corrective statement, the Code of Practice Appeal Board decided that Merck Sharp & Dohme will be publicly reprimanded and undergo an audit of its procedures and policies for ensuring compliance with the Code. The matter is also the subject of a report to the ABPI Board of Management for it to consider whether further sanctions are necessary.

Should you have any further questions, please contact medical information at Merck Sharp & Dohme on 01992 45 5000.

As with all cases considered under the Code the case report giving full details will be published in due course (www.pmcpa.org.uk).

Yours sincerely

UK Managing Director
Merck Sharp & Dohme Limited'

Complaint received **15 March 2006**
Undertaking received **9 June 2006**
ABPI Board consideration **5 September 2006**

NOVARTIS v APOPHARMA and SWEDISH ORPHAN

Promotion of Ferriprox

Novartis complained about a Ferriprox (deferiprone) banner advertisement which appeared on the homepage of the electronic British Journal of Haematology and about an article on Ferriprox in the March edition of the UK Thalassaemia Society Patient Newsletter. Ferriprox was distributed by Swedish Orphan International (UK) and the marketing authorization was held by Apotex Europe. Novartis supplied Desferal (desferoxamine).

In response to a request by the Authority for clarification, it was informed that ApoPharma was the Innovative Drug Division of Apotex Inc. Apotex was a Canadian generic pharmaceutical company and relied on distributor agreements in markets around the world for its sales and marketing requirements. Swedish Orphan was the exclusive distributor of Ferriprox in many European markets, including the UK.

Case AUTH/1822/4/06 concerned the banner advertisement. Novartis alleged that the strapline 'Life is getting longer' was an exaggerated claim that the use of Ferriprox was associated with increased survival generally; no reference was cited to substantiate such a broad claim and it was a hanging comparative. In addition, the claim did not state the disease area in which the product was to be used and hence was inconsistent with the terms of the marketing authorization, which stated that Ferriprox was licensed for the 'treatment of iron overload in patients with thalassaemia major when deferoxamine therapy is contraindicated or inadequate'. Failing to include the indication whilst suggesting that use of the product prolonged life could be seen as promoting outside the product licence. Finally, no consideration had been given to the provision of the prescribing information.

ApoPharma responded in relation to these allegations.

The Panel considered that the banner advertisement in the British Journal of Haematology was an advertisement covered by the UK Code. The journal would be widely read round the world but, given its title, it was intended for, *inter alia*, a UK audience.

The Panel ruled the failure to include a direct link to the Ferriprox prescribing information in the banner advertisement in breach of the Code. The Panel did not accept that the failure to indicate the disease area meant that the claim was inconsistent with the summary of product characteristics (SPC) as alleged. No breach of the Code was ruled in that regard.

The Panel ruled a breach of the Code as the claim 'Life is getting longer' was a hanging comparison. Under the Code there was no need to reference all claims, only those that referred to published studies. ApoPharma had not provided any material to substantiate the claim. The Panel ruled a breach of the Code.

Case AUTH/1823/4/06 concerned the claim 'New Data Show Ferriprox Tablets are More Efficacious than Desferoxamine in Removing Iron from the Heart and in Preventing Early Death in Patients with Thalassaemia'. This was the title of an article in the UK Thalassaemia Society Patient Newsletter – March 2006.

Novartis alleged that this article, which appeared to have been written by Swedish Orphan, had a promotional tone and thus constituted clear advertising by the company of a prescription only medicine to the public.

In the second paragraph the article described 'a stunning report on the morbidity and mortality of thalassaemia patients…'. This information was not provided in a factual manner. Both the trials reported in the article included patients who were either randomised or switched to Ferriprox from Desferal. The information provided indicated that these patients were not within the licensed indication for Ferriprox which included the statement: 'when deferoxamine therapy is contraindicated or inadequate'. In addition, despite it being clearly stated that 'Full prescribing information is printed overleaf', this was not so and there was no prescribing information for Ferriprox in the entire newsletter. The inclusion of this statement suggested that the company recognised that this was a promotional item and that the original intention for this item was as a promotional item directed to health professionals rather than patients. Its inclusion in a patient group newsletter was therefore entirely inappropriate. The article also displayed the previously described advertisement 'Life is getting Longer'.

Swedish Orphan responded in relation to these allegations.

The Panel noted that the UK Code applied to press releases of corporate interest. The Code prohibited the advertising of prescription only medicines to the public. The Code permitted information to be made available if presented in a balanced way. It must not raise unfounded hopes of successful treatment and not be misleading with respect to the safety of the product. Statements must not be made for the purpose of encouraging a member of the public to ask their health professional to prescribe a specific prescription only medicine.

The Panel noted that the actual press release had not been supplied to it by Swedish Orphan. The company submitted that the UK Thalassaemia Society's patient newsletter had reproduced the UK press release including the prescribing information. This was unusual. Thus the Panel made its decision on the content of the patient newsletter which was in effect Swedish Orphan's press release.

The Panel did not consider that the article itself was an advertisement for a prescription only medicine to the public. No breach of the Code was ruled.

The article referred to the results of the study as being 'stunning' and 'exciting'. The Panel considered that in that regard the article was not balanced and would encourage readers to ask their

health professional to prescribe Ferriprox. A breach of the Code was ruled.

The Panel noted that the supplementary information to the Code stated that it was good practice to include the SPC with a press release. There was no prohibition in Clause 20 on including the prescribing information, which was different to the SPC, with a press release. The prescribing information was required when a product was promoted to health professionals for prescribing. A press release to the media must not constitute advertising of a prescription only medicine to the public.

The Panel considered that its rulings with regard to the claim 'Life is getting longer' in Case AUTH/1822/4/06, above applied here. The Panel ruled a breach as the advertisement was for a prescription only medicine to the public. The advertisement was not advertising to health professionals and prescribing information was thus not required and no breach was ruled in that regard.

Novartis Pharmaceuticals UK Ltd complained about a Ferriprox (deferiprone) banner which appeared in the electronic British Journal of Haematology homepage and about an article on Ferriprox in the March 2006 edition of the United Kingdom Thalassaemia Society Patient Newsletter. Ferriprox was distributed by Swedish Orphan International (UK) Ltd and the marketing authorization was held by Apotex Europe Ltd. Contact with Apotex had failed to resolve the matter. Novartis supplied Desferal (desferoxamine).

In response to a request from the Authority for clarification, it was informed that ApoPharma was the Innovative Drug Division of Apotex Inc. Apotex was a Canadian generic pharmaceutical company and relied on distributor agreements in markets around the world to satisfy its sales and marketing requirements. Swedish Orphan was the exclusive distributor of Ferriprox in many European markets, including the UK.

Case AUTH/1822/4/06 (ApoPharma)

Ferriprox banner advertisement 'Life is getting longer'

COMPLAINT

Novartis stated that the supplementary information to Clause 1.1 of the Code clearly stated that the Code applied to the advertising of medicines in professional journals which were produced in the UK and/or intended for a UK audience. This requirement included both print and electronic versions of such journals. Clearly the British Journal of Haematology fitted this definition and this advertising was therefore, Novartis believed, subject to the Code.

The strapline 'Life is getting longer' at the top of the menu page for the electronic journal was clearly visible to UK health professionals accessing the British Journal of Haematology via this route. In isolation the banner represented a clearly exaggerated claim that the use of Ferriprox was associated with increased survival generally with no reference source to substantiate such a broad claim and a hanging comparative.

In addition, the claim did not state the disease area in which the product was to be used and hence was inconsistent with the terms of the marketing authorization, which stated that Ferriprox was licensed for the 'treatment of iron overload in patients with thalassaemia major when deferoxamine therapy is contraindicted or inadequate'. It could be argued that failing to include the indication whilst at the same time suggesting that use of the product prolonged life could be seen as promoting the product outside of the licence.

Novartis alleged that the claim was misleading, exaggerated, unsubstantiable and a hanging comparison. Finally, no consideration had been given to the provision of the prescribing information with this banner advertisement. There was no weblink, nor any indication as to the location of the Ferriprox prescribing information on the banner itself. This banner advertisement was therefore in breach of Clauses 3.2, 4.1, 7.2 and 7.4 of the Code.

RESPONSE

ApoPharma stated that it had made the changes that Novartis requested to the banner advertisement on the British Journal of Haematology website, specifically, the disease area, thalassaemia major had been added. In addition, a link on the banner advertisement had been provided that would allow the user access to the prescribing information, or the reference sources that supported the claim of increased survival.

With regard to Novartis' concerns regarding the *Ferriprox.com* website, ApoPharma did not agree with its assertion that the British Journal of Haematology was intended solely for a UK audience. The British Journal of Haematology might be published in the UK, but it was certainly promoted and sold on a global basis. For this reason ApoPharma felt that providing access to a website targeted to a population outside of the UK was not inappropriate if the proper disclaimer was provided.

PANEL RULING

The Panel considered that the banner advertisement in the British Journal of Haematology was an advertisement covered by the UK Code and noted that ApoPharma was responsible for the advertisement which appeared in a professional journal intended for a UK audience. The journal would be widely read round the world but, given its title, it was intended for, *inter alia*, a UK audience.

The Panel noted the supplementary information to Clause 4.1 of the Code, Electronic Journals. The Panel considered that the failure to include a direct link to the prescribing information for Ferriprox in the banner advertisement was a breach of Clause 4.1 of the Code and ruled accordingly.

The Panel did not accept that the failure to indicate the disease area meant that the claim in the banner advertisement was inconsistent with the summary of product characteristics (SPC) as alleged. No breach of Clause 3.2 was ruled.

The Panel considered that the claim 'Life is getting longer' was a hanging comparison; it was not clear with what Ferriprox was being compared. A breach of Clause 7.2 of the Code was ruled. Under the Code there was no need to reference all claims, only those that referred to published studies (Clause 7.6). ApoPharma had not provided any material to substantiate the claim. The Panel ruled a breach of Clause 7.4.

Case AUTH/1823/4/06 (Swedish Orphan)

Claim 'New Data Show Ferriprox Tablets are More Efficacious than Desferoxamine in Removing Iron from the Heart and in Preventing Early Death in Patients with Thalassaemia'

This was the title of an article in the UK Thalassaemia Society Patient Newsletter – March 2006.

COMPLAINT

Novartis alleged that this article, which appeared to have been written by Swedish Orphan had a promotional tone and thus constituted clear advertising by the company of a prescription medicine to the public in breach of Clause 20.1.

In the second paragraph the article described 'a stunning report on the morbidity and mortality of thalassaemia patients…'. This information was not provided in a factual manner and so a breach of Clause 20.2 was alleged.

Both the trials reported in the article included patients who were either randomised or switched to Ferriprox from Desferal. The information provided indicated that these patients were not within the licensed indication for Ferriprox which included the statement: 'when deferoxamine therapy is contraindicated or inadequate'.

In addition, despite it being clearly stated that 'Full prescribing information is printed overleaf', this was not the case and in fact there was no prescribing information for Ferriprox in the entire newsletter. The inclusion of this statement suggested that the company recognised that this was a promotional item and that the original intention for this item was as a promotional item directed to health professionals rather than patients. Its inclusion in a patient group newsletter was therefore entirely inappropriate.

The article also displayed the previously described advertisement 'Life is getting Longer' and so for the reasons given above, Case AUTH/1822/4/06, in breach of Clauses 3.2, 4.1, 7.2 and 7.4 as well as of Clause 20.1.

RESPONSE

Swedish Orphan stated that when new important data from two studies with Ferriprox became known a global press release was developed. The results from the two studies were regarded to be 'breakthrough data' and of high importance to patients (lifesaving), the medical community as well as for the corporations and the investor community.

In the UK the global press release was slightly adapted and the UK prescribing information for Ferriprox was added. This was common practice, not only at Swedish Orphan, but a practice applied by many if not most pharmaceutical companies and adding the SPC or local labelling was part of communicating balanced information on the product.

The global press release (with local adaptations) went out in many countries to the medical press and other relevant publications for a corporate announcement.

As far as Swedish Orphan could understand the codes for marketing (EFPIA, ABPI and others) did not apply to press releases of corporate interest.

Swedish Orphan could not confirm if the publisher of the UK Thalassaemia Society Newsletter received the press release directly from its local office or if it was picked up from somewhere else. There was a press conference at a congress in Dubai (The Thalasaemia International Federation Congress 2006) shortly before the press release was distributed in UK. The UK Thalassaemia Society was represented at the congress.

As was noted by Novartis it was an article in the newsletter – not an advertisement. Swedish Orphan International had obviously not written the article. It was simply an article which was based on the press release. What was a bit unusual was that the article included most of the press release, which also explained why there was a reference to prescribing information and contact details if further information was wanted. It was common practice to provide contact details and attach the SPC/labelling in a press release.

In summary: Novartis' conclusion that the article represented an 'advertisement by the company' was false. It was an article based on a well justified press release as the study results had a corporate (public) interest. Also, this meant Novartis was implying that the UK Thalassaemia Society, a well respected patient organisation, would allow Swedish Orphan to write articles containing product promotion in its newsletter. This was a serious allegation against the society.

Novartis' conclusion that the reference to the prescribing information '… suggested that the company recognized that this was a promotional item…' was false. Swedish Orphan, as well as other pharmaceutical companies, commonly attached prescribing information (SPC or local labelling) to press releases concerning products in order to provide balanced information and to name a company contact person.

PANEL RULING

The Panel noted that the UK Code did apply to press releases of corporate interest. Clause 20.1 prohibited the advertising of prescription only medicines to the public. Clause 20.2 permitted information to be made available if presented in a balanced way. It must not raise unfounded hopes of successful treatment and not be misleading with respect to the safety of the product. Statements must not be made for the purpose of encouraging a member of the public to ask their health professional to prescribe a specific prescription only medicine.

The supplementary information to Clause 20.2, Financial Information, referred to information made available to inform shareholders, the stock exchange and the like. The press material at issue in this case did not appear to be a business press release as set out in this supplementary information.

The Panel noted that the actual press release had not been supplied to it by Swedish Orphan. The company submitted that the UK Thalassaemia Society's patient newsletter had reproduced the UK press release including the prescribing information. This was unusual. Thus the Panel made its decision on the content of the patient newsletter which was in effect Swedish Orphan's press release.

The Panel did not consider that the article itself was an advertisement for a prescription only medicine to the public. No breach of Clause 20.1 of the Code was ruled.

The article referred to the results of the study as being 'stunning' and 'exciting'. The Panel considered that in that regard the article was not balanced and would encourage readers to ask their health professional to prescribe Ferriprox. A breach of Clause 20.2 of the Code was ruled.

The Panel noted that the supplementary information to Clause 20.2 of the Code stated that it was good practice to include the SPC with a press release. There was no prohibition in Clause 20 on including the prescribing information, which was different to the SPC, with a press release. The prescribing information was required by Clause 4.1 of the Code when a product was promoted to health professionals for prescribing. A press release to the media must not constitute advertising a prescription only medicine to the general public.

The Panel noted that an advertisement issued by Swedish Orphan appeared immediately following the article in the newsletter. The advertisement stated 'With licensed oral iron chelation life is getting longer' and included the Swedish Orphan International mission statement. Novartis had complained about this advertisement.

The Panel considered that its rulings with regard to the claim 'Life is getting longer' in Case AUTH/1822/4/06, above, applied here. Thus breaches of Clauses 7.2 and 7.4 of the Code were ruled and no breach of Clause 3.2 was ruled. The Panel ruled a breach of Clause 20.1 as the advertisement was for a prescription only medicine to the general public. The Panel ruled no breach of Clause 4.1 as the advertisement was not advertising to health professionals and prescribing information was thus not required.

Case AUTH/1822/4/06	
Complaint received	**4 April 2006**
Company agreed to comply with the Code and accept the Authority's jurisdiction	**5 July 2006**
Case completed	**23 August 2006**

Case AUTH/1823/4/06	
Complaint received	**4 April 2006**
Company agreed to comply with the Code and accept the Authority's jurisdiction	**14 July 2006**
Case completed	**18 August 2006**

GENERAL PRACTITIONER v JANSSEN-CILAG

Durogesic DTrans email

A general practitioner complained that an unsolicited email about Durogesic DTrans (fentanyl patches) which he had received from Janssen-Cilag seemed to be a misuse of the NHS net for advertising purposes.

The Panel noted that the parties' accounts differed. The complainant stated that the email was unsolicited. Janssen-Cilag stated that the email was only sent to those who had given prior permission for it to send them promotional material. It was impossible to know where the truth lay. No breach of the Code was ruled.

A general practitioner complained about an unsolicited email about Durogesic DTrans (fentanyl patches) which he had received, via an agency, from Janssen-Cilag Ltd.

COMPLAINT

The complainant stated that the unsolicited email from the Durogesic DTrans Team [DurogesicDTrans@ehealthinfo.co.uk] seemed to be a misuse of the NHS net for advertising purposes. The email promoted Durogesic DTtrans and was from the product manager. Recipients were offered an opportunity to take part in a survey, and receive a free 64mb memory stick.

When writing to Janssen-Cilag, the Authority asked it to respond in relation to Clause 9.9 of the Code.

RESPONSE

Janssen-Cilag stated that it was not in breach of Clause 9.9 since recipients of the email had given permission for promotional materials to be sent to them electronically.

The agency which had sent the email was contracted to Janssen-Cilag to undertake certain activities, such as distribution of the email in question. The contract between the two parties stated that the agency would obtain all necessary permissions from health professionals in line with certain regulatory requirements, the Data Protection Act and the Code, and that its practices would comply with the Code. Implicit within this, was that only those doctors who had given prior permission would be sent Janssen-Cilag material by electronic mailing. The contract also specified that the agency would record how and when the permission was obtained, ensuring that permission could be traced on an individual basis and provided to the Authority if necessary.

Following receipt of the complaint, Janssen-Cilag contacted the agency requesting it to confirm that prior permission had been given by health professionals to receive the email in question and also to address other issues raised within the letter.

The agency confirmed that the email address referred to in the complaint 'ehealthinfo.co.uk' belonged to it and was not an NHS email address; therefore, the complainant's concern as to what was perceived to be a misuse of the NHS net for advertising purposes was unfounded.

In respect of the generation of mailing lists and obtaining health professionals' permission to receive promotional materials, the agency had told Janssen-Cilag that the mailing list was generated from information received directly from health professionals or, as sometimes happened, from practice managers with the approval of the doctors. Questionnaires had been sent out to every surgery and NHS trust in the country. This was followed up by a letter requesting the return of the questionnaire (if necessary). This was then followed by a personal call. Much of the updating was done online and in view of the longstanding relationship built up between the agency and NHS personnel, a lot of the updates were now simply a matter of a quick telephone call. However, in every case the health professionals were told that they were giving this information to a private organisation and that they would from time to time receive information, some from government departments, some educational and some of a promotional nature, all forwarded by the agency on behalf of other organisations. At that stage they gave the agency the information and opted in for the receipt of e-mails.'

It was therefore within the context of Janssen-Cilag's contract with the agency and its processes as outlined above, that the Durogesic DTrans promotional email was distributed to health professionals on the agency's distribution list of those who had given permission to receive such promotional items. The email indicated that it had been forwarded by the agency on behalf of Janssen-Cilag and in addition, there was an opportunity for health professionals to unsubscribe and therefore not receive any further emails.

As the identity of the complainant was not known to Janssen-Cilag, it was unable to comment specifically with regard to how he had consented to receive emails from agency. However the contract between the agency and Janssen-Cilag stipulated that permissions could be traced on an individual basis and provided to the Authority if so requested. Any such request would remain confidential between the Authority, the agency, and the individual general practitioner.

Janssen-Cilag denied a breach of Clause 9.9 of the Code.

PANEL RULING

The Panel noted that in its preliminary consideration of this case it had decided to send Janssen-Cilag's response to the complainant for comment before it

made its ruling. Permission was also sought to reveal the complainant's identity to Janssen-Cilag thus allowing it to search its records to determine if permission had been granted for it to send promotional emails to the complainant. No response was received from the complainant.

The Panel noted that the parties' accounts differed. The complainant stated that the email was unsolicited. Janssen-Cilag stated that the email was only sent to those who had given prior permission for it to send them promotional material. It was impossible to know where the truth lay. No breach of Clause 9.9 was ruled.

Complaint received **24 April 2006**

Case completed **8 August 2006**

CASE AUTH/1833/5/06

ASTRAZENECA v GLAXOSMITHKLINE

CONCEPT study leavepiece

AstraZeneca complained that a leavepiece issued by Allen & Hanburys, part of GlaxoSmithKline, did not present a fair and balanced account of the CONCEPT (CONtrol CEntred Patient Treatment) study which had compared stable dosing of GlaxoSmithKline's product Seretide (salmeterol/fluticasone propionate) with symptom led (variable) dosing of AstraZeneca's product Symbicort (formoterol/budesonide) in the management of asthma. The leavepiece implied that Seretide was compared with clinically equivalent doses of Symbicort as it did not explicitly state that like-for-like steroid doses were not used (82% Symbicort patients were stepped down to the lowest possible dose, compared with all Seretide patients being maintained at 500mcg per day). The leavepiece did not explicitly state that in the Symbicort arm the steroid dose could only be increased in response to symptoms, thus predetermining a higher symptom level in this group. The leavepiece did not reflect the balance of the evidence in that it did not refer to the results of the SUND study (where comparable steroid doses were used, which resulted in significantly fewer exacerbations in the Symbicort arm).

The CONCEPT study had consisted of a 2 week run-in, a 4 week stabilisation phase and a 48 week variable maintenance phase. During the 4 week stabilisation phase patients remained on either Seretide 250mcg bd or Symbicort 200mcg 2 puffs bd which equated to comparing a daily dose of 500mcg fluticasone with 800mcg budesonide (delivered via a turbohaler device) respectively. AstraZeneca stated that these doses were approximately equivalent.

Following 4 weeks on approximately equivalent doses patients entered the variable maintenance phase if they were completely symptom free. During the variable maintenance phase, Seretide patients remained on fixed Seretide 250mcg 1 inhalation bd. Symbicort patients could adjust their therapy according to a predefined treatment plan; they could halve their dose and subsequently step up or down as indicated by the presence or absence of various asthma symptoms and changes in morning peak expiratory flow measurements. If Symbicort patients were well controlled they were instructed to further reduce the dose to only 1 inhalation once daily in the evening which equated to a daily steroid dose of only 200mcg of budesonide. This was important as Seretide patients remained on a fixed daily dose of 500mcg fluticasone. Results showed that during the variable maintenance phase 82% of Symbicort patients stepped down to 1 inhalation per day at some time during the trial. Only when they developed symptoms were they instructed to step up the dose to regain asthma control. Thus the majority of Symbicort patients were instructed to down titrate to the lowest possible maintenance dose of inhaled steroid and remain on this dose until they developed asthma symptoms. It was therefore not surprising that these patients experienced more asthma symptoms and exacerbations compared to those taking comparatively higher steroid levels of Seretide 250mcg bd.

The dose for dose steroid comparison chosen for this trial was alleged to be unfair and likely to have significantly influenced the efficacy results. In order to fairly compare two different treatment approaches for asthma using either a fixed or an adjustable dosing regime one would need to have compared a more equivalent overall dose for dose steroid comparison.

Furthermore, the summaries of product characteristics (SPCs) for Symbicort and Seretide supported a reduction in dosing to 1 puff daily. The CONCEPT study design did not allow well controlled Seretide patients to step down to once daily dosing as recommended in the SPC. Restricting once daily dosing to Symbicort created an unfair dose comparison increasing the probability of a favourable outcome for patients taking twice daily Seretide.

AstraZeneca stated that it had conducted 8 studies, involving over 10,000 patients, using Symbicort as an adjustable dosing regime whereby patients could adjust therapy according to a patient asthma management plan. In all of these trials patients could down titrate their Symbicort dose if well controlled to a minimum dosage of 2 inhalations per day. In those trials comparing adjustable maintenance dosing with fixed dosed Symbicort, adjustable maintenance dosing provided at least as good or superior asthma control compared to fixed

dose Symbicort but at reduced overall medication doses. AstraZeneca noted in particular that the SUND study demonstrated that Symbicort adjustable maintenance dosing was equivalent in terms of achieving the primary endpoint of odds of achieving a well-controlled asthma week compared to fixed dose Seretide and significantly more effective at reducing the clinically important secondary endpoint of severe exacerbations.

AstraZeneca submitted that the previous studies, in contrast to the CONCEPT study, had shown adjustable dosing with Symbicort to be either as or more efficacious than using fixed dose maintenance therapy. This was because the dosing regimes used in the previous studies had been more equivalent.

Finally, recent research indicated that in normal clinical practice only 0.3% of patients were instructed by their health professional to take Symbicort at all strengths 1 puff once daily. Hence the doses of Symbicort used in the CONCEPT study did not reflect UK clinical practice.

AstraZeneca noted that the CONCEPT study design depicted in the leavepiece did not show that the majority of Symbicort patients were down-titrated to one inhalation a day. This was important as the relative doses of corticosteroid used in the maintenance part of the study were a critical determinant in the evaluation of relative efficacy. Hence the statement regarding once daily dosing in small font at the bottom was not sufficiently prominent nor did the page indicate the high percentage of Symbicort patients (82%) who were down-titrated to 1 inhalation daily at some point in the trial. Not including this data was clearly misleading and unfair and did not allow the reader to reach a balanced view.

AstraZeneca alleged that the claim 'Seretide stable dosing achieves superior asthma control compared to formoterol/budesonide symptom led dosing' was all encompassing, exaggerated and misleading and did not reflect fairly the body of clinical evidence. Also the symptom led dosing approach used in the study was not one that was used routinely in clinical practice.

The Panel noted that CONCEPT was a comparative study of two different treatment approaches for asthma – fixed maintenance dosing with Seretide or adjustable maintenance dosing with Symbicort. Patients in the study were previously symptomatic on either 200-500mcg inhaled corticosteroid plus long acting beta$_2$ agonist or >500-1000mcg inhaled corticosteroid alone. Patients were initially stabilized, over four weeks, on Seretide 250 1 puff twice daily (total daily dose (tdd) salmeterol 100mcg/fluticasone 500mcg) or Symbicort 2 puffs twice daily (tdd formoterol 24mcg/budesonide 800mcg twice daily). During this stabilization phase, when both groups received fixed doses, the percentage of symptom-free days was similar between the two treatments. Having been stabilized over 4 weeks, patients in the Symbicort group were instructed to halve their dose to 1 puff twice daily (tdd formoterol 12mcg/budesonide 400mcg). At subsequent clinic visits patients who continued to be controlled could halve the dose again to 1 puff daily (formoterol 6mcg/budesonide 200mcg daily). Such low dosing was not inconsistent with the Symbicort SPC. If after stepping down to this lowest dose patients subsequently lost control of their asthma, as defined by certain criteria, they were instructed to go back to not less than 1 puff twice daily (tdd formoterol 12mcg/budesonide 400mcg) throughout the rest of the 52 week period. The study was not a comparison of steroid dose *per se*.

During the course of the study 83.1% of patients in the Symbicort group stepped down their dose to 1 puff daily at some time and 41.6% increased their dose to 4 puffs twice daily for 7-14 days at least once. Over the 52 week treatment period the mean daily dose of fluticasone (from Seretide two puffs daily) was 463mcg and the mean daily dose of budesonide (from adjustable dosing of Symbicort) was 480mcg. Diary card data showed that Symbicort patients used a mean of 1.8 inhalations daily (equivalent to 360mcg budesonide).

The Panel noted that the leavepiece did not detail the mean daily dose of product or the mean daily number of inhalations. Further the leavepiece gave no details as to how patients, in practice, had adjusted the dose of Symbicort. It was thus difficult for readers to fully understand the clinical significance of the results. The Panel considered that in this regard the leavepiece was misleading. Breaches of the Code were ruled.

The Panel noted AstraZeneca's comments regarding the design of the CONCEPT study, the fact that its results seemed to contradict other studies and that the symptom led dosing approach used was not one that was routinely used in clinical practice. However, other studies had been open-label as opposed to the CONCEPT study which was double-blind. Additionally the CONCEPT study had allowed Symbicort to be dosed at 1 puff daily which, although lower than in other studies, was nonetheless consistent with the Symbicort SPC. In that regard, whilst noting its ruling above, the Panel did not consider that claims such as 'Seretide stable dosing achieves superior asthma control compared to formoterol/budesonide symptom led dosing' regarding the symptom led dosing of Symbicort *per se* were misleading. No breaches of the Code were ruled.

AstraZeneca UK Limited complained about a leavepiece (ref SFL/LVP/05/19527/2-FP/July 2005) issued by Allen & Hanburys Limited, part of GlaxoSmithKline UK Ltd. The leavepiece concerned the CONCEPT (**CON**trol **CE**ntred **P**atient **T**reatment) study which compared stable dosing of GlaxoSmithKline's product Seretide (salmeterol/fluticasone propionate) with symptom led (variable) dosing of AstraZeneca's product Symbicort (formoterol/budesonide).

COMPLAINT

AstraZeneca alleged that the leavepiece did not present a fair and balanced representation of the data in breach of Clauses 7.2 and 7.3 of the Code.

The leavepiece compared two different approaches for asthma control, however:

- it implied that Seretide was compared with clinically equivalent doses of Symbicort as it did not explicitly state that like-for-like steroid doses were not used (82% Symbicort patients were stepped down to the lowest possible dose, compared with all Seretide patients being maintained at 500mcg per day),
- it did not explicitly state that in the Symbicort arm the steroid dose could only be increased in response to symptoms, thus predetermining a higher symptom level in this group,
- it did not reflect the balance of the evidence in that it did not refer to the results of the SUND study (where comparable steroid doses were used, which resulted in significantly fewer exacerbations in the Symbicort arm).

Study design and relative inhaled steroid doses chosen

AstraZeneca explained that the CONCEPT study design, as outlined in the leavepiece, consisted of a 2 week run-in, a 4 week stabilisation phase and a 48 week variable maintenance phase. During the 4 week stabilisation phase patients remained on either Seretide 250mcg bd or Symbicort 200mcg 2 puffs bd which equated to comparing a daily dose of 500mcg fluticasone with 800mcg budesonide (delivered via a turbohaler device) respectively. These doses of the two inhaled corticosteroids were considered to be approximately equivalent. According to its summary of product characteristics (SPC) fluticasone was twice as potent as budesonide. In section 4.2 of the fluticasone SPC under posology and method of administration '100mcg of fluticasone propionate is approximately equivalent to 200mcg dose of beclometasone dipropionate (CFC containing) or budesonide'.

Following the 4 weeks stabilisation phase on approximately equivalent doses patients then entered the variable maintenance phase if they were completely symptom free. During the variable maintenance phase, patients in the Seretide arm remained on fixed Seretide 250mcg 1 inhalation bd. Symbicort patients were able to adjust their therapy according to a predefined treatment plan; they could halve their dose and subsequently step up or down as indicated by the presence or absence of various asthma symptoms and changes in morning peak expiratory flow measurements. If patients in the Symbicort arm were well controlled, they were instructed to further reduce the daily dose to only 1 inhalation once daily in the evening. One inhalation per day of Symbicort dose equated to a total inhaled steroid daily dose of only 200mcg of budesonide when delivered via a turbohaler device. This was important as Seretide patients remained on a fixed Seretide dose that equated to a total inhaled steroid daily dose of 500mcg fluticasone.

According to the published CONCEPT paper, during the variable maintenance phase 82% of Symbicort patients stepped down to 1 inhalation per day at some time during the trial. Only when they developed symptoms were they then instructed to step up the dose again to achieve asthma control. This meant that the majority of patients taking Symbicort were instructed to down titrate to the lowest possible maintenance dose of inhaled steroid and remain on this dose until they developed asthma symptoms. It was therefore not surprising that these patients experienced more asthma symptoms and exacerbations compared to those taking comparatively higher steroid levels of Seretide 250mcg bd.

The dose for dose steroid comparison chosen for this trial was therefore unfair and likely to have significantly influenced the efficacy results for this trial. In order to fairly compare two different treatment approaches for asthma using either a fixed or an adjustable dosing regime one would need to have compared a more equivalent overall dose for dose steroid comparison.

Comparative SPC dosing recommendations

Furthermore, the SPCs for Symbicort and Seretide supported a reduction in dosing to 1 puff daily. The Symbicort SPC stated 'in usual practice when control of symptoms is achieved with the twice daily regimen, titration to the lowest effective dose could include Symbicort Turbohaler given once daily, when in the opinion of the prescriber, a long-acting bronchodilator would be required to maintain control'. Similarly the Seretide SPC stated 'Where the control of symptoms is maintained with the lowest strength of the combination given twice daily then the next step could include a test of inhaled corticosteroid alone. As an alternative, patients requiring a long acting beta-2-agonist could be titrated to Seretide given once daily if, in the opinion of the prescriber, it would be adequate to maintain disease control'.

The CONCEPT study design did not allow well controlled Seretide patients to step down to once daily dosing as recommended in the SPC. Restricting once daily dosing to Symbicort created an unfair dose comparison between the two groups hence increasing the probability of a favourable outcome for patients taking twice daily Seretide.

Contradicts the balance of evidence supporting adjustable maintenance dosing vs fixed dosing

AstraZeneca stated that it had conducted 8 studies involving over 10,000 patients using Symbicort as an adjustable dosing regime whereby patients could adjust therapy according to a patient asthma management plan. In all of these trials patients could down titrate their Symbicort dose if well controlled to a minimum dosage of 2 inhalations per day. In those trials comparing adjustable maintenance dosing with fixed dosed Symbicort, adjustable maintenance dosing provided at least as good or superior asthma control compared to fixed dose Symbicort but at reduced overall medication doses.

Another trial compared adjustable dosing Symbicort with fixed dose Seretide. The AstraZeneca SUND study compared a fairer overall dose for dose inhaled corticosteroid comparison. In the SUND study, patients could adjust their Symbicort 200mcg dose down to a minimum of 2 inhalations per day whilst patients remained on a fixed dose of Seretide 250mcg twice daily. The design of the SUND study attempted

to select a fair dose for dose comparison so that the two different treatment approaches could be fairly evaluated. Symbicort patients could adjust their dose using a defined patient management plan, from 2 to 8 inhalations per day depending on asthma control. An open design was selected for this trial due to the practicable difficulties for patients in using a double-dummy study design for such comparison.

The SUND trial demonstrated that Symbicort adjustable maintenance dosing was equivalent in terms of achieving the primary endpoint of odds of achieving a well-controlled asthma week compared to fixed dose Seretide. However it also demonstrated that adjustable Symbicort was significantly more effective at reducing the clinically important secondary endpoint of severe exacerbations by 40% compared to fixed dose twice daily Seretide. Overall patients in the Symbicort adjustable dosing group used a mean of 544mcg/day of budesonide versus 500mcg/day of fluticasone in the Seretide fixed dosing group during the entire study.

Hence these trials in a large number of patients had shown adjustable dosing with Symbicort to be either as or more efficacious than using fixed dose maintenance therapy either as Symbicort or Seretide. The difference compared to the CONCEPT trial related to the dosing regime selected. In the aforementioned trials a more equivalent inhaled steroid dose for dose comparator between adjustable and fixed dosing was selected.

An independent article (Murphy 2005) outlined the case for improving asthma care for patients by outlining the treatment options and the different treatment approaches. In the section on fixed versus adjustable therapy the author discussed the clinical data to support the respective approaches. The fifth paragraph detailed the CONCEPT study and stated: 'However the results of the study need to be interpreted carefully. This study contradicts the findings of eight other studies investigating adjustable maintenance dosing with the formoterol/budesonide combination. The mean dose of the formoterol/budesonide combination used in this study was 1.8 inhalations per day, with 82% of patients on a maintenance dose as low as one inhalation per day, while patients in the salmeterol/fluticasone arm were maintained throughout on two inhalations per day'.

Finally, recent research indicated that in normal clinical practice only 0.3% of patients were instructed by their health professional to take Symbicort at all strengths 1 puff once daily. (As assessed by AstraZeneca using IMS Disease Analyzer December 2005). Hence the doses chosen by the CONCEPT study for Symbicort did not reflect actual clinical practice in the UK.

In view of the above, AstraZeneca alleged that the CONCEPT study leavepiece was in breach of Clauses 7.2 and 7.3.

1 'A comparison of two treatment approaches for asthma'

Page 1 of the leavepiece described the objectives of the CONCEPT trial with an illustration of the study design. The study design illustrated the different stages and dosing regimes used in the two arms of the trial. However it did not illustrate that the majority of Symbicort patients were down-titrated to one inhalation a day. This was important as the relative doses of corticosteroid used in the maintenance part of the study were a critical determinant in the evaluation of relative efficacy. Hence the statement regarding once daily dosing in small font at the bottom was not sufficiently prominent nor did the page indicate the high percentage of Symbicort patients (82%) who were down-titrated to 1 inhalation daily at some point in the trial. Not including this data was clearly misleading and unfair and did not allow the reader to reach a balanced view and was therefore in breach of Clauses 7.2 and 7.3.

2 'Seretide stable dosing achieves superior asthma control compared to formoterol/ budesonide symptom led dosing'

Pages 2 and 3 of the leavepiece outlined the results from the CONCEPT trial. The nature of the CONCEPT study design, as discussed, meant that these statements were all encompassing, exaggerated and misleading and did not reflect fairly the body of clinical evidence.

Also the symptom led dosing approach used in the study was not one that was used routinely in clinical practice and hence these statements were in breach of Clauses 7.2 and 7.3.

In conclusion, AstraZeneca considered that this promotional use of the CONCEPT study represented a serious breach of the letter and the spirit of the Code and due to the nature of these breaches sought immediate withdrawal of this item and any other promotional items that detailed the CONCEPT results in this manner.

RESPONSE

GlaxoSmithKline stated that the promotion of the CONCEPT study had been the subject of intercompany dialogue without resolution although it had agreed to include comments on the average steroid dose in each arm of the study as part of a conciliatory process to resolve the differences without recourse to the Authority.

As regards the leavepiece itself, GlaxoSmithKline did not agree that it was in breach of the Code for the following reasons:

- It represented an important and clinically relevant study that compared two different approaches for asthma control that were within the SPC recommendations for both products. It compared alternative dosing regimes that could be used for asthmatic patients, but did not imply that Seretide was compared with pharmacologically equivalent doses of Symbicort. GlaxoSmithKline noted that the study addressed a question that was particularly relevant to clinical practice and in that regard was a valid and fair comparison of therapeutic options. The depiction of the study design and the accompanying bullet points stated quite clearly that the objective of the CONCEPT

study was to compare the effect of two different treatment approaches on asthma control, a stable dosing approach and a symptom led dosing approach. This comparison was represented in the diagram with symptom led dosing being shown as a large block accompanied by a statement of the dosing range for Symbicort, and with stable dosing being shown as a single line accompanied by a statement of the consistent dosing for Seretide.

- The leavepiece explicitly stated that in the Symbicort arm the steroid dose could only be increased according to symptoms. This was reinforced in the study design pictorial where the statement concerning symptom led dosing was asterisked to a footnote '1 inhalation bd stepped down to 1 od if controlled and temporarily stepped up to 4 bd for 7-14 days as needed according to symptoms'. As this was a well constructed study in line with the Symbicort SPC and AstraZeneca promotion, GlaxoSmithKline did not agree that this approach predetermined a higher symptom level in this group. It was not known prior to this study whether a stable dosing approach that addressed underlying inflammation over a longer period of time actually resulted in lower symptoms when compared to a reactive approach that adjusted treatment in response to individual symptoms. If the flexible dosing achieved the aim of controlling underlying inflammation then it was possible that more symptoms would have been recorded in the stable dosing arm of the trial. Clinical trials were conducted to answer such questions.

- AstraZeneca's reference to 82% of patients being stepped down to the lowest licensed dose of Symbicort, reflected the control achieved at higher doses. The value of 82% however was a cumulative value and reflected the number of patients who received the lowest dose at any time during the study. It was not a true reflection of overall levels of Symbicort use throughout the study.

- The leavepiece reflected the balance of evidence as it referred to the only randomised controlled trial that had compared the two different treatment approaches which were promoted by the two companies, stable dosing and symptom led dosing. By definition symptom led dosing would lead to variations in dosing within individuals over time, whereas stable dosing would provide longer time consistent dosing. It was unreasonable to expect that pharmacologically comparable steroid doses would be delivered to patients, but this design of study allowed the comparison of clinically relevant therapeutic pathways. It was therefore appropriate to provide evidence for physicians of any differences in the efficacies of these different dosing strategies when used in the clinical setting which might come about because of these different steroid doses received. The SUND study would not provide clinicians with this evidence since it compared pharmacologically equivalent steroid doses with the two products Seretide and Symbicort. The data from SUND provided no evidence on the clinical effect of the Symbicort symptom led adjustable maintenance dosing strategy, widely promoted by AstraZeneca, and might actually provide a misleading picture of the effect of Symbicort as promoted by AstraZeneca since the data represented the effect of a stable dosing strategy. Furthermore as an open-label study which did not reach significance in its primary end-point SUND did not add to the weight of evidence when compared against the robust design of the CONCEPT study, a randomised, double-dummy, placebo-controlled study which reached significance in its primary end-point.

Study design and relative inhaled steroid dose chosen

GlaxoSmithKline acknowledged that the design of the CONCEPT study and specifically the relative doses of inhaled corticosteroid were important issues for the understanding of the CONCEPT results. However AstraZeneca's understanding of the study was fundamentally flawed.

AstraZeneca had correctly noted that during the initial 4 week stabilisation phase patients remained on Seretide 250mcg 1 inhalation bd or Symbicort 200mcg 2 inhalation bd, an approximately equivalent dose of steroid, and during the variable maintenance phase of the trial patients in the Seretide arm remained fixed on Seretide 250mcg 1 inhalation bd whereas patients in the Symbicort arm were instructed to adjust their therapy according to symptoms.

However, Symbicort patients adjusted their dose according to a pre-defined treatment plan and stepped up or stepped down treatment according to the presence or absence of symptoms in accordance with the Symbicort SPC. Furthermore, the step up and step down criteria defined in the patient action plan accurately reflected guidance that had been provided by AstraZeneca to physicians for the use of Symbicort in their symptom led adjustable maintenance dosing strategy and product monograph:

- the AstraZeneca 'dose wheel' physicians' leavepiece clearly showed that a dose of 1 inhalation once daily had been recommended by AstraZeneca. In addition the step down and step up criteria on the dose wheel showed that the criteria set in the CONCEPT trial for step up and step down of Symbicort treatment were almost identical:
  - Step down in the AstraZeneca dose wheel was indicated when patients on 2 consecutive days needed no more than 1 puff of reliever medicine and had no night-time awakenings, and in the CONCEPT trial was indicated when patients had 2 consecutive days with no rescue medication use, no night-time awakenings and morning PEF at least 85% of baseline
  - Step up in the AstraZeneca dose wheel was indicated when patients on 2 consecutive days used more reliever than normal or had night-time awakenings, and in the CONCEPT trial was indicated when patients had 2 consecutive days with rescue medication used 3 or more times per day or night-time awakenings or morning PEF less than 85% of baseline

- the AstraZeneca product monograph from 2001 clearly showed the use of a dose of 2 inhalations twice a day initially to control symptoms and then reduction to 1 inhalation twice a day when symptom control had been achieved with subsequent step-up to 4 inhalations twice a day and step down to 1 inhalation twice a day according to symptoms and the possible reduction to 1 inhalation once a day if symptoms were sufficiently well controlled. This product monograph formed the basis for the dosage adopted for Symbicort in the CONCEPT trial and corresponded exactly to the dosage regime recommended by AstraZeneca for patients at the time the CONCEPT study was initiated.

AstraZeneca also stated that 'the majority of patients were instructed to down titrate to the lowest possible maintenance dose of inhaled steroid and remain on this dose until they developed symptoms'. This suggested that there was active involvement by investigators to push patients down to lower doses of Symbicort. This was not the case as patients followed a pre-defined action plan based on AstraZeneca's own materials, where adjustments in dose were made according to symptoms, reflecting the real clinical situation for patients if they were following the symptom led adjustable maintenance dosing strategy endorsed and promoted by AstraZeneca for Symbicort. The percentage of patients who stepped down to the lowest dose simply reflected the degree of control they and their supervising physicians (since a patient could not step down without the endorsement of an investigator) felt had been achieved using Symbicort in a symptom led adjustable maintenance dosing approach using step up and step down criteria in accordance with those recommended by AstraZeneca.

GlaxoSmithKline also noted that AstraZeneca had stated that in the CONCEPT study the dose for dose steroid comparison was unfair. As stated above, it was not the objective of this trial to compare like-for-like doses of the two steroids. The objective was to compare two treatment approaches, stable dosing versus symptom led dosing, the latter of which, by its very definition, would result in variable amounts of treatment being received. Consequently, no steroid dose was 'chosen' for this study, rather the steroid dose received in the Symbicort arm was a **result** of the trial, and indicated what might occur in patients in the clinical setting if the symptom led adjustable maintenance dosing approach was used. It was appropriate to undertake this trial as the symptom led adjustable maintenance dosing approach was the treatment strategy endorsed and promoted by AstraZeneca for Symbicort, and clinicians should know about the clinical outcome of using Symbicort in this way to help guide them as to the selection of the appropriate dosing strategy for their patients.

Comparative SPC dosing recommendations

GlaxoSmithKline noted that AstraZeneca had correctly pointed out the respective SPC dosing recommendations of both Symbicort and Seretide, and the fact that the CONCEPT study did not allow well controlled Seretide patients to step down to once daily dosing, an option included in the Seretide SPC.

However, the design of the CONCEPT study did not require Seretide patients to step down to once daily dosing as this was **not** part of the treatment approach that GlaxoSmithKline had adopted for the use of Seretide. The treatment strategy for Seretide, based on the GOAL study, and investigated in the CONCEPT study was fixed stable dosing with Seretide for a prolonged period to control underlying inflammation, not symptom led adjustable dosing. It was known that control of underlying inflammation required long term treatment, possibly for as long as a year in the context of bronchial hyper-responsiveness (Woolcock 2001), and the GlaxoSmithKline treatment strategy was based on addressing this underlying problem. Therefore it was appropriate that Seretide treatment was not stepped down during the year-long period of the trial since within this time frame GlaxoSmithKline considered that patients would not have gained control of their underlying inflammation and therefore symptoms. The evidence clearly showed that long-term treatment was needed to control symptoms such as bronchial hyper-responsiveness. Consequently, it would only be after the period of this trial that patients would have gained control of all their symptoms and therefore be appropriate for consideration of step down of their treatment as suggested in the SPC.

In contrast, the treatment approach for Symbicort, as promoted and endorsed by AstraZeneca, required adjustment of treatment by patients in the short-term in response to more obvious symptoms such as coughing, wheezing and peak flow. It was known that control of these symptoms could be gained much more quickly than other less obvious symptoms such as bronchial hyper-responsiveness (Woolcock), therefore it was appropriate that short-term treatment changes were made for Symbicort as recommended in its SPC and in accordance with the promotional guidance provided by AstraZeneca.

The Code required promotion to be within the SPC, but did not require that promotion followed the entirety of the SPC. It was therefore not misleading to promote a study which investigated some, but not all of the individual aspects of the SPC indication and dosing statements. It would be unrealistic to expect every study to reflect every aspect of the SPC. The leavepiece clearly detailed the study design and the dosages of Seretide and Symbicort that were used as well as what dose adjustments were made. All of these doses were consistent with the SPCs for the two products and the different treatment regimens were clearly set out for the reader.

Contradicts the balance of evidence supporting adjustable maintenance dosing vs fixed dosing

GlaxoSmithKline acknowledged that AstraZeneca had conducted studies involving over 10,000 patients in 8 trials using Symbicort in a symptom led adjustable maintenance dosing regime, and in these trials patients were able to step down to a minimum dosage of 2 inhalations twice a day. However, to compare non comparative studies with different designs might be misleading, and although AstraZeneca studies had shown this, this minimum dosing recommendation was not in accordance with the Symbicort SPC and

AstraZeneca's own dosing recommendations which included a dose of 1 inhalation once a day. Furthermore all of these trials used an open-label design which, in contrast to the extremely robust randomised, double-blind, double-dummy controlled design of the CONCEPT study, were known to be open to potential bias from investigators and patients, and were of a much shorter duration than the CONCEPT trial. (In contrast to the CONCEPT trial which lasted 52 weeks, the AstraZeneca trials included four trials of 3 months, one of 4 months and three which lasted 6 months.) Consequently, it was appropriate that the CONCEPT study was considered as the only robustly designed long-term trial which provided level 1 evidence of the comparison between fixed dosing and symptom led adjustable maintenance dosing, and included the appropriate minimum dosage as recommended by AstraZeneca in its promotional materials.

GlaxoSmithKline noted that NICE and other such review bodies only considered level 1 (randomised study) evidence. GlaxoSmithKline's position with this leavepiece was thus consistent with well accepted principles.

GlaxoSmithKline disagreed with AstraZeneca's statement that the SUND study provided a comparison of a 'fairer' overall dose of inhaled corticosteroid; in the SUND study the minimum inhaled dose of Symbicort was 2 inhalations per day, not 1 as in CONCEPT, and this did not reflect the treatment recommendations for physicians which clearly included a dose of 1 inhalation once a day. Furthermore, once again AstraZeneca had not considered that SUND was a 6 month open-label study open to potential bias from investigators and patients, that failed to achieve its primary end point. AstraZeneca had defended this design due to the 'practicable difficulties for patients in using a double-dummy study design' for such a trial. However, the CONCEPT study demonstrated that these problems could be overcome and a much more robust randomised, double-blind, double-dummy controlled trial could be performed in asthmatic patients to more appropriately determine the effects of two different treatment approaches. GlaxoSmithKline did not agree that SUND demonstrated that Symbicort adjustable maintenance dosing was equivalent in terms of achieving the primary end-point of odds of achieving a well-controlled asthma week when compared to fixed dose Seretide as this study was not designed as an equivalence study. The design of the SUND study, and numbers of patients involved, clearly indicated that it was set up as a superiority study to investigate whether Symbicort was better than Seretide at achieving a well-controlled asthma week. In not achieving any significant difference in its primary end-point SUND only showed that Symbicort was not superior to Seretide in achieving a well-controlled asthma week. However, equivalence could not be inferred from this result and AstraZeneca was wrong to suggest that it could.

Consequently, GlaxoSmithKline did not agree that these trials showed adjustable maintenance dosing to be more efficacious than fixed dose therapy. The difference between these was not an issue of 'appropriate comparison doses' more an issue of study design, since the evidence from open-label short-term trials could not be compared with evidence from randomised, double-blind, double-dummy, controlled trials looking at long-term outcomes.

GlaxoSmithKline stated that it was inappropriate for it to comment on the article by Murphy other than to say that the other studies referred to in the article had also been raised by AstraZeneca in its complaint. GlaxoSmithKline's response to this was detailed above.

AstraZeneca had also quoted recent prescribing data to indicate that in normal clinical practice only a small minority of patients were instructed by their health professional to take Symbicort 1 inhalation once daily. GlaxoSmithKline failed to see the relevance of this point in a complaint about a well designed clinical study that robustly examined the two companies' treatment approaches and would inform clinical practice to a much greater extent than prescribing data.

It was not the objective of the CONCEPT study, as already stated, to compare clinical practice but to compare the two treatment approaches recommended by the two companies in a randomised, double-dummy, double-blind, controlled trial looking at long-term clinical outcomes. CONCEPT was the only trial that offered robust evidence for clinicians of the comparison between fixed dosing and symptom led dosing strategies.

Specific points

GlaxoSmithKline did not believe that the CONCEPT leavepiece was misleading or that it presented an inaccurate, unfair or unbalanced representation of the available evidence, since CONCEPT was designed to compare two treatment approaches, not pharmacologically comparable steroid dosing; it was the only long-term robustly designed clinical trial investigating this question. Furthermore, CONCEPT used dosing strategies for Seretide and Symbicort as recommended for health professionals in promotional materials.

1 'A comparison of two treatment approaches for asthma'

The study design in the leavepiece illustrated the different stages and dosing regimes used in the trial appropriately. However, it did not show that 82% of patients were stepped down to 1 inhalation once a day. GlaxoSmithKline believed that this piece of information was in itself misleading since 82% of patients were actually stepped down to 1 inhalation once a day at some point during the trial. What the figure of 82% did not convey was how long patients actually spent at this dosage level, and that if patients stepped down to 1 inhalation once a day but then subsequently had an increase in symptoms or an exacerbation such that they had to step up their treatment they were not allowed to step back down to a dose of 1 inhalation once a day at any further point during the trial. Consequently, GlaxoSmithKline did not consider that including the percentage of patients in the Symbicort arm that stepped down to 1

inhalation once a day would be helpful as it raised more questions than it answered and in itself could actually mislead health professionals into thinking that patients stepped down and remained at that dose.

The page complained about by AstraZeneca fully and faithfully represented the design of the study and reflected the ability of patients to down titrate to doses compatible with the Symbicort SPC and in line with AstraZeneca's promotional strategy. As such GlaxoSmithKline refuted any breach of Clauses 7.2 or 7.3.

2 'Seretide stable dosing achieves superior asthma control compared to formoterol/ budesonide symptom led dosing'

GlaxoSmithKline considered that this claim was an accurate, fair and objective summary of all the available evidence and was not exaggerated or misleading since all the conflicting evidence for the efficacy of Symbicort had been gained from short-term open-label trials that were open to considerable bias and did not provide sufficient weight of evidence to challenge the data gained from a long-term robustly designed randomised, double-blind, double-dummy, controlled trial such as CONCEPT.

CONCEPT was the only study that examined the two different dosing strategies of the individual products as promoted by the individual companies. The design of CONCEPT was such as to investigate the effects of two different treatment approaches, not pharmacologically comparable steroid dosing, which would provide evidence to health professionals of the clinical outcomes that would be seen in patients for each of these treatment strategies. By its very nature, symptom led adjustable maintenance dosing resulted in variable dosing in individual patients and the corticosteroid dosage received by patients in this arm of the trial was actually a result of this treatment approach not a pre-determined factor defined in the protocol. The data from CONCEPT were extremely important for health professionals such that they provided further knowledge of the clinical efficacy of a fixed dosing approach compared with an adjustable dosing approach as recommended by AstraZeneca.

AstraZeneca's assertion that the details of the dosages used for symptom led adjustable maintenance dosing in current clinical practice did not reflect entirely those used in the CONCEPT trial were surprising since the dosage regime used in CONCEPT was based on that recommended by AstraZeneca itself.

In conclusion, GlaxoSmithKline did not consider that the promotional use of the CONCEPT study represented any breach of the Code.

PANEL RULING

The Panel noted that CONCEPT was a comparative study of two different treatment approaches for asthma – fixed maintenance dosing with Seretide or adjustable maintenance dosing with Symbicort. Patients in the study were previously symptomatic on either 200-500mcg inhaled corticosteroid plus long acting $beta_2$ agonist or >500-1000mcg inhaled corticosteroid alone. Patients were initially stabilized, over four weeks, on Seretide 250 1 puff twice daily (total daily dose (tdd) salmeterol 100mcg/fluticasone 500mcg) or Symbicort 2 puffs twice daily (tdd formeterol 24mcg/budesonide 800mcg twice daily). During this stabilization phase, when both groups received fixed doses, the percentage of symptom-free days was similar between the two treatments. Having been stabilized over 4 weeks, patients in the Symbicort group were instructed to halve their dose to 1 puff twice daily (tdd formoterol 12mcg/budesonide 400mcg). At subsequent clinic visits patients who continued to be controlled could halve the dose again to 1 puff daily (formoterol 6mcg/budesonide 200mcg daily). Such low dosing was not inconsistent with the Symbicort SPC. If after stepping down to this lowest dose patients subsequently lost control of their asthma, as defined by certain criteria, they were instructed to go back to not less than 1 puff twice daily (tdd formoterol 12mcg/budesonide 400mcg) throughout the rest of the 52 week period. The study was not a comparison of steroid dose *per se*.

During the course of the study 83.1% of patients in the Symbicort group stepped down their dose to 1 puff daily at some time and 41.6% increased their dose to 4 puffs twice daily for 7-14 days at least once. Over the 52 week treatment period the mean daily dose of fluticasone (from Seretide two puffs daily) was 463mcg and the mean daily dose of budesonide (from adjustable dosing of Symbicort) was 480mcg. Diary card data showed that Symbicort patients used a mean of 1.8 inhalations daily (equivalent to 360mcg budesonide).

The Panel noted that the leavepiece did not detail the mean daily dose of product or the mean daily number of inhalations. Further the leavepiece gave no details as to how patients, in practice, had adjusted the dose of Symbicort. It was thus difficult for readers to fully understand the clinical significance of the results. The Panel considered that in this regard the leavepiece was misleading. Breaches of Clauses 7.2 and 7.3 were ruled.

The Panel noted AstraZeneca's comments regarding the design of the CONCEPT study, the fact that its results seemed to contradict other studies and that the symptom led dosing approach used was not one that was routinely used in clinical practice. However, other studies had been open-label as opposed to the CONCEPT study which was double-blind. Additionally the CONCEPT study had allowed Symbicort to be dosed at 1 puff daily which, although lower than in other studies, was nonetheless consistent with the Symbicort SPC. In that regard, whilst noting its ruling above, the Panel did not consider that claims such as 'Seretide stable dosing achieves superior asthma control compared to formoterol/budesonide symptom led dosing' regarding the symptom led dosing of Symbicort *per se* were misleading. No breach of Clauses 7.2 and 7.3 was ruled.

Complaint received **8 May 2006**

Case completed **25 July 2006**

CASE AUTH/1841/5/06

TAKEDA v DAIICHI-SANKYO

Promotion of Olmetec

Takeda complained that a comparison of its product Amias (candesartan) with Olmetec (olmesartan) by Daiichi-Sankyo was unfair. The comparison was based upon Brunner *et al* 2003 which had compared olmesartan 20mg with candesartan 8mg in patients with hypertension. Both medicines currently had three doses within their usual dosing regimen for hypertension; patients were titrated according to response. Patients started on candesartan 8mg or olmesartan 10mg and would remain (be maintained) on those doses unless their blood pressure was not adequately controlled, at which time the dose of either might be doubled. If additional blood pressure reduction was required then the doses might be doubled again to candesartan 32mg or olmesartan 40mg. Brunner *et al* had compared the 'usual maintenance dose' of candesartan with the 'optimal' dose of olmesartan which was misleading. When the study was designed the starting dose for candesartan was only 4mg; the authors' statement that the approved dose range for candesartan was 4, 8 and 16mg was out of date and inconsistent with the current summary of product characteristics (SPC) for Amias.

Takeda considered that the most appropriate comparison of the two products was candesartan 16mg vs olmesartan 20mg. Supporting data was provided including a meta-analysis of the dose response data for candesartan which showed that the 'optimal' dose for lowering blood pressure was 16mg and that the incremental benefit of moving from candesartan 8mg (starting and usual maintenance dose) to the optimal dose of 16mg was 2/2mmHg (Elmfeldt *et al*, 1997). A meta-analysis of the dose response data for olmesartan (Püchler *et al*, 2001) showed that the incremental benefit achieved by moving from the starting dose of 10mg to the 'optimal' dose of 20mg was 2.42/1.77mmHg. Takeda noted that in the US, the starting dose for olmesartan was 20mg (maximum dose of 40mg) and the starting dose for candesartan was 16mg (maximum dose of 32mg). This further supported Takeda's stance that the most appropriate comparison would be between olmesartan 20mg and candesartan 16mg.

Takeda complained about a leavepiece and a journal advertisement which featured the allegedly unfair comparison. Takeda also complained about the promotional use of reprints of Brunner *et al*.

The Panel noted that Brunner *et al* stated that for candesartan, the approved dosage range was 4mg once daily as the starting dose, 8mg once daily as the usual maintenance dose and 16mg once daily as the maximum dose. This information was outdated. Since the paper was written the dose of Amias in hypertension had been revised upwards. The recommended initial dose and usual maintenance dose was now 8mg once daily which could be increased to 16mg once daily and thereafter further increased to a maximum of 32mg once daily if necessary. The SPC stated that the average additional effect of a dose increase from 16mg to 32mg once daily was small but that due to inter-individual variability a more than average effect could be expected in some patients.

The Olmetec SPC stated that the recommended starting dose was 10mg once daily. In patients inadequately controlled this dose could be increased to the optimal dose of 20mg. If patients remained inadequately controlled the dose could be increased to a maximum of 40mg daily. It was thus clear from the SPC that some patients would be controlled on Olmetec 10mg although the Panel had no way of knowing what percentage that might be.

The Panel considered that it was unfortunate that the Amias SPC and the Olmetec SPC used different terms to describe various doses. The Panel did not accept that 'optimal dose' and 'usual maintenance dose' necessarily meant one and the same thing as submitted by Daiichi-Sankyo.

The Panel noted that although Brunner *et al* had originally compared the midpoint doses of both candesartan and olmesartan, due to the upward revision in the candesartan dosing it now meant that the lowest dose of candesartan had been compared with the middle dose of Olmetec.

The leavepiece included a bar chart depicting the mean change in daytime blood pressure following once daily treatment with Olmetec 20mg and candesartan 8mg. The bar chart, however, did not state that the dose for Olmetec was the optimal dose whilst the candesartan dose was the starting and usual maintenance dose. It was thus difficult for readers to fully understand the clinical significance of the results. The Panel considered that in this regard the comparison in the leavepiece was misleading. Breaches of the Code were ruled. This ruling was appealed.

The advertisement featured the claim 'Olmetec 20mg delivers more potent BP reduction than… candesartan 8mg'. A footnote stated that the medicines had been compared at their usual maintenance dose. This was not so. The dose for Olmetec was the optimal dose and the candesartan dose was the starting dose and usual maintenance dose. The Panel noted its comments above regarding the leavepiece. Further breaches of the Code were ruled. This ruling was appealed.

The Panel noted that the promotional use of an unsolicited reprint of an article about a medicine constituted promotion of that medicine and all relevant requirements of the Code must be observed. Brunner *et al* contained out of date information regarding the dose of candesartan. Unsolicited use of that paper was therefore misleading with regard to candesartan. Breaches of the Code were ruled. This ruling was accepted by Daiichi-Sankyo.

Upon appeal by Daiichi-Sankyo, the Appeal Board noted the bar chart in the leavepiece which compared the response to Olmetec 20mg and candesartan 8mg did not state that the Olmetec dose was the optimal dose which according to the SPC was only for those patients not adequately

controlled at the recommended starting dose of 10mg, whilst the candesartan dose was the recommended starting and usual maintenance dose. It was thus difficult for readers to fully understand the clinical significance of the results. The Appeal Board considered that in this regard the comparison was misleading. The Appeal Board upheld the Panel's rulings of breaches of the Code.

The advertisement featured the claim 'Olmetec 20mg delivers more potent BP reduction than… candesartan 8mg'. A footnote stated that the medicines had been compared at their usual maintenance dose. The Appeal Board noted the dose for Olmetec was the optimal dose and the candesartan dose was the starting dose and usual maintenance dose. The Appeal Board considered that in practice such doses would be considered comparable. In this particular instance the Appeal Board considered that the basis of the comparison was clear. The Appeal Board ruled no breach of the Code.

Takeda UK Limited complained about the promotion of Olmetec (olmesartan) by Sankyo Pharma UK Ltd (now Daiichi-Sankyo). The items at issue were a leavepiece (ref OLM 212.1), a journal advertisement (ref OLM359) and the promotional use of a reprint of Brunner *et al* (2003) by representatives. Takeda supplied Amias (candesartan).

COMPLAINT

Takeda considered that a study comparing olmesartan 20mg with candesartan 8mg in patients with hypertension (Brunner *et al*, 2003), was an unfair comparison of the two products. Takeda alleged that use of data from this study in promotional materials was in breach of Clauses 7.2 and 7.3 because:

- Candesartan and olmesartan currently had three doses within their usual dosing regimen for hypertension; patients moved through the dose range for both according to blood pressure response.
  - o patients started on candesartan 8mg or olmesartan 10mg.
  - o patients would remain (be maintained) on candesartan 8mg or olmesartan 10mg unless their blood pressure was not adequately controlled, at which time the dose might be increased to candesartan 16mg or olmesartan 20mg.
  - o if additional blood pressure reduction was required then the dose might be increased to candesartan 32mg or olmesartan 40mg.
- The 'usual maintenance dose' of candesartan had been compared with the 'optimal' dose of olmesartan. Takeda alleged that this comparison was misleading.
- Brunner *et al* was designed prior to the starting dose for candesartan increasing from 4mg to 8mg. The publication stated that the approved dose range for candesartan was 4, 8 and 16mg which was now out of date and inconsistent with the current summary of product characteristics (SPC) for Amias.
- During intercompany discussions, and also in a previous case (Case AUTH/1523/10/03), Daiichi-Sankyo had stated its belief that the word 'optimal' (relating to the 20mg dose of olmesartan) was interchangeable with and had the same meaning as 'maintenance'. Takeda disagreed and could not find any evidence to support Daiichi-Sankyo's assumption. The meaning/definition of optimal in the Oxford dictionary was 'best or most favourable'; 'most conducive to a favourable outcome', whereas 'maintenance' was to 'preserve' or 'keep up'.

Takeda considered that the most appropriate comparison of the two products was candesartan 16mg vs olmesartan 20mg.

- A published meta-analysis of the dose response data for candesartan showed that the 'optimal' dose for lowering blood pressure was 16mg and that the incremental benefit of moving from candesartan 8mg (starting and usual maintenance dose) to the optimal dose of 16mg was 2/2mmHg (Elmfeldt *et al*, 1997). Further titration from 16mg to the maximum dose of 32mg might provide additional benefit in some patients (Section 5.1 (Hypertension) Amias SPC).
- A published meta-analysis of the dose response data for olmesartan (Püchler *et al*, 2001) showed that the incremental benefit achieved by moving from the starting dose of 10mg to the 'optimal' dose of 20mg was 2.42/1.77mmHg.
- Takeda noted that in the US, the starting dose for olmesartan was 20mg (maximum dose of 40mg) and the starting dose for candesartan was 16mg (maximum dose of 32mg). This further supported Takeda's stance that the most appropriate comparison would be between olmesartan 20mg and candesartan 16mg. The US dosing schedule had previously been used by Daiichi-Sankyo to support its case regarding the head-to-head comparison with losartan, valsartan and irbesartan (Case AUTH/1523/10/03).

Associated with the above, Takeda believed that the use of the Brunner *et al* as a promotional item (eg reprints provided by sales representatives) was also in breach of Clauses 7.2 and 7.3. In the discussion section of the paper, it clearly stated that the approved dosage range for candesartan was 4mg once daily as the starting dose, 8mg once daily as the usual maintenance dose and 16mg once daily as the maximum dose. This information was inaccurate, misleading and not consistent with the Amias SPC for candesartan in the UK.

Since Takeda's intercompany discussions with Daiichi-Sankyo the journal advertisement had been published. This also contained the comparison at issue above in the claim 'Olmetec potency puts you in control. Olmetec 20mg delivers more potent BP reduction than losartan 50mg, valsartan 80mg, irbesartan 150mg and candesartan 8mg. That's the power you could prescribe'.

Takeda maintained that promotion using data from Brunner *et al* was inaccurate, misleading and not consistent with the SPC. These claims were in breach

of Clauses 7.2 and 7.3 and hence these items (and any others that included this data) should be withdrawn from use.

RESPONSE

Daiichi-Sankyo firmly believed that Brunner *et al* was a fair and just comparison of the recognised maintenance doses of olmesartan (20mg) and candesartan (8mg) in the UK. The company therefore denied that the use of this data was in breach of Clauses 7.2 and 7.3.

Brunner *et al* was carried out in 2002 across 44 European centres and involved 643 patients. The study was conducted before Olmetec was launched in Europe and formed part of the regulatory submission. When the study was conducted the recognised doses of candesartan and the proposed dosing schedule of olmesartan for Europe were:

	candesartan	*olmesartan*
Renal or hepatic impairment	2mg (severe renal or mild to moderate hepatic or renal/ hepatic impairment in the elderly)	No initial dose adjustment (maximum dose 20mg in elderly or mild to moderate renal impairment. CI in hepatic impairment)
Start	4mg	10mg
Maintenance	**8mg**	**20mg**
Maximum	16mg	40mg

In effect four dose titrations (2mg, 4mg, 8mg and 16mg) existed for candesartan and three dose titrations (10mg, 20mg and 40mg) were proposed for olmesartan.

In March 2002 Olmetec was first approved in the EU in Germany via the Mutual Recognition Procedure with the three dose titration schedule ie 10mg as the start dose, 20mg as the maintenance dose and 40mg as the maximum dose. Market authorization in the UK was issued in May 2003. The SPC described the 20mg maintenance dose of olmesartan as 'optimal'. As far as Daiichi-Sankyo was aware this term only appeared in the Olmetec SPC and not in the SPCs for other medicines in the same pharmacological class.

The dosing schedule for olmesartan had thus remained since launch as outlined above as 10, 20 and 40mg.

Following its EU launch in March 2002, and as part of the European promotional strategy for Olmetec, Brunner *et al* was used to support a comparison of the recognised maintenance doses for olmesartan (20mg) and for candesartan (8mg).

The data was first made available by Brunner in 2003 and then in the publication that followed later in 2003. More recently it had been made available in Brunner and Arakawa (2006). Hence, the data had been available in the scientific literature for over four years in a number of publications as well as being a secondary reference in other publications.

Daiichi-Sankyo believed that Takeda changed the starting dose of Amias from 4mg to 8mg in March 2003. A further change occurred in September 2004 when a 32mg maximum dose was introduced. However most notably the maintenance dose had remained as 8mg since the launch of the product in 1998.

Candesartan thus currently had five doses within the usual dose regimen whereas olmesartan had three.

	candesartan	*olmesartan*
Hepatic impairment	2mg (mild to moderate hepatic impairment)	(CI in hepatic impairment)
Renal impairment	4mg	No initial dose adjustment (maximum dose 20mg in elderly or mild to moderate renal impairment)
Start	8mg	10mg
Maintenance	**8mg**	**20mg**
Maximum	16-32mg*	40mg

Dosing schedule in 2006

*The SPC for candesartan stated that *'According to a meta-analysis, the average additional effect of a dose increase from 16mg to 32mg once daily was small. Taking into account the inter-individual variability, a more than average effect can be expected in some patients'.*

Daiichi-Sankyo believed that the dose changes that had occurred with candesartan had not changed the validity of the study comparison as the maintenance doses for the two products had remained the same since launch. Currently, it remained fair, accurate and was not misleading and was thus not in breach of Clauses 7.2 and 7.3.

In the arguments presented by Takeda to support the opinion that olmesartan 20mg should be compared with candesartan 8mg it considered two meta-analyses. For candesartan (Elmfedt *et al*) and for olmesartan (Püchler *et al*). Although these might appear similar in design there were some obvious differences which might make such a comparison invalid. The key difference between the two analyses were:

- The olmesartan analysis was twice the size of the candesartan analyses and thus the conclusions from the candesartan analyses were likely to be less robust
- The range of hypertension considered in the two analyses differed and groups were not comparable. Patients in the olmesartan group were more difficult to treat and had more severe hypertension (100-120mmHg) compared to (95-114mmHg) in the candesartan group.
- The studies used in the candesartan analysis lasted 4-12 weeks whereas some studies included in the

olmesartan analyses lasted 52 weeks (minimum 6 weeks). Longer term control was harder to maintain and this would influence the results analysed.

- The candesartan analysis was of a fixed dose nature with a defined group of patients receiving each therapy. The olmesartan analysis included some patients who were titrated to higher doses and thus were counted in more than one group.
- Normalisation rate analyses were not conducted in the candesartan analysis
- Responder rate and normalisation rate were not analysed as primary objective measures in the candesartan analysis

Daiichi-Sankyo did not agree with the scientific credibility of comparing the results of individually conducted analyses for different products with each other, particularly where there were differences in study size, patient type, study length and degree of hypertension being analysed. It was of the opinion therefore that this argument was weak.

In addition the conclusion drawn by Takeda was supported by selectively picking data just to show the incremental benefit of increasing the dose of olmesartan from 10 to 20mg being similar to that of moving from candesartan 8 to 16mg. As a consequence Daiichi-Sankyo believed Takeda's conclusion was flawed since it did not consider the comparative placebo corrected BP response at the specific doses mentioned or across the remainder of the dose profile. If it were scientifically valid to draw conclusions from and compare results of two individually conducted meta-analyses then in Daiichi-Sankyo's view this could only be done by looking at the entire dose range and the placebo corrected responses.

If one considered the placebo corrected diastolic blood pressure (DBP) and systolic blood pressure (SBP) reductions across the dose ranges reported ie 10-40mg olmesartan and 4-16mg candesartan there was very little difference in the comparative BP reductions as reported by Elmfedt *et al* and Püchler *et al*.

The placebo corrected reductions in DBP and SBP for olmesartan 20mg and candesartan 8mg were reported as being the same in both individually conducted analyses. This argument supported a fair maintenance dose comparison at 20mg and 8mg of olmesartan with candesartan.

Takeda stated that up-titrating candesartan from 16mg to 32mg might provide 'some additional benefit'. This was also stated in the SPC. Takeda then suggested that this supported the supposition that by moving from 20mg to 40mg of olmesartan this would be the most appropriate comparison. Daiichi-Sankyo disagreed strongly with this opinion. If one considered the effect of upwards titration from 20mg to 40mg with olmesartan then the 40mg dose was statistically superior in terms of SBP lowering compared to 20mg (p=0.002), removal of the placebo effect provided similarly significant results (p=0.04) in favour of olmesartan 40mg for SBP reduction alone. Furthermore, although the statistical significance was not analysed, the 40mg dose also provided higher SBP normalisation rates (SBP≤130mmHg) 49% vs 45%, and (SBP≤135mmHg) 28% vs 20%.

When one considered DBP the greatest mean decrease from baseline in sitting DBP was observed for patients on the 40mg dose, 15.7mmHg compared with 7.6mmHg for patients on placebo. Again, although the statistical significance was not analysed, the 40mg dose also provided a higher DBP responder rate (DBP≤90mmHg or DBP decrease ≥10mmHg) 81% compared to 70% and higher normalisation rates (DBP≤90mmHg) 62% vs 51%, (DBP≤85mmHg) 31% vs 28%.

It was clear therefore that there was a difference that was both significant and measurable between the olmesartan 20mg and 40mg dose following up-titration. This differed from the small additional benefit seen when titrating up from 16mg candesartan to 32mg.

There was thus no clear scientific rationale in this respect to make a comparison as suggested by Takeda of the 16mg and 32mg doses with 20mg and 40mg of olmesartan.

Further support was gained for this argument by comparing the 80mg dose of olmesartan with candesartan 32mg to look at the indicative response.

If the results were further extrapolated to include doses up to 32mg candesartan (Reif *et al*) then the 80mg dose of olmesartan (not licensed) was similar in response to candesartan 32mg. Clearly this would remain to be evaluated and supported by a head-to-head clinical study but this would indicate the most fair comparison if this approach were to be used.

Daiichi-Sankyo believed that on the balance of evidence it remained fair, accurate and was not misleading to compare olmesartan 20mg with candesartan 8mg and thus the use of this comparison in clinical data was not in breach of Clauses 7.2 and 7.3.

Daiichi-Sankyo acknowledged that the Olmetec SPC did not explicitly specify a maintenance dose of olmesartan and that this differed from other medicines in the same class. Further complexity occurred due to the wording of the SPC which stated that the dose of Olmetec 20mg was the 'optimal' dose.

However Daiichi-Sankyo continued to believe, as it had maintained in its promotional material that since the launch of Olmetec, and as proven in Case AUTH/1523/10/03, the recognised maintenance dose of olmesartan was 20mg. This had been recognised independently by competitors, within the NHS, and in the published scientific literature. Furthermore the WHO ATC Daily Defined Dose (DDD) classification which listed the recognised comparative doses of molecules within a therapy class stated that the usual recognised DDD of candesartan and olmesartan were 8mg and 20mg respectively. This supported the rationale that the comparison of olmesartan 20mg with candesartan 8mg was valid and appropriate and that the recognised maintenance dose of olmesartan was 20mg. Daiichi-Sankyo was not aware of any evidence which suggested that 10mg of olmesartan should be the maintenance dose as stated by Takeda or that the appropriate comparator for olmesartan 20mg should be candesartan 16mg.

Daiichi-Sankyo disagreed with Takeda's assertion that the terms 'optimal' and 'maintenance' were not interchangeable. The optimal effect was the best or most favourable outcome the best outcome must be to 'maintain or preserve' in this instance a patient's blood pressure to the desired level. This would mean avoiding a sub-optimal or supra-optimal response by using too high or too low a dose which could have adverse consequences.

Daiichi-Sankyo also noted that Elmfeldt *et al* used the terminology 'optimal' with reference to candesartan. Within this publication it was stated that 8mg was an optimal dose for candesartan within the usual maintenance dose range of 8-16mg. This further supported the rationale for an interchangeable use of the terminology.

In its correspondence with Takeda, Daiichi-Sankyo maintained the clinical data comparison of candesartan 8mg and olmesartan 20mg was a fair and just comparison and the provision of this reprint was also fair as it supported the efficacy of olmesartan and candesartan at UK maintenance doses. However Daiichi-Sankyo acknowledged that the provision of the reprint with a now out-of-date start dose of 4mg and maximum dose of 16mg for candesartan was potentially misleading; although it did not change the meaning or conclusions of the study as this was a comparison of recognised maintenance doses which had not changed. Daiichi-Sankyo had offered to label the page in question with the correct dose schedule for candesartan on reprints provided by its salesforce. This offer was declined due to the difference in opinion with regards to the validity of the comparison.

Daiichi-Sankyo did not believe that the use of Brunner *et al* to support a maintenance dose comparison was misleading or inaccurate and had tried to ensure consistency with the Amias SPC. As a consequence Daiichi-Sankyo not consider that there was a breach of Clause 7.2 or 7.3 in this regard.

In summary Daiichi-Sankyo submitted that the maintenance dose of olmesartan had remained as 20mg since launch of the product and this was well recognised.

The 8mg maintenance dose of candesartan had remained unchanged since its launch in 1998 and also remained well recognised. However, the candesartan dose schedule had changed at least twice since 1998 and it was now relatively complex with the availability of five possible doses dependent on patient type.

As a consequence Brunner *et al* remained a valid comparison of current recognised maintenance doses in the UK and its use and interpretation remained unaffected by the changes in dose titration scheme for candesartan that had occurred.

Daiichi-Sankyo therefore believed that it was not in breach of Clauses 7.2 and 7.3 as alleged.

PANEL RULING

The Panel noted that Brunner *et al* stated that for candesartan, the approved dosage range was 4mg once daily as the starting dose, 8mg once daily as the usual maintenance dose and 16mg once daily as the maximum dose. This information was out dated. Since the paper was written the dose of Amias in hypertension had been revised upwards. The SPC stated that the recommended initial dose and usual maintenance dose was 8mg once daily. The dose could be increased to 16mg once daily and if blood pressure was not sufficiently controlled after 4 weeks of treatment with 16mg once daily, the dose could be further increased to a maximum of 32mg once daily. The SPC stated that the average additional effect of a dose increase from 16mg to 32mg once daily was small but that due to inter-individual variability a more than average effect could be expected in some patients.

The Olmetec SPC stated that the recommended starting dose was 10mg once daily. In patients where blood pressure was inadequately controlled at this dose, the dose could be increased to the optimal dose of 20mg. If patients remained inadequately controlled the dose could be increased to a maximum of 40mg daily. It was thus clear from the SPC that some patients would be controlled on Olmetec 10mg although the Panel had no way of knowing what percentage that might be.

The Panel considered that it was unfortunate that the Amias SPC and the Olmetec SPC used different terms to describe various doses. The Panel did not accept that 'optimal dose' and 'usual maintenance dose' necessarily meant one and the same thing. In the Panel's view the 'usual maintenance dose' of an antihypertensive was that dose which controlled most people's blood pressure. In the Panel's view the 'optimal dose' of a medicine encompassed consideration of its efficacy vs side effects and was the most favourable balance of the two but what was an optimal dose (and possibly also the usual maintenance dose) in one patient might be a sub-optimal dose in another.

The Panel noted that although Brunner *et al* had originally compared the midpoint doses of both candesartan and olmesartan, due to the upward revision in the candesartan dosing it now meant that the recommended initial dose and usual maintenance (lowest) dose of candesartan had been compared with the optimal (middle) dose of Olmetec.

The leavepiece included a bar chart depicting the mean change in daytime blood pressure following once daily treatment with Olmetec 20mg and candesartan 8mg. The bar chart, however, did not state that the dose for Olmetec was the optimal dose whilst the candesartan dose was the starting and usual maintenance dose. It was thus difficult for readers to fully understand the clinical significance of the results. The Panel considered that in this regard the comparison in the leavepiece was misleading. Breaches of Clauses 7.2 and 7.3 were ruled. This ruling was appealed by Daiichi-Sankyo.

The advertisement featured the claim 'Olmetec 20mg delivers more potent BP reduction than… candesartan 8mg'. A footnote stated that the medicines had been compared at their usual maintenance dose. This was not so. The dose for Olmetec was the optimal dose

and the candesartan dose was the starting dose and usual maintenance dose. The Panel noted its comments above regarding the leavepiece. Further breaches of Clauses 7.2 and 7.3 were ruled. This ruling was appealed by Daiichi-Sankyo.

The Panel noted that the promotional use of an unsolicited reprint of an article about a medicine constituted promotion of that medicine and all relevant requirements of the Code must be observed. Brunner *et al* contained out of date information regarding the dose of candesartan. Unsolicited use of that paper was therefore misleading with regard to candesartan. Breaches of Clauses 7.2 and 7.3 were ruled. This ruling was accepted by Daiichi-Sankyo.

During its consideration of the advertisement the Panel noted that the supplementary information to Clause 7 stated that claims must be capable of standing alone; in general they should not be qualified by the use of footnotes and the like. The Panel requested that Daiichi-Sankyo be reminded of this advice.

APPEAL BY DAIICHI-SANKYO

Daiichi-Sankyo submitted that the bar chart in the leavepiece and claim in the advertisement were valid, stand alone statements. As a result, Daiichi-Sankyo did not accept the Panel's ruling that the claims in these materials were misleading in breach of Clauses 7.2 and 7.3.

Daiichi-Sankyo stated that the leavepiece at issue was no longer in use.

Daiichi-Sankyo submitted that the following points formed the basis of its appeal:

- In Case AUTH/1523/10/03, the Panel held that a comparison of Olmetec 20mg was a fair comparison with the start and maintenance doses of valsartan, losartan and irbesartan (in each case where such start and maintenance doses were identical);
- The maintenance dose of candesartan had remained unchanged at 8mg since its launch in 1997. The entire dosage scheme of Olmetec (including in particular the 20mg recognised 'optimal' dose) had not changed since its launch in 2003. Accordingly the scientific validity of the comparison in Brunner *et al* between the maintenance dose of candesartan (8mg) with the optimal dose of Olmetec (20mg) remained sound;
- It was not appropriate to take a semantic approach to the significance of the wording in SPCs in cases (such as with sartans) where there was inconsistent terminology. Four of the seven sartans did not specifically use the 'maintenance dose' terminology.
- Data on actual use and dosing trends should be taken into account. In this regard over the 36 months since its launch, Olmetec 20mg had become the most used dose of Olmetec in the UK (International Marketing Services (IMS) British Pharmaceutical Index (BPI) to June 2006), indicated by packs sold. The trend was also towards Olmetec 20mg being the most used dose of Olmetec in terms of patients being prescribed any single dose. Furthermore, Olmetec 20mg had a higher persistence on therapy compared to Olmetec 10mg indicating that more patients remained on this dose once they were placed on it (IMS DIN-LINK data to May 2006).
- Well respected and authoritative published data including the WHO and Martindale (34th edition) recognised that Olmetec 20mg was the usual dose or maintenance dose.

Daiichi-Sankyo submitted that the Panel's view that the term 'optimal' was not interchangeable with that of 'maintenance' seemed to contradict its ruling in Case AUTH/1523/10/03 where it was considered fair to compare Olmetec 20mg, as the 'optimal' dose, with the starting and maintenance dose of losartan 50mg, valsartan 80mg and irbesartan 150mg (Oparil *et al*).

Daiichi-Sankyo submitted that in Case AUTH/1523/10/03 the Panel appeared to accept its argument to the effect that the maintenance dose of Olmetec was 20mg and thus the comparison of these doses in the UK as maintenance doses was valid. In particular Daiichi-Sankyo noted the Panel's comment that in relation to the treatment of hypertension the start and maintenance doses of each of the compared sartans considered were one and the same and the Panel did not consider that the claims at issue compared the titration dose [20mg] of Olmetec with the starting doses of losartan, valsartan and irbesartan as alleged. Therefore it must be concluded that the comparison was of recognised maintenance doses. As discussed below there had been no change in the maintenance dose of either Olmetec or candesartan during this period.

Daiichi-Sankyo was extremely concerned that the Panel's ruling was in apparent contradiction of its 2003 ruling which substantially informed the company's use of Brunner *et al* in the promotion of Olmetec since that time. Daiichi-Sankyo's surprise and disappointment was heightened by the fact that Brunner *et al* had been used since the launch of Olmetec (and since the 2003 Panel ruling) without complaint despite the candesartan dosage changes of which the starting and maintenance amalgamation occurred in May 2003.

Daiichi-Sankyo noted that in the previous ruling in favour of Olmetec the middle dose was accepted as being a fair comparison to the lowest dose of the other products using the above rationale. This ruling appeared to show significant inconsistency in the ruling made by the Panel in the current case.

Daiichi-Sankyo noted that the Panel had noted that the dosing of candesartan had been revised upwards. Whilst the maximum dose had increased to 32mg (December 2004) and the start dose to had been revised to 8mg from 4mg (May 2003) the maintenance dose had remained as 8mg since the launch of the product in 1997. Furthermore the Olmetec dose had not changed since its launch with 10mg being the start dose, 20mg the quoted 'optimal' dose and 40mg the maximum dose. Since the maintenance doses in question had not changed during this period for either Olmetec or candesartan, Daiichi-Sankyo considered the comparison of these doses was justified.

Daiichi-Sankyo noted that Takeda had cited the 'Oxford dictionary' definitions of 'maintenance' and 'optimal'. The Panel considered it to be 'unfortunate' that the candesartan SPC and Olmetec SPC used different terms. In the circumstances the Panel considered that it was entitled to 'assume' (without giving any reasoning therefore) that the 'usual maintenance dose' of an antihypertensive was one which controlled most people's blood pressure. It further decided (again without giving any rationale) that the 'optimal dose' was a dose which 'encompassed consideration of its efficacy vs side effects and was the most favourable balance of the two but what was an optimal dose (and possibly also the usual maintenance dose) in one patient might be sub-optimal in another'.

Daiichi-Sankyo noted that only three of the seven marketed sartans had a specifically defined maintenance dose. The SPCs for Micardis (telmisartan), Teveten (eprosartan), Diovan (valsartan), and Olmetec, did not specify a recognised maintenance dose. Instead terminology such as 'usually effective dose' and 'recommended dose' as well as Daiichi-Sankyo's 'optimal dose' was used in relation to other sartans. It was generally accepted that such terms corresponded in the mind of clinicians to the term 'maintenance dose'.

Daiichi-Sankyo further challenged the Panel's 'assumed' definitions for 'usual maintenance dose' and 'optimal dose'. The Panel defined 'usual maintenance dose' 'as the dose which controlled most patients' blood pressure'. Daiichi-Sankyo did not regard either of the terms, 'usually effective dose' (telmisartan) or 'recommended dose' (valsartan, eprosartan) to come within the Panel's definition of the maintenance dose. A 'usually effective dose' was normally defined as that dose which was 'commonly encountered, experienced, or observed providing an expected response'; whilst a recommended dose would be considered the 'approved, favoured or endorsed dose'. Despite this, these doses were widely regarded as the individual maintenance doses of the products in question. In short, if Olmetec 20mg was not to be considered a valid comparator for candesartan 8mg for maintenance purposes on the apparently sole basis that 'optimal' and 'maintenance' were not synonymous then it would seem that telmisartan 40mg, eprosartan 600mg, and valsartan 80mg, would each face similar difficulties.

Daiichi-Sankyo submitted that the Panel's definition of 'optimal dose' of the medicine as one which encompassed consideration of its efficacy vs side effects and was the most favourable balance of the two but what was an optimal dose (and possibly also the usual maintenance dose) in one patient might be sub-optimal in another must also be challenged. It was equally arguable that the dose required as the maintenance dose in one patient might be different to that required in another and thus might similarly be 'sub-optimal'.

Daiichi-Sankyo submitted that with specific reference to the Panel's definition of optimal dose referred to above it noted that in the regulatory process the determination of what was the optimal dose was made with reference to efficacy. With respect to the Panel's view that side effects should form part of the criterion of the definition of optimal, the tolerability of sartans was not dose-related and this had been demonstrated with Olmetec (Smith 2002).

Daiichi-Sankyo agreed with the Panel and with Takeda that the maintenance dose of a product was that dose which controlled most patients' blood pressure, however this could not be determined just by reference to the wording in the SPC (which was divergent) but by reference to actual clinical and use data and by other published data and information as a product's usage became established.

Daiichi-Sankyo submitted that where SPC language was inconsistent (as with sartans), consideration must also be given to actual data during use as indicating a product's most frequent actual maintenance dose. In this regard the period of time a product had been made available, its relative growth and the trend in dosing since launch, as prescribers became familiar with the product, must be considered as indicators.

Daiichi-Sankyo noted that the Panel had stated that some patients would be controlled on Olmetec 10mg but it had no way of knowing what percentage that might be. Daichi-Sankyo thus set out various sets of data which demonstrated that Olmetec 20mg was either the most used dose of Olmetec or was trending quite clearly towards this in the UK; comparable data for candesartan over the same time period since its launch was also provided.

Daiichi-Sankyo submitted that it was evident from the information provided that over the 3 years since its launch, the 20mg dose would now become the most used dose in the UK. In particular Daiichi-Sankyo noted that over the last six months and in particular at the time of the publication of the promotional item in question, the 20mg dose was either the most used, or had achieved equivalent sales levels and when one took into account the volume of new patients, (Olmetec was one of the fastest-growing sartans in the UK market (IMS BPI to June 2006)) this clearly indicated the predominant use of the 20mg dose for maintenance purposes.

Over the same time period in the candesartan life cycle ie 3 years since launch, the 8mg dose did not at any time surpass that of 4mg dose despite the fact that the SPC clearly stated that the 8mg dose was the 'maintenance dose'.

Daiichi-Sankyo recognised that the data related to packs sold and did not directly indicate patients on a specific dose. However there was additional supportive data which reinforced its argument that Olmetec 20mg dose had in effect become the usual maintenance dose. In the 6-month period to June 2006, 46% of patients received Olmetec 20mg, compared with 42% who reeived Olmetec 10mg. The information provided showed the actual number of patients on a particular dose of Olmetec since launch in the UK. Again the trend 3 years into launch indicated a growing percentage of patients on Olmetec 20mg.

Daiichi-Sankyo submitted that although it did not have access to equivalent data for candesartan since launch in 1997 it had data from 2001 onwards, a full

four years into launch. This demonstrated that even though candesartan was stated throughout to have a maintenance dose of 8mg, more patients still received the 4mg as a starting dose than the 8mg dose until 2004, some seven years after launch.

Daiichi-Sankyo submitted that it was of value to consider the persistence rate on treatment (the rate at which patients stayed on any one particular dose). It would be expected that the persistence rate for a maintenance dose would be higher than the persistence for the starting dose, as better control would be evident.

Daiichi-Sankyo submitted that Olmetec 20mg had a higher rate of persistence to therapy than Olmetec 10mg with more patients being maintained on treatment over a 12-month period following initiation on therapy. Reasons for this included the need for upwards titration of dose, lack of efficacy, change of treatment, and non-compliance. This further demonstrated that more patients were maintained on Olmetec 20mg following initiation.

Daiichi-Sankyo submitted that its position that Olmetec 20mg was the maintenance or usual dose of Olmetec was supported by: the World Health Organisation; Martindale; Brunner and Arakawa and promotional material for Micardis and Aprovel.

Finally Daiichi-Sankyo noted that the Panel referred extensively to Elmfedt *et al* and Püchler *et al*. Whilst there was no direct reference to the meta-analyses in question in the Panel's ruling, in the event that it did inform to any extent the Appeal Board's thinking on this matter Daiichi-Sankyo specifically repeated its arguments in response to the complaint in that it was generally accepted that this method of comparing individual meta-analyses conducted independently with differing patient populations was not scientifically valid. Daiichi-Sankyo reiterated points relevant to the appeal from its response to the complaint.

In conclusion Daiichi-Sankyo submitted that on the balance of evidence it was fair, accurate and not misleading to compare Olmetec 20mg with candesartan 8mg and thus the use of this comparison in clinical data was not in breach of Clauses 7.2 and 7.3. In addition, Daiichi-Sankyo was particularly concerned that the Panel's ruling contradicted its 2003 ruling in relation to the dosing of Olmetec. Daiichi-Sankyo understood that the two cases might differ in certain respects but there had been no change to the specific doses in question and it was not unreasonable to expect the Panel to be consistent in its rulings on such matters.

COMMENTS FROM TAKEDA

Takeda noted that the sartans involved in Case AUTH/1523/10/03 (losartan, irbesartan and valsartan) had only two doses within their usual treatment range (excluding special populations where tolerability considerations were of particular importance, such as those with renal or hepatic impairment) unlike olmesartan and candesartan which had three. These other sartans had a single combined starting and maintenance dose and a maximum dose. There was not a third (middle) dose that allowed further titration and optimisation of their maintenance dose. For this reason, the issues involved in the present case, Case AUTH/1841/5/06, were different to those in Case AUTH/1523/10/03 which rendered it invalid as a suitable case precedent.

Takeda noted that when Brunner *et al* was designed and conducted, candesartan had three doses within its usual range for hypertension – 4mg starting dose, 8mg maintenance dose and 16mg maximum dose. In 2003 this changed to two doses with the removal of the 4mg as the starting dose. The change to the dosing schedule of candesartan was completed in December 2004 when the maximum dose was increased to 32mg, thereby shifting the whole dosing schedule upwards. Therefore, the dosing regimen that was applicable when Brunner *et al* was designed in the early 2000s was not appropriate today.

Takeda also noted that the treatment regimens used in Brunner *et al* (8 week duration) were not consistent with recognised and current medical practice or the current SPCs for either olmesartan or candesartan. In line with the UK SPC for candesartan, patients should commence treatment on 8mg and after 4 weeks should have their blood pressure monitored and the dose increased to 16mg if necessary (most of the antihypertensive effect of an individual dose was achieved after 4 weeks). In line with the SPC for olmesartan, patients should commence treatment on 10mg before up titrating to 20mg (the maximal effect was seen after 8 weeks). Patients in Brunner *et al* did not have the option of up-titration to candesartan 16mg after 4 weeks.

Takeda noted that hypertension was a chronic condition and treatment was long-term and usually lifelong. Patients were treated according to their response to a medicine and subsequent reduction in blood pressure. A patient would be titrated on a particular treatment until they achieved their target blood pressure. The dose of a medicine that enabled a patient to achieve target was used to maintain that patient and became their 'maintenance' dose. Patients usually commenced treatment with candesartan 8mg and if sufficient BP lowering was achieved they stayed and were 'maintained' on this dose. Patients whose blood pressure was not sufficiently lowered with 8mg had their dose increased in line with the SPC to 16mg and if sufficient BP reduction was achieved they were maintained on this dose. For some patients, additional benefit might be gained by increasing the dose further to 32mg, or alternatively adding in a different class of antihypertensive in line with NICE recommendations. When the dosing range for candesartan shifted upwards, the 16mg dose changed from being the maximum dose to becoming a 'maintenance' dose and based on the dose response data was clearly the optimal maintenance dose for candesartan.

Takeda stated that it was unfortunate that wording used by regulatory authorities could sometimes be ambiguous and inconsistent. This was particularly so when the inconsistencies occurred within a single class of medicines. What was consistent, however (and not dependent on the nuances of language), was the patient path for each medicine.

Candesartan and olmesartan had three doses within their usual dosing regimen for hypertension; patients moved through the dose range for both according to blood pressure response:

- Patients started on candesartan 8mg or olmesartan 10mg
- Patients remained (maintained) on candesartan 8mg or olmesartan 10mg unless their blood pressure was not adequately controlled, at which time the dose might be increased to candesartan 16mg or olmesartan 20mg. The SPCs for both products clearly stated that the dose was increased only if the patient required additional blood pressure lowering. If the patient's BP was lowered sufficiently on these doses (candesartan 16mg, olmesartan 20mg) then they would remain (be maintained) on these doses.
- If further blood pressure reduction was required then the dose might be increased to the maximum doses of candesartan (32mg) and olmesartan (40mg).

Takeda alleged that based on the dose response meta-analyses previously submitted for each of the products (Elmfeldt *et al* and Püchler *et al*), it was clear that the optimal dose for each product was 16mg (candesartan) and 20mg (olmesartan).

Takeda noted the timing of the licensing of these two medicines. Candesartan was one of the first sartans to be launched in 1997. At this time, the sartans were a new class of medicines with little long-term safety data and therefore, the dosing regimens tended to be on the conservative (low) side. Olmesartan was launched in 2003 (6 years later) when there was significant safety data and greater confidence in the class along with data from several large outcome studies. Takeda (in collaboration with AstraZeneca) had aimed to address this by submitting variations to the regulatory authorities to increase and shift the dosing range of candesartan upwards from that originally approved in 1997.

Takeda noted that data and claims used within promotional material should be based on robust scientific data and not sales data which was not statistically valid and subject to commercial influences.

Takeda alleged that all the usage data presented by Daiichi-Sankyo had to be viewed with consideration of the following potential biases:

- It was not appropriate to compare the launch/uptake dynamics of a product launched into a brand new class and one launched 6 years later when the class had matured and there was more safety data available and confidence in the class (ie 1997 vs 2003).
- The uptake of various strengths of a product would be significantly influenced by many factors including the level of promotion around each strength, pricing and available discount schemes. It should be noted that the promotion for Olmetec in the UK was heavily focussed on the 20mg dose.
- The fact that there was such a difference in dosage use across Europe (vs UK) for olmesartan further supported the influence that outside factors other than scientific data might have.
- It was not clear whether some of Daiichi-Sankyo's data took account of the different pack sizes of 4mg candesartan (available in 7s and 28s). If it did not then it would be biased towards the 4mg strength. The most appropriate unit would be '28 day equivalents'.

Takeda noted that in the data presented by Daiichi-Sankyo, it could clearly see that over time (and consistent with increased confidence and comfort with the sartan class and changes to the dose range of candesartan) the use of the higher strengths of candesartan had increased. This was particularly noticeable for the 16mg dose, which overtook the 4mg strength in 2004 and was clearly catching up with the 8mg dose. Takeda also noted that since May 2004 it had not had a traditional sales force promoting candesartan and this shift in use was therefore not biased by promotional activity. During 2005, Takeda's share of the sartan market was 2.4% (share of calls and share of total promotional spend; IMS MPI Overview, MAT Dec 2005). The equivalent share for Olmetec was: 12.4% and 13.7% for calls and total promotional spend respectively (IMS MPI Overview, MAT Dec 2005).

Takeda alleged that it also appeared that in its response, Daiichi-Sankyo had misinterpreted the data presented which clearly showed that most patients received the 8mg dose of candesartan. This was consistent throughout 2001-2006. It was the 4mg and 16mg strengths that crossed over in 2004 (as discussed above).

Takeda noted as discussed previously, hypertension was a chronic disease and all doses could be 'maintenance' doses. Different patients required different doses to maintain their blood pressure at an acceptable level. Both 8mg and 16mg of candesartan were maintenance doses. Based on its dose response data (Elmfeldt *et al*), Takeda alleged that candesartan 16mg was its optimal maintenance dose (i.e. the most efficacious dose for lowering BP). For olmesartan, both 10mg and 20mg were 'maintenance' doses with the appropriateness of either dose being determined by patient response. Olmesartan 20mg was viewed to be the optimal maintenance dose of olmesartan.

Takeda noted that Daiichi-Sankyo had referred to the World Health Organisation (WHO) daily defined dose (DDD). Takeda noted from the WHO website that the DDD was a unit of measurement and did not necessarily reflect the recommended or prescribed daily dose. The DDD was not designed to necessarily reflect therapeutically equivalent doses and it was acknowledged that the average daily dose might change over time. The DDD was designed solely to maintain a stable system of medicine consumption measurement which could be used to follow trends in utilization of medicines within and across therapeutic groups. The WHO specifically stated that the recommendation of a substance in the ATC/DDD system was not a recommendation for use, nor did it imply any judgements about efficacy or relative efficacy of medicines and groups of medicines. The DDD for candesartan was allocated at the time of

launch within the EU (1997) at which time the starting dose was 4mg, maintenance dose was 8mg and maximum dose was 16mg. WHO requested that any changes to the DDD were kept to a minimum and avoided as far as possible. Too many alterations would always be disadvantageous for long-term studies on medicine utilization.

Takeda considered that the most appropriate comparison would be between candesartan 16mg and olmesartan 20mg (ie their optimal maintenance doses). With the upward shift of the whole dosing range for candesartan since Brunner *et al* was designed and conducted, what might have been a fair comparison then (early 2000s) was no longer appropriate and valid. The appropriateness of candesartan 16mg vs olmesartan 20mg being the most fair and scientifically valid comparison was further supported by the approved dosing in the US where the starting dose of candesartan was 16mg with 32mg as the maximum dose and for olmesartan, 20mg was the starting dose with 40mg being the maximum.

In conclusion, Takeda considered that the comparison of olmesartan 20mg with candesartan 8mg was not fair and was misleading, in breach of Clauses 7.2 and 7.3.

APPEAL BOARD RULING

The Appeal Board examined the case report for the previous case, Case AUTH/1523/10/03, referred to by Daiichi-Sankyo. The Panel's ruling had not been appealed and the complaint was from Novartis not Takeda. The case considered in 2003 was distinguishable in that it had been considered before the change of the starting dose for candesartan from 4mg to 8mg and the introduction of the 32mg dose. These changes were completed in December 2004. Each case under the Code had to be considered on its own particular merits.

The Appeal Board noted the bar chart in the leavepiece depicted the mean change in daytime blood pressure following once daily treatment with Olmetec 20mg and candesartan 8mg. There was no statement, however, as to what these doses were ie that the dose for Olmetec was the optimal dose which according to the SPC was only for those patients not adequately controlled at the recommended starting dose of 10mg, whilst the candesartan dose was the recommended starting and usual maintenance dose. It was thus difficult for readers to fully understand the clinical significance of the results. The Appeal Board considered that in this regard the comparison in the leavepiece was misleading. The Appeal Board upheld the Panel's rulings of breaches of Clauses 7.2 and 7.3. The appeal on this point was unsuccessful.

The advertisement featured the claim 'Olmetec 20mg delivers more potent BP reduction than… candesartan 8mg'. A footnote stated that the medicines had been compared at their usual maintenance dose. The Appeal Board noted the dose for Olmetec was the optimal dose and the candesartan dose was the starting dose and usual maintenance dose. The Appeal Board considered that in practice such doses would be considered comparable. In this particular instance the Appeal Board considered that the basis of the comparison was clear. The Appeal Board ruled no breaches of Clauses 7.2 and 7.3 of the Code. The appeal on this point was successful.

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During its consideration of this case, the Appeal Board noted that the Olmetec SPC stated that the recommended starting dose was 10mg once daily. In patients whose blood pressure was inadequately controlled at this dose, the dose might be increased to the optimal dose of 20mg once daily. Further, according to the SPC, the antihypertensive effect of Olmetec was substantially present within 2 weeks of initiating therapy and maximal by about 8 weeks after initiating therapy which should be borne in mind when considering changing the dose regimen. Thus 20mg was not the optimal dose for all patients, only for those whose blood pressure was inadequately controlled on 10mg. This was not made clear in the materials at issue.

Complaint received **31 May 2006**

Case completed **28 September 2006**

SENIOR COMMUNITY MENTAL HEALTH NURSE/ MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY v JANSSEN-CILAG

Promotion of Risperdal and Risperdal Consta

A senior community mental health nurse complained to the Medicines and Healthcare products Regulatory Agency (MHRA) about a three page mailing for Risperdal (risperidone) sent by Janssen-Cilag. The front cover of the mailing showed a bedroom and two clothed, silhouetted figures: a woman standing in the doorway and man sitting on the bed. Across the top of the front cover a brief profile of the woman read 'Convinced she's a siren, Tricia lures total strangers back from the park and from taxi queues for unprotected sex. To date she's had two terminations and one divorce'. In the middle of the front cover was the caption 'Mania wrecks lives'.

The MHRA considered that whilst the content of the mailing might not be in good taste, its particulars were not in breach of the Advertising Regulations. With the complainant's agreement, the matter was accordingly referred to the Authority for consideration in relation to the Code.

The complainant stated that the mailing had been received by all sixteen members of his multi-disciplinary team. They found the front cover to be extremely stigmatising; not one of them had ever encountered a case as outlined in the mailing.

All received the mailing despite having never provided names/addresses to the company voluntarily. It appeared that in 2005 a Janssen-Cilag representative had asked a secretary for all the names of the team members and this material was then put on a database. The complainant queried if this was ethical.

The team had also been subjected to very heavy marketing of the injectable form of Risperdal (Risperdal Consta) throughout the autumn of 2005 when virtually on a weekly basis a representative would visit and distribute large amounts of office material ie diaries, wrist pads and paper shredders.

The Panel noted that as an example of how mania wrecked lives, the mailing had profiled a fictional patient who exhibited inappropriate sexual behaviour. Janssen-Cilag submitted that such characteristics of mania were commonly encountered in clinical practice. This appeared to be at odds with the complainant's experience. Hirschfeld *et al*, however, showed that increased sexual interest or sexual activity was not uncommon in patients suffering from mania. The Panel thus did not consider that the mailing failed to recognise the special nature of medicines or the professional standing of the audience. The issue highlighted was relevant to the disease area. The mailing had caused some concern to the complainant but the Panel did not consider that it was likely to offend the majority of those who would see it. No breach of the Code was ruled.

With regard to the frequency of visits by sales representatives, the Panel noted that there were two sales forces promoting Risperdal; the schizophrenia team and the bipolar/mania team. The complainant's mental health unit had sixteen health professionals and was the base for a large number of others. There thus appeared to be multiple representatives calling on multiple health professionals. The sales team for Risperdal Consta had held 28 meetings in the unit in the first five months of the year which included nine with nurses. Six meetings were held, including four with nurses, by members of the bipolar/mania sales team. According to Janssen-Cilag's records the complainant had not met any Janssen-Cilag representatives. From the material supplied by Janssen-Cilag it appeared that the Code had been followed. Thus the Panel ruled no breach of the Code.

With regard to the distribution of the mailing the Panel noted that Janssen-Cilag used mailing lists compiled by a third party. This was quite usual in the industry. The Panel considered that the mailing had been sent to people whose need for, or interest in, it could reasonably be assumed. Thus no breach of the Code was ruled.

A senior community mental health nurse complained to the Medicines and Healthcare products Regulatory Agency (MHRA) about a three page mailing (ref 06799b) for Risperdal (risperidone) received from Janssen-Cilag Ltd. The front cover of the mailing showed a bedroom and two clothed, silhouetted figures: a woman standing in the doorway and man sitting on the bed. Across the top of the front cover a brief profile of the woman read 'Convinced she's a siren, Tricia lures total strangers back from the park and from taxi queues for unprotected sex. To date she's had two terminations and one divorce'. In the middle of the front cover was the caption 'Mania wrecks lives'.

The MHRA considered that whilst the content of the mailing might not be in good taste, its particulars were not in breach of the Advertising Regulations. With the complainant's agreement, the matter was accordingly referred to the Authority for consideration in relation to the Code and, in particular, the requirements of Clause 9 relating to suitability and taste.

COMPLAINT

The complainant stated that the mailing had been received by all the members of his multi-disciplinary team. They found the front cover to be extremely stigmatising of the diagnosed mental illness the product was aimed at. They also considered that the mailing had picked a very rare complication of mania and presented it in a way as to suggest an actual case history. Within the team of sixteen mental health professionals, each with between 6 to 25 years'

experience in psychiatric settings, not one had ever encountered a case as outlined in the mailing.

All received the mailing despite having never provided names/addresses to the company voluntarily. It appeared that in 2005 a Janssen-Cilag representative has asked a secretary for all the names of the team members and this material was then put on a database. The complainant queried if this was ethical particularly given the disturbing nature of the mailing.

The team had also been subjected to very heavy marketing of the injectable form of Risperdal (Risperdal Consta) throughout the autumn of 2005 when virtually on a weekly basis a representative would visit and distribute large amounts of office material ie diaries, wrist pads, paper shredders; some offices now resembled a Janssen-Cilag stock depot.

When writing to Janssen-Cilag the Authority asked it to respond in relation to Clauses 9.2, 12.1 and 15.4 of the Code.

RESPONSE

Janssen-Cilag noted that the mailing, which described the benefits of Risperdal in the treatment of mania, was mailed to mental health nurses earlier this year. The imagery and text had been used across various media for two and a half years and had been well received by many health professionals. An analysis of the Hospital Readership Survey 2005/2006 revealed that a 99.99% coverage of senior grade psychiatrists had been achieved during the previous two years, allowing them several opportunities to view this material. This was the first complaint about this material.

Tricia, the fictional character depicted on the front cover, was based on a real patient described to Janssen-Cilag by a community psychiatric nurse, although the details had been changed to ensure patient confidentiality. Janssen-Cilag submitted that the scenario described was a fair and accurate representation of some of the characteristics experienced by patients with mania. Tricia represented a patient who was sexually disinhibited, who was behaving recklessly and was consequently vulnerable and at risk of further harm. Such characteristics of mania were well documented throughout the literature and featured prominently in two of the most widely used sets of diagnostic criteria for psychiatric illness, the International Classification of Disease (ICD 10, World Health Organization) and the Diagnostic and Statistical Manual of Mental Disorder (DSM IV, American Psychiatric Association).

According to the ICD 10, patients in the hypomanic phase of the illness might exhibit a persistent mild elevation of mood, increased energy and activity, and usually marked feeling of well-being, and both physical and mental efficiency. Increased sociability, talkativeness, over-familiarity, increased sexual energy, and a decreased need for sleep were often present but not to the extent that they led to severe disruption of work or resulted in social rejection (ICD 10 Ch 5 F30.0).

Furthermore, in full-blown mania, mood was elevated out of keeping with the patient's circumstances and might vary from carefree joviality to almost uncontrollable excitement. Elation was accompanied by increased energy, resulting in overactivity, pressure of speech, and a decreased need for sleep. Attention could not be sustained and there was often marked distractibility. Self-esteem was often inflated with grandiose ideas and overconfidence. Loss of normal social inhibitions might result in behaviour that was reckless, foolhardy, or inappropriate to the circumstances, and out of character (ICD 10 Ch 5 F30.1).

The DSM IV offered a similar classification of disease, although it was more often used in the US. It identified criteria that needed to be fulfilled for a manic episode. During the period of mood disturbance, three (or more) of the following symptoms had persisted (four if the mood was only irritable) and had been present to a significant degree: inflated self-esteem or grandiosity; decreased need for sleep; more talkative than usual or pressure to keep talking; flight of ideas or subjective experience that thoughts were racing; distractibility; increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation; excessive involvement in pleasurable activities that had a high potential for painful consequences eg engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments.

The mood disturbance was sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalisation to prevent harm to self or others, or there were psychotic features.

In a questionnaire-based study which examined the perceptions and impact of bipolar discorder, the majority of respondents experienced excessive irritability or aggressive behaviour, reckless behaviour, erratic eating, or increased sexual interest or sexual activity (Hirschfeld *et al* 2003). Furthermore during the time that the illness was untreated or improperly treated, the most frequently experienced psychosocial problems were relationship problems (80%), including interpersonal conflicts with family and friends (68%) and marital difficulties (49%). Some of these features were reflected by the mailing.

A study of sexual and reproductive behaviours among people with mental illness found that women with mental illness had more lifetime sexual partners than women in the comparative group representative of the US population matched for age and race. The authors concluded that this finding might reflect the chaotic pattern of sexual relationships and the high rate of non-consensual sex that had been observed among women with mental illness (Dickerson *et al* 2004).

Janssen-Cilag submitted that the evidence cited above supported the fact that the characteristics of mania represented in the mailing were commonly encountered in clinical practice and demonstrated the vulnerability of such patients. It was thus entirely appropriate to highlight these issues to health professionals in marketing materials. On the contrary, rather than stigmatizing patients with mania, the mailing drew much needed attention to the sexual

and relationship problems they sometimes had. Janssen-Cilag did not suggest that this issue affected all patients with mania.

With reference to Clause 9.2 of the Code, Janssen-Cilag was aware of the special nature of medicines, and recognised the professional standing of the target audience for its marketing materials. It did not consider that this mailing undermined or contravened Clause 9.2.

With reference to Clause 12.1, Janssen-Cilag knew that promotional material should only be distributed to those persons whose need for, or interest in, the particular information could be reasonably assumed. The mailing was created for, and distributed to, mental health nurses as they were fundamentally involved in the management of patients with mania. Therefore Janssen-Cilag did not consider that the distribution of the mailing undermined or contravened Clause 12.1.

With regard to the concern about the use of address details on a mailing list, Janssen-Cilag noted that like many other pharmaceutical companies it relied on an agency to supply accurate details about health professionals for its promotional mailings. If someone wanted to be removed from the company's mailing list there were processes in place to allow them to do that.

In response to the complainant's concern regarding the volume of promotional activity seen at his unit by Janssen-Cilag representatives promoting Risperdal Consta, it was of course company policy to ensure strict adherence to the Code. For this reason representatives did not see any health professional more than three times per year on average except in the following circumstances (Clause 15.4 of the Code): attendance at group meetings, including audio-visual presentations and the like; a visit which was requested by a doctor or other prescriber or a call which was made in order to respond to a specific enquiry; a visit to follow up a report of an adverse reaction.

In a unit of sixteen health professionals such as the one in which the complainant worked, this could reasonably be expected to amount to approximately one visit from a representative per week to see different individuals. Records for the first five months of 2006 of one-to-one meetings between health professionals and Janssen-Cilag staff at the unit in question revealed that 28 such meetings were held, including nine with nurses, with members of the Risperdal Consta team (schizophrenia). Six such meetings were also held, including four with nurses, with members of the bipolar/mania team. The unit in question was a large one and was the base for a large number of mental health professionals, far in excess of sixteen. Records revealed the complainant had not had a one-to-one meeting with anyone from Janssen-Cilag in either 2005 or 2006 and therefore had not been inconvenienced directly by legitimate promotional activity. Other health professionals in the unit were happy to see representatives from Janssen-Cilag.

Therefore Janssen-Cilag did not consider that the behaviour of its representatives, or the frequency with which they had visited health professionals at the complainant's unit, undermined or contravened Clause 15.4.

Janssen-Cilag trusted that its response demonstrated that the mailing, rather than being misleading and stigmatizing was a fair representation of one aspect of a patient with bipolar mania, exhibiting some of the important and not uncommon characteristics and vulnerabilities that this patient group might display. Furthermore it considered that the material was relevant and appropriate for the intended audience of health professionals. Janssen-Cilag believed that it had demonstrated that the quantity and frequency of the promotional activity undertaken by its representatives was appropriate and thus it refuted the alleged breaches of the Code.

PANEL RULING

The Panel noted that as an example of how mania wrecked lives, the mailing had profiled a fictional patient who exhibited inappropriate sexual behaviour. Janssen-Cilag submitted that such characteristics of mania were commonly encountered in clinical practice. This appeared to be at odds with the complainant's experience. Data supplied by Janssen-Cilag (Hirschfeld *et al*), however, showed that increased sexual interest or sexual activity was not uncommon in patients suffering from mania. The Panel thus did not consider that the mailing failed to recognise the special nature of medicines or the professional standing of the audience. The issue highlighted was relevant to the disease area. The mailing had caused some concern to the complainant but the Panel did not consider that it was likely to offend the majority of those who would see it. No breach of Clause 9.2 of the Code was ruled.

With regard to the frequency of visits by sales representatives, the Panel noted that there were two sales forces promoting Risperdal; the schizophrenia team and the bipolar/mania team. The complainant's mental health unit had sixteen health professionals and was the base for a large number of others. There thus appeared to be multiple representatives calling on multiple health professionals. The sales team for Risperdal Consta had held 28 meetings in the unit in the first five months of the year which included nine with nurses. Six meetings were held, including four with nurses, by members of the bipolar/mania sales team. According to Janssen-Cilag's records the complainant had not met any Janssen-Cilag representatives.

The limits in the Code referred to frequency of calls by a representative to a doctor or other prescriber. The wishes of individuals on whom representatives wished to call and the arrangements in force at any particular establishment must be observed. The supplementary information to Clause 15.4 of the Code stated that the number of calls made on a doctor or other prescriber by a representative each year should not normally exceed three on average. From the material supplied by Janssen-Cilag it appeared that the supplementary information to the Code had been followed. Thus the Panel ruled no breach of Clause 15.4.

With regard to the distribution of the mailing the Panel noted that Janssen-Cilag used mailing lists compiled by a third party. This was quite usual in the industry. Janssen-Cilag had not commented on the point raised by the complainant regarding a representative asking a secretary for names of team members. Individuals could ask for their names to be removed from lists (Clause 12.3 of the Code). The Panel considered that the mailing had been sent to people whose need for, or interest in, it could reasonably be assumed. Thus no breach of Clause 12.1 of the Code was ruled.

Complaint received **2 June 2006**

Case completed **7 August 2006**

CASE AUTH/1843/6/06

ANONYMOUS v SERONO

Representative call rates

An anonymous complainant complained about call rates for Serono representatives and provided a copy of 'Activity Standards and Definitions', updated 1 January 2006. The call targets were split into four different therapy areas, reproductive health, multiple sclerosis, myalgic encephalomyelitis and dermatology. Details of the call rates which were described as minimum requirements over an average period were provided. The frequency for a cycle from September to December for doctors was three times in one therapeutic area and twice in another. The complainant stated that the document detailed the minimum level of activity expected. The activity levels were per cycle and there were three cycles per year.

The Panel noted Serono's submission that the document provided by the complainant had been altered. Nonetheless both the original document supplied by Serono and that provided by the complainant included for some therapy areas the statement 'For Sept-Dec 04' which thus implied that the stated call frequency, eg 3 calls for some doctors in rheumatology, was for that period of time only, thus resulting in the possibility of 9 calls a year based on 3 cycles per year. Serono submitted that the statement 'For Sept-Dec 04' had been a typographical error; the statement should have read 'As agreed with Manager'. The Panel noted that other supporting documents and the training on the Code had made the requirements of the Code clear with regard to call rates. The 'Activity Standards and Definitions' document, however, had to stand alone. The inclusion of the typographical error had given the wrong impression about call rates. A breach of the Code was ruled.

An anonymous complainant complained about the call rates Serono required of its key account managers (KAMs). A copy of 'Activity Standards and Definitions', updated 1 January 2006, sent with the complaint had a definitions section followed by a section on 'Activity – Target Levels'. The call targets were split into four different therapy areas, reproductive health, multiple sclerosis, myalgic encephalomyelitis and dermatology. The call rates which were described as minimum requirements over an average period were provided. The frequency for a cycle from September to December for doctors was 3 times in one therapeutic area and twice in another. The tables set out daily call rate, daily contact rate, coverage per cycle, frequency per cycle for various target groups in relation to activity with doctors, nurses and others.

COMPLAINT

The complainant stated that the document detailed the minimum level of activity expected of all of Serono's KAMs. The activity levels were per cycle and there were three cycles per year.

When writing to Serono, the Authority asked it to respond in relation to Clause 15.4 of the Code.

RESPONSE

Serono stated that the document sent by the complainant was an out of date document which was revised in January 2006 from a previous version in 2004 (a copy of which was provided) and was superseded by additional documentation including: December 2005 Standard Operating Procedures (SOP), January 2006 Cycle meeting booklet, January 2006 ABPI presentation, January 2006 individual performance objectives detailing activity standards and Serono 2006 policy statements.

The updated document sent to the Authority was amended by the sender; Serono provided a copy of the original document.

The SOP applicable and relevant during the period (dated 21/12/05) clearly stated under the heading 'ABPI Code of Practice – Key points from the Code (2006)', that the number of calls on a doctor should not exceed three in one year. All KAMs were extensively briefed and trained on these SOPs and the new 2006 Code during business unit meetings and the Serono business cycle meeting in January 2006. All employees had completed the ABPI Wellards on-line training and validation course on the 2006 Code, where the level of calls was discussed and was confirmed to all sales staff.

The document at issue clearly stated that Serono did not believe in a call rate culture.

The tables under 'Activity – Target Levels' listed daily call rates, contact rates, both of which were 'As agreed with manager'. The frequency per cycle bullet point

in the table clearly showed the cycle to be 'For Sept – Dec 04'. The inclusion of this on the updated document was a typing error and should have been removed and replaced with the aforementioned 'As agreed with Manager'. The revised table was issued on 17 January 2006.

The call volume listed was the per annum rate, which was also confirmed by the performance objective document (provided) that clearly showed the amount of calls permissible and how it was personally discussed with the KAM during their performance objectives in January and July of each year. This was further confirmed with the opening statement in bold type face above the tables that stated 'Cycle Call volume – As agreed per cycle with manager and on an individual basis'.

Serono stated that it did not have a call rate culture of seeing any health professional 12 times per year.

The 2006 cycle booklet issued and discussed with KAMs on 17 January clearly showed that activity levels were to be only 3 unsolicited calls per annum. The table in the multiple sclerosis section clearly showed that the level of call rate activity permitted by Serono was and always had been only 3 calls per year in line with the 2006 Code.

Serono's portfolio included several complex products and services and therefore the calls on any health professional were by necessity segmented into three categories: KAM initiated calls (3 per annum); customer requested calls (as requested) and group meetings (as requested and authorised).

Serono had recently conducted a thorough revision of all policies and procedures with the SOPs being revised from the December 2005 versions to become more detailed and robust. These were now in force.

There were now policy statements related to all areas of the Code for quick reference by all employees regarding meetings, patient groups, contact with health professionals and a series of statements detailing the many aspects of the 2006 Code. The current certified statement on contact with health professionals, that showed that the level of contact allowable remained within the new 2006 Code parameters, was provided.

All KAMs from late 2005 had been fully briefed both as groups and as individuals on the level of contact permissible and at no time was there any confusion relating to this.

Serono submitted in summary that the document upon which the complaint was based had been altered. The original document entitled 'Activity Standards and Definitions' updated January 2006, was an out of date document superseded immediately after issue by many other clearly defined pieces that made it very clear that KAMs were not permitted to make an unsolicited call on a health professional more than 3 times in a year. There had been no confusion about this from any of the sales staff, particularly with the detailed briefings all staff had received in relation to the Code which reinforced this position. The sales director and managers alike enforced this with vigour and ensured that these were included within individual performance objectives.

PANEL RULING

The Panel noted that Clause 15.4 of both the 2003 and the 2006 Codes stated, *inter alia*, that representatives must ensure that the frequency, timing and duration of calls on health professionals, administrative staff in hospitals and health authorities and the like, together with the manner in which they were made, did not cause inconvenience. The supplementary information to Clause 15.4 of the 2006 Code stated, *inter alia*, that the number of calls made on a doctor or other prescriber and the intervals between successive visits were relevant to the determination of frequency. The number of calls made on a doctor or other prescriber by a representative each year should not normally exceed three on average. This did not include attendance at group meetings, a visit requested by a doctor or other prescriber or a call made to respond to a specific enquiry or a visit to follow up a report of an adverse reaction, all of which were additional to the three visits. The reference to 'other prescriber' in the supplementary information was newly introduced in 2006; the supplementary information to Clause 15.4 in the 2003 Code referred only to doctors.

The Panel noted Serono's submission that the document provided by the complainant had been altered. Nonetheless both the original document supplied by Serono and that provided by the complainant included for some therapy areas the statement 'For Sept-Dec 04' which thus implied that the stated call frequency eg 3 calls for target group A doctors in rheumatology, was for that period of time only, thus resulting in the possibility of 9 calls a year based on 3 cycles per year. Serono submitted that the statement 'For Sept-Dec 04' had been a typographical error; the statement should have read 'As agreed with Manager'. The Panel noted that other supporting documents and the training on the Code had made the requirements of the Code clear with regard to call rates. The 'Activity Standards and Definitions' document, however, had to stand alone. The inclusion of the typographical error had given the wrong impression about call rates. A breach of Clause 15.4 was ruled.

During its consideration of this case the Panel noted that the 'Activity Standards and Definitions' document should state how long a cycle was. If the cycle was a year then this should be stated. With regard to the call rates for nurses and others, if these groups included prescribers then the supplementary information to Clause 15.4 needed to be followed.

Complaint received **1 June 2006**

Case completed **15 August 2006**

CASE AUTH/1844/6/06

PRIMARY CARE TRUST HEAD OF PRESCRIBING v SANOFI-AVENTIS

Rimonabant email

The head of prescribing at a primary care trust (PCT) alleged that an email which he had received from Sanofi-Aventis which discussed the licensing status of rimonabant and how the recipient could receive information about it, was in breach of the Code because it was unsolicited and referred to an unlicensed medicine. Further, despite the email referring to a medicine no prescribing information was included.

The supplementary information to Clause 3.1, Advance Notification of New Products or Product Changes, noted that PCTs and the like needed to receive advance information about the introduction of new medicines, which might significantly affect their future expenditure. When this information was required, the medicines concerned would not be the subject of marketing authorizations (though applications would often have been made) and it would thus be contary to the Code for them to be promoted. Information might, however, be provided as long as, *inter alia*, it was directed to those responsible for making policy decisions on budgets, rather than those expected to prescribe, and the likely cost and budgetary implications were indicated and such that they would make significant differences to likely expenditure. Only factual information could be provided which should be limited to that sufficient to provide an adequate and succinct account of the product's properties.

The Panel noted that the subject of the email was stated as 'new Product Horizon Scanning Information' and asked the recipient if they wished to receive information regarding the projected introduction of a new product. The email gave brief details of rimonabant, describing it as the first of a new class of medicines. It was stated that the licensing process was considering data for possible use in the treatment of obesity and associated cardiovascular/cardiometabolic risk factors. The recipient was told that information on the cost of the medicine, patient types suitable for treatment, a summary of the numbers of such patients in the local PCT and an estimate of the uptake rate could be provided on request.

The Panel considered that the primary purpose of the email was to elicit interest in rimonabant and prompt the recipient to seek further information; the information provided in the email was not sufficient to provide an adequate but succinct account of the product's properties as required and nor did the email indicate the likely cost and significant budgetary implications of rimonabant. The email thus failed to meet the requirements of the supplementary information. A breach of the Code was ruled.

The Panel noted the complainant's concern that the email had not contained prescribing information. The supplementary information to the Code, however, stated that advance notification of new products should not include mock up drafts of summaries of product characteristics or patient information leaflets. In that regard the Panel considered that mock up prescribing information should also not be provided. No breach of the Code was ruled.

The Panel noted that the email in question had been sent without the prior permission of the recipient. A breach of the Code was ruled.

The head of prescribing at a primary care trust (PCT) complained about an email which he had received from Sanofi-Aventis at the end of May 2006. The email discussed the licensing status of rimonabant and how the recipient could receive information about it.

COMPLAINT

The complainant alleged that the email was in breach of the Code, firstly because it was unsolicited and secondly, because it gave the generic name, rimonabant, of a medicine that was, to the complainant's knowledge, unlicensed. Finally, despite the email referring to a medicine produced by Sanofi-Aventis, the prescribing information was not included.

When writing to Sanofi-Aventis, the Authority asked it to respond in relation to Clauses 3.1 and 9.9 of the Code. If rimonabant had a marketing authorization then Clause 4.1 should also be borne in mind.

RESPONSE

Sanofi-Aventis stated that it expected the rimonabant marketing authorization to be granted in June 2006. The complainant had not given prior permission to receive promotional material electronically.

The email was a personal letter, albeit in email format, which provided information on a new product expected to have significant budgetary impact to the PCT. Sanofi-Aventis considered that the email complied with Clause 3.1 of the Code (advance notification of new products).

The author, a Sanofi-Aventis employee, considered that the complainant would, as a pharmaceutical advisor to a PCT, have significant influence on policy decisions on the prescribing budgetary, as required by Clause 3.1. This consideration was stated within the email; also included was a request to forward the email to a more appropriate person should the complainant not fulfil this role (although there was no reason to believe that this would not be the case). The email continued in a factual manner to outline the essential information required by the Code with respect to advance notification of new medicines. In particular, it contained details that this concerned a new medicine that was subject to review by the European Medicines Evaluation Agency, a brief factual account of the product sufficient to enable the recipient to understand where the new medicine would be likely to be used in practice, and an indication that a price band and an estimate of the impact on the local budget was available upon which further discussions could be based if desired. The letter did not provide any information beyond that

required by Clause 3.1 and was not constructed nor supplemented by any material that might give the impression that this was a promotional item.

Sanofi-Aventis was confident that the email represented a *bona fide* non-promotional personal communication, and that it complied with Clause 3.1 of the Code.

With respect to the complainant's allegations, Sanofi-Aventis submitted that no breach of the Code had occurred and that high standards had been maintained for the following reasons.

- Firstly, although the email was sent unsolicited, it was factual rather than promotional in nature, and was a personal communication as opposed to any form of direct electronic promotion. Whilst agreeing that an unsolicited promotional email would be a breach of Clause 9.9, in view of the non-promotional nature of this letter, Sanofi-Aventis considered that no breach of Clause 9.9 had occurred and that high standards had been maintained.
- Secondly, the complainant was correct in stating that rimonabant did not yet have a marketing authorization. For this reason, the contact was made in full compliance with Clause 3.1 as outlined above. In complying with these requirements in full, Sanofi-Aventis again considered that no breach had occurred and that high standards had been maintained.
- Finally, with respect to the allegation that no prescribing information was included, this was clearly in line with the requirements of the Code not to provide mock-ups of such material prior to marketing authorization and Sanofi-Aventis again considered that it had complied with Clause 3.1 and thus maintained high standards.

In response to a request for further information Sanofi-Aventis stated that the cost of rimonabant was assumed to be between £30 to £50 for 28 days' treatment. In comparison to other marketed anti-obesity products, the most frequently used was orlistat which had an NHS cost of £41.60 for the same duration. The anticipation was that rimonabant would be prescribed for a wider population than orlistat given its anticipated indication and expected utility. Sanofi-Aventis thus considered that rimonabant would present a major budgetary impact to the NHS, over and above that of orlistat. Sanofi-Aventis later confirmed the price of £55.20 for rimonabant.

PANEL RULING

The Panel noted that the supplementary information to Clause 3.1, Advance Notification of New Products or Product Changes, noted that various healthcare organizations, including PCTs, needed to estimate their likely budgets two to three years in advance in order to meet Treasury requirements and so they needed to receive advance information about the introduction of new medicines, or changes to existing medicines, which might significantly affect their level of expenditure during future years. At the time this information was required, the medicines concerned (or the changes to them) would not be the subject of marketing authorizations (though applications would often have been made) and it would thus be contrary to the Code for them to be promoted. Information might, however, be provided as long as, *inter alia*, it was directed to those responsible for making policy decisions on budgets, rather than those expected to prescribe, and the likely cost and budgetary implications were indicated and such that they would make significant differences to the organizations likely expenditure. Only factual information could be provided which should be limited to that sufficient to provide an adequate and succinct account of the products' properties.

The subject of the email was stated as 'new Product Horizon Scanning Information' and asked the recipient if they wished to receive information regarding the projected introduction of a new product. The email then went on to give brief details of rimonabant describing it as the first of a new class of medicines. It was stated that the licensing process was considering data for possible use in the treatment of obesity and associated cardiovascular/cardiometabolic risk factors. The recipient was told that Sanofi-Aventis could provide, on request, information on the cost of the medicine, patient types suitable for treatment, a summary of the numbers of such patients in the local PCT and an estimate of the uptake rate.

The Panel considered that the primary purpose of the email was to elicit interest in rimonabant and prompt the recipient to seek further information; the information provided in the email was not sufficient to provide an adequate but succinct account of the product's properties as required and nor did the email indicate the likely cost and significant budgetary implications of rimonabant. The email thus failed to meet the requirements of the supplementary information. A breach of Clause 3.1 was ruled.

The Panel noted the complainant's concern that the email had not contained prescribing information for rimonabant. The supplementary information to Clause 3.1, however, stated that advance notification of new products should not include mock up drafts of either summaries of product characteristics or patient information leaflets. In that regard the Panel considered that mock up prescribing information should also not be provided. No breach of Clause 3.1 was ruled in that regard.

Clause 9.9 of the Code stated, *inter alia*, that emails must not be used for promotional purposes except with the prior permission of the recipient. The Panel noted its ruling of a breach of Clause 3.1 of the Code. The email in question had been sent without the prior permission of the recipient. A breach of Clause 9.9 was ruled.

Complaint received **6 June 2006**

Case completed **15 August 2006**

CASE AUTH/1845/6/06

PRIMARY CARE TRUST ASSISTANT DIRECTOR OF PUBLIC HEALTH v ASTRAZENECA

Arimidex journal advertisement

An assistant director of public health at a primary care trust, complained about an advertisement for Arimidex (anastrozole), issued by AstraZeneca. Arimidex was indicated for the treatment of advanced breast cancer in postmenopausal women and as an adjuvant treatment of postmenopausal women with hormone receptor positive early invasive breast cancer. The advertisement showed a large rectangle subdivided into four smaller rectangles. Three of the smaller rectangles featured a picture of a woman and the fourth contained the claim '26% is a very big difference in breast cancer recurrence if you are that 1 in 4'.

The complainant alleged that the advertisement implied that 1 in 4 breast cancer sufferers would benefit from taking Arimidex ie the number-needed-to-treat (NNT) was 4. The complainant noted that the 26% quoted referred to the relative risk reduction seen in the ATAC study for the endpoint of time-to-recurrence. A relative risk reduction of 26% did not correspond to an NNT of 4. From the figures quoted in the published paper, the complainant calculated the NNT to be 59 at 3 years, 36 at 5 years, and 27 at 6 years. The complainant alleged that the advertisement was very misleading and implied that Arimidex was far more beneficial than it actually was.

The Panel noted the claim '26% is a very big difference in breast cancer recurrence if you are that 1 in 4' was asterisked to a footnote which explained that the 26% was risk reduction with Arimidex over tamoxifen in hormone receptor positive postmenopausal women. The Panel noted that the footnote thus contained information which was fundamental to understanding the claim at issue. Without reading the footnote the Panel considered that the advertisement implied that 1 in every 4 patients treated with Arimidex would not have a recurrence of their breast cancer. This was not so. The Panel considered that the advertisement was misleading as alleged. A breach of the Code was ruled.

An assistant director of public health at a primary care trust complained about an advertisement (ref ARIM 06 18600) for Arimidex (anastrozole), issued by AstraZeneca UK Limited, which had appeared in Prescriber on 19 May. Arimidex was indicated for the treatment of advanced breast cancer in postmenopausal women and as an adjuvant treatment of postmenopausal women with hormone receptor positive early invasive breast cancer. The advertisement showed a large rectangle subdivided into four smaller rectangles. Three of the smaller rectangles featured a picture of a woman and the fourth contained the claim '26% is a very big difference in breast cancer recurrence if you are that 1 in 4'.

The advertisement had variously appeared in Prescriber, the BMJ and Hospital Doctor between 5 May and 22 June 2006.

COMPLAINT

The complainant alleged that the advertisement implied that 1 in 4 breast cancer sufferers would benefit from taking Arimidex ie the number-needed-to-treat (NNT) was 4.

The complainant noted that the 26% quoted referred to the relative risk reduction seen in the ATAC study for the endpoint of time-to-recurrence. A relative risk reduction of 26% did not correspond to an NNT of 4. From the figures quoted in the published paper, the complainant calculated the NNT to be 59 at 3 years, 36 at 5 years, and 27 at 6 years. None of these was close to 4. No data was provided in the paper beyond 6 years. Time-to-recurrence was not even the primary endpoint in the ATAC study.

The complainant alleged that the advertisement was very misleading and implied that Arimidex was far more beneficial than it actually was. The advertisement should be withdrawn and a correction published, preferably quoting the true NNTs. It would be a great step forward if advertisements had to quote NNTs.

RESPONSE

AstraZeneca submitted that the advertisement was an attempt to convey the patient perspective of a statistical endpoint and the image reflected a visual representation of a relative reduction in recurrence. The claim '26% is a very big difference …' was aligned to the empty box, to show the fourth woman who might recur on tamoxifen but be saved from recurrence by Arimidex.

The claim '26% is a very big difference …' was amplified in the footnote 'ATAC shows that in hormone receptor positive postmenopausal women, Arimidex gives a 26% risk reduction over tamoxifen; this is in addition to the 47% risk reduction previously shown for tamoxifen versus placebo'. This made it quite clear that it was referring to recurrence relative to tamoxifen-treated patients. In addition the inclusion of safety information further ensured prominence of this text.

The complainant had alleged that 'A relative risk reduction of 26% did not correspond to a NNT of 4 ….a correction should be published preferably quoting the true NNTs'. AstraZeneca noted that in the context of reduction in recurrence in patients taking tamoxifen, the 26% risk reduction did equate to a NNT of 4. However, AstraZeneca noted that in the advertisement it had only included data quoted in the source reference, the ATAC Trialists' Group publication from The Lancet 2005. This reference did not contain any NNT data and indeed there were no such data in either of the previous ATAC publications,

in The Lancet 2002 and Cancer 2003. In addition, the hazard ratios from the ATAC study, rather than figures for NNT were quoted in the Arimidex summary of product characteristics (SPC).

AstraZeneca noted the complainant's comment that time to recurrence was not even a primary endpoint in the ATAC study and submitted that time to recurrence was a protocol-defined secondary endpoint of the study. It included all recurrences, new breast cancers and deaths due to breast cancer. In the treatment of early breast cancer, patients and their doctors found the prevention of recurrence, which in turn was likely to delay death from breast cancer, was hugely important and this information was what was represented.

AstraZeneca submitted that the ATAC primary endpoint of 'disease-free survival' covered not only recurrence and breast cancer death, but also death due to any cause and was also significantly in favour of Arimidex compared to tamoxifen. Death due to any cause was not a sign of the return of breast cancer and therefore not a predictor of the efficacy of breast cancer treatment. This composite endpoint would therefore be less informative to doctors when deciding on the optimal treatment for their patients.

AstraZeneca noted the complainant's allegation that the advertisement was very misleading and implied that Arimidex was far more beneficial than it actually was. AstraZeneca submitted that it had addressed the complainant's points, showing that the advertisement related to the relative risk of recurrence in patients on Arimidex compared with those given tamoxifen; that it was not appropriate to calculate NNTs from the data and that time to recurrence was a meaningful endpoint in this context. The above points demonstrated that the advertisement was not misleading and did not suggest an unrealistic benefit from prescribing Arimidex.

PANEL RULING

The Panel noted that the supplementary information to Clause 7.2 of the Code stated that in general claims should not be qualified by the use of footnotes and the like. The claim '26% is a very big difference in breast cancer recurrence if you are that 1 in 4' was asterisked to a footnote which explained that the 26% was risk reduction with Arimidex over tamoxifen in hormone receptor positive postmenopausal women. The Panel noted that the footnote thus contained information which was fundamental to understanding the claim at issue. Without reading the footnote the Panel considered that the advertisement implied that 1 in every 4 patients treated with Arimidex would not have a recurrence of their breast cancer. This was not so. The Panel considered that the advertisement was misleading as alleged. A breach of Clause 7.2 of the Code was ruled.

Complaint received **7 June 2006**

Case completed **28 July 2006**

CASE AUTH/1846/6/06 *NO BREACH OF THE CODE*

FORMER EMPLOYEE v MERCK SHARP & DOHME

Memorandum and briefing document

A former employee of Merck Sharp & Dohme complained about internal memoranda relating to the matters at issue in Case AUTH/1814/3/06 and a field force briefing document concerning the creation of partnership development managers (PDMs) by Schering-Plough as part of a Schering-Plough/Merck Sharp & Dohme co-promotion agreement.

The complainant provided copies of two memoranda sent to all of Merck Sharp & Dohme's sales teams involved in the promotion of Cozaar (losartan). The complainant noted that the memorandum sent from the cardiovascular business unit stated *inter alia*, that Merck Sharp & Dohme considered that the audit protocol (at issue in Case AUTH/1814/3/06) complied with the Code.

The complainant considered that this statement was remarkable as it clearly contradicted Merck Sharp & Dohme's acceptance of the likely breach of the Code on 29 March 2006. The complainant alleged that the memorandum failed to maintain high standards of behaviour when telling internal audiences about matters related to alleged breaches of the Code.

The complainant also provided a briefing document that was issued to relevant field force members regarding the creation of PDMs. The scope and responsibilities of the PDM's role appeared to be that of a provider of medical and educational goods and services as opposed to that of a representative. Accordingly, the complainant was surprised and concerned to see that the PDM role also appeared to have commercial responsibilities. The complainant questioned whether the stated objectives of the PDM role were consistent with the Code.

The Panel noted Merck Sharp & Sharp's submission that the reference in the memorandum from the cardiovascular business unit was to the audit protocol and to the proformas which, as noted in Case AUTH/1814/3/06, had been revised to comply with the Code and reissued in September 2005. The Panel considered that the proformas referred to could be those formally certified by Merck Sharp & Dohme as opposed to those which had not been approved for use and which had been in question in

Case AUTH/1814/3/06. It was very important that correspondence about the proformas should be clear about which document was being referred to. The memorandum at issue was not entirely clear about which proformas were referred to but the Panel did not consider that it was inconsistent with Merck Sharp & Dohme's response in Case AUTH/1814/3/06. No breach of the Code was ruled.

With regard to the briefing document for the PDM role, the Panel did not consider there was any evidence that the role as described in the briefing document was in breach of the Code. It appeared that the role was a commercial/promotional one rather than providing medical and educational goods and services. The Panel considered that the Merck Sharp & Dohme briefing document was not inconsistent with the Code. No breach of the Code was ruled.

A former employee of Merck Sharp & Dohme Limited complained about internal memoranda relating to the matters at issue in Case AUTH/1814/3/06 and a field force briefing document concerning the creation of partnership development managers (PDMs) by Schering-Plough Ltd as part of the Schering-Plough/Merck Sharp & Dohme co-promotion of Ezetrol (ezetimibe) and Inegy (ezetimibe/simvastatin).

COMPLAINT

The complainant provided copies of two memoranda dated 2 and 8 May 2006 sent to all of Merck Sharp & Dohme's sales teams involved in the promotion of Cozaar (losartan). The memoranda had recently been brought to the complainant's attention by an ex-colleague within Merck Sharp & Dohme's field force.

The complainant referred to the memorandum sent from the cardiovascular business unit and dated 2 May 2006 which stated *inter alia*:

> 'MSD believes that … audit protocol complies with code guidance regarding audit activity save for the BHS ABCD guidance which was has [sic] been amended in light of a previous case to reflect accurately the original BHS guidance.'

The complainant noted that Merck Sharp & Dohme's response to the complaint in Case AUTH/1814/3/06 regarding the nurse audit programme, dated 29 March 2006, stated the following in respect of the Hypertension and Type 2 diabetes proformas that were a central component of Merck Sharp & Dohme's implementation of the nurse advisor programme:

> 'They were not reviewed internally and we believe that they breach Clause 18.1 of the Code. We would like to take this opportunity to apologise to the Authority that these proformas were sent out in this form for use by representatives. We are conducting an internal investigation into the matter and once that investigation is completed disciplinary action will be taken if appropriate.'

The complainant noted that given that the author of the memorandum reported directly to the managing director and in light of the seriousness with which the company claimed to view adherence to the Code, the statement to the entire field force that 'Merck Sharp & Dohme believes that the … audit protocol complies with the code guidance regarding audit activity…' was remarkable when it clearly contradicted the company's acceptance of the likely breach of Clause 18.1 on 29 March 2006. The complainant alleged that the memorandum was in breach of Clause 9.1 of the 2003 Code in that it failed to maintain high standards of behaviour when communicating to internal audiences on matters pertaining to alleged breaches of the Code.

The complainant also provided a briefing document that was recently issued by Merck Sharp & Dohme to its relevant field force members in relation to the creation of partnership development managers (PDMs) as a component of Schering-Plough/Merck Sharp & Dohme's co-promotion of Inegy and Ezetrol. The scope and responsibilities of the PDM role appeared to be that of a provider of medical and educational goods and services as distinct from that of a medical/generic sales representative. Accordingly, the complainant was surprised and concerned to see that the PDM role also appeared to have commercial responsibilities:

> 'PDMs will build partnerships in key accounts and local clinical networks, working alongside the existing Regional Sales teams. The PDM will identify commercial opportunities and develop partnerships across key accounts and their clinical and managerial networks resulting in incremental market share growth for Schering-Plough brands.
>
> Identify and realise commercial opportunities (patient identification and management). Work with commissioning locality groups to cement the environment for SP products.'

The complainant questioned whether the stated objectives of the PDM role were consistent with the Code. The complainant explained that the PDM initiative and roles were attributable to Schering-Plough. However, the briefing document had been subject to Merck Sharp & Dohme's medico-legal review process, as the case for all bulletins provided by Merck Sharp & Dohme to its field force. The purpose of this bulletin was to ensure that Merck Sharp & Dohme staff involved in the co-promotional venture with Schering-Plough were fully apprised of activities undertaken by its partner company. The complainant explained that he raised his concerns about the potential Code compliance of the Schering-Plough PDM role because the bulletin had been subject to Merck Sharp & Dohme's medico-legal review process which suggested that the company saw no issue with the appropriateness of the PDM role.

When writing to Merck Sharp & Dohme the Authority asked it to respond in relation to Clauses 2, 9.1, 15.9, 18.1 and 18.4 of the Code.

RESPONSE

Merck Sharp & Dohme refuted the allegation that the memorandum from the cardiovascular business unit was inconsistent with Merck Sharp & Dohme's response to Case AUTH/1814/3/06.

Merck Sharp & Dohme submitted that its response to the previous case had referred to the original

proforma which formed part of the complaint. The memorandum from the cardiovascular business unit clearly referred to the revised proforma, issued in September 2005 and to which reference was made in the response as well. Merck Sharp & Dohme was confident that the revised proformas were consistent with the Code. Accordingly Merck Sharp & Dohme submitted that this allegation had no substance.

Merck Sharp & Dohme noted that the complainant had also asked the Authority to consider whether the stated objectives of the PDM role were consistent with the Code. As the complainant acknowledged, the PDM was a Schering-Plough role. The briefing document in question was circulated by Merck Sharp & Dohme to staff in order that they would better understand the work undertaken by PDMs, with whom they would be working to further the commercial aims of the partnership. So far as Merck Sharp & Dohme was aware, there was no prohibition under the Code of jobs which encompassed both service provision and overt selling; the two must however be kept distinct in terms of actual delivery, hence representatives must not offer both the service and promote at the same visit. Merck Sharp & Dohme submitted that the PDM role was clearly a commercial one and did not seem to involve providing '…..medical and educational goods and services,' as alleged by the complainant. In any event, there was nothing in the document which supported the complainant's view that the role was not consistent with the Code. Merck Sharp & Dohme submitted that if the Authority had specific questions regarding the job and its responsibilities, it respectfully suggested that they might like to pose them to Schering-Plough Ltd.

Merck Sharp & Dohme trusted therefore that the above would satisfy the Panel that the company had not engaged in any activities which breached the Code and in particular Clauses 2, 9.1, 15.9, 18.1 and 18.4.

PANEL RULING

The Panel noted Merck Sharp & Sharp's submission that the reference in memorandum at issue was to the APMS audit protocol and to the proformas which, as noted in Case AUTH/1814/3/06, had been revised to comply with the Code and reissued in September 2005. The Panel considered that the proformas referred to could be those formally certified by Merck Sharp & Dohme as opposed to those which had not been approved for use and which had been in question in Case AUTH/1814/3/06. The complainant's quotation from Merck Sharp & Dohme's response to Case AUTH/1814/3/06 referred to these 'unapproved' proformas which the company submitted had been created by the Cozaar marketing team. It was very important that correspondence about the proformas should be clear about which document was being referred to. The memorandum on 2 May stated that the audit was suspended and then referred to the representative practice proformas. The memorandum was not entirely clear about which proformas were referred to but the Panel did not consider that the memorandum was inconsistent with Merck Sharp & Dohme's response in Case AUTH/1814/3/06. Thus the Panel ruled no breach of Clause 9.1 of the Code.

With regard to the briefing document for the PDM role, the Panel did not consider there was any evidence that the role as described in the briefing document was in breach of the Code. It appeared that the role was a commercial/promotional one rather than providing medical and educational goods and services. The Panel considered that the Merck Sharp & Dohme briefing document was not inconsistent with the Code. No breaches of Clauses 15.9, 18.1 and 18.4 of the Code were ruled.

Complaint received **1 June 2006**

Case completed **5 July 2006**

CASE AUTH/1847/6/06

PRIMARY CARE TRUST HEAD OF PRESCRIBING v ALTANA PHARMA

Conduct of representative

The head of prescribing at a primary care trust (PCT) complained about the promotion of Alvesco (ciclesonide) by representatives from Altana. The complainant stated that he and a GP colleague met two of the representatives to discuss the evidence, cost and place in therapy of Alvesco. The representatives intimated that Altana had placed its product after beclometasone dipropionate (BDP), but as an alternative to other steroids and to step 3 of the British Thoracic Society (BTS) asthma guidelines. One of the representatives repeatedly asked the complainant to endorse this placement of the product in therapy. This request was repeatedly refused. The complainant stated that the PCT would not, and could not endorse what was a significant deviation from the BTS asthma guidelines. The complainant told the representatives that he could not stop them promoting Alvesco in this way but made it clear that he most certainly would not endorse this place for the product.

The complainant later learnt that another Altana representative had told a practice nurse that the complainant had endorsed the product in the position as described above. The complainant alleged that this was in breach of the Code and morally and ethically objectionable. He was appalled that having repeatedly stated, very clearly, that he would not endorse individual products in this way, Altana had ignored this and misquoted him in order to gain product endorsement.

The complainant alleged that the information Altana had used, and attributed to him, was inaccurate and misleading. In addition, the company could not substantiate the claims.

Commenting on Altana's response to the complaint, the complainant stated that he had placed Alvesco at step 2 of the BTS guidelines only in patients who got oral side effects from the first line choice, BDP. Furthermore, that Alvesco should not be used in patients who were uncontrolled at step 2, before moving to step 3, as it was not his, or his colleague's, place to amend the BTS guidelines for local use.

The Panel considered that it was beholden upon representatives to be abundantly clear when using the names of health professionals to endorse a promotional message. The circumstances were complicated in that the complainant had met two Altana representatives to discuss Alvesco and its place in therapy. As a result of that discussion the representatives had presumably briefed another Altana representative who had in turn discussed the outcome of the meeting, at which he was not present, with a practice nurse. It was a remark made to the practice nurse which had prompted the complaint.

The complaint focussed on when Alvesco should be used within the BTS guidelines. Step 2 of the guidelines involved the 'as required' use of a short-acting B_2 agonist plus the regular use of inhaled corticosteroids, BDP or equivalent. If asthma worsened then patients progressed to step 3 and a long-acting B_2 agonist was added to the existing corticosteroid therapy. The complainant had given permission for representatives to state that they had discussed the use of Alvesco with him but he had not endorsed their placement of Alvesco in therapy, ie as an alternative to BDP in patients uncontrolled at step 2 of the BTS guidelines instead of progressing to step 3. In the complainant's view, Alvesco should only be used at step 2 of the BTS guidelines in the small number of patients who were uncontrolled with BDP therapy (the PCT's first choice inhaled steroid) because compliance was compromised by oral side effects.

Altana's response stated that the representative who had spoken to the practice nurse had understood that the complainant had endorsed the use of Alvesco once BDP had not been successful and before resorting to combination therapy. This was not so.

The promotional literature for Alvesco placed the product as an alternative to BDP at step 2 of the BTS guidelines in patients uncontrolled on BDP without any reference to poor compliance. The BTS guidelines, however, did not indicate that patients uncontrolled at step 2 on one inhaled steroid should try an alternative inhaled steroid; patients in whom asthma was uncontrolled should progress to step 3. The Panel noted that Altana had referred to the 'tight confines of the agreement with the complainant'. In the Panel's view, however, the promotional literature positioned Alvesco for a wide range of patients.

The Panel considered it unlikely that the complainant, head of prescribing at a PCT, would endorse a course of action which was not referred to in the BTS guidelines and this was supported by the complainant's comments. The complainant's name had been used, with his permission, by a representative during the course of promoting Alvesco. The promotional literature positioned Alvesco in a way which was not referred to in the BTS guidelines, ie as an alternative for use in any patient uncontrolled on BDP. The Panel thus considered that, on the balance of probability, the practice nurse had been led to believe that the complainant endorsed Altana's positioning of Alvesco which was not so. The Panel considered that the representatives had failed to maintain a high standard of ethical conduct and had failed to comply with all relevant requirements of the Code. Formal permission had not been obtained in relation to the quotation used by the representative with the practice nurse, ie the misquotation. Breaches of the Code were ruled. The Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 of the Code.

Upon appeal by Altana, the Appeal Board noted that one of the representatives who had met with the complainant had emailed an account of that meeting

to, *inter alia*, the representative who had subsequently visited the practice nurse. The Appeal Board considered that the email showed that the representative had had to work extremely hard to get any agreement out of the complainant. Agreements gained in such circumstances should be treated with caution. The Appeal Board considered that following such a protracted discussion the representative should have written to the complainant so that both parties could confirm their understanding of what had been agreed. It was beholden upon representatives to be abundantly clear when using the names of health professionals to endorse a promotional message. In circumstances where companies sought to gain the endorsement of public bodies, ie PCTs and the like, for their products, the Appeal Board considered that they would be well advised to confirm formal agreement before making such endorsement known.

On the evidence before it, the Appeal Board was satisfied on the balance of probabilities that the complainant's views about the positioning of Alvesco had been misrepresented. The Appeal Board upheld the Panel's rulings of breaches of the Code.

The head of prescribing at a primary care trust (PCT) complained about the promotion of Alvesco (ciclesonide) by representatives from Altana Pharma Limited.

COMPLAINT

The complainant stated that he and a GP colleague met two representatives to discuss the evidence, cost and place in therapy of Alvesco. The representatives intimated that Altana had placed its product after beclometasone dipropionate (BDP), but as an alternative to other steroids and to step 3 of the British Thoracic Society (BTS) asthma guidelines. During the meeting one of the representatives repeatedly asked for a written endorsement for the product and this position in therapy from the PCT. This request was repeatedly refused. Furthermore, the complainant had stated that the PCT would not, and could not endorse this position for any product as it was a significant deviation from the BTS asthma guidelines.

The complainant was asked how he would react if representatives promoted Alvesco in this way locally. The complainant told the representatives that he could not stop them and again made it clear that he most certainly would not endorse this place for the product.

To his consternation, the complainant learnt on 9 June that a GP representative from Altana, had told a practice nurse that the complainant had endorsed the product in the position as described above. The complainant alleged that this was in breach of the Code and morally and ethically objectionable. He was appalled that having repeatedly stated, very clearly, that he would not endorse individual products in this way, Altana had ignored this and misquoted him in order to gain product endorsement.

The complainant alleged that the information Altana had used, and attributed to him, was inaccurate and misleading. In addition, the company could not substantiate the claims. The complainant alleged breaches of Clauses 7.2, 7.4, 7.6 and 11.3 of the Code.

When writing to Altana, the Authority asked it to respond in relation to Clauses 2, 9.1 and 15.2, in addition to Clauses 7.2, 7.4, 7.6 and 11.3 cited by the complainant.

RESPONSE

Altana explained that Alvesco was an inhaled corticosteroid for the treatment of persistent asthma in adults and adolescents (12 years and older). According to the BTS guidelines inhaled steroids were the most effective preventer medicine for achieving overall treatment goals. Step 2 of the guidelines involved the regular inhalation of a corticosteroid to reduce the frequency of asthma exacerbations (by decreasing lung inflammation) and the use of a short acting beta-2-agonist to relieve the symptoms of an asthma exacerbation (by dilating the small airways). Step 3 included the regular usage of a long-acting beta-2-agonist (to help maintaining airway dilatation) in addition to medication given at step 2 if asthma control was inadequate with step 2 therapy only.

Alvesco had clearly been marketed for use at step 2 which advised inhaled steroids as first choice preventer drug, it did not mention a particular inhaled steroid as first choice preventer drug. From a marketing perspective Altana positioned Alvesco after BDP and before combination inhalers. It should be considered as an alternative to other inhaled steroids in step 2 patients who were having symptoms of asthma despite step 2 therapy. Alvesco might be of considerable benefit to patients who had compliance problems due to oral pharyngeal side effects or complex treatment regimen with other inhaled steroids.

It was appropriate medical practice for a physician to consider changing a step 2 patient to Alvesco if the physician believed that the patient might benefit from the alternative characteristics of the product before exposing the patient to the additional medication of step 3 therapy. Clearly for patients with increasing asthma symptoms despite compliance at step 2 it would be inappropriate to remain at step 2 and they should be immediately commenced on the increased medical regimen of step 3. Determination of therapy was for the prescribing physician to decide on the basis of their clinical judgement.

The positioning of Alvesco was within the BTS guidelines and was supported by a large number of physicians and formulary inclusions. The briefing notes and sales materials showed that Alvesco was clearly positioned in step 2 therapy.

Altana submitted that this complaint hinged on the content of two meetings between Altana representatives and health professionals:

From the meeting report and notes of the first meeting (provided) and subsequent interviews with relevant employees, it was clear that the meeting with the complainant was productive and good-natured. It lasted an hour and a half and two of the outcomes that illustrated the mutually productive nature of the

meeting were that he agreed to see a representative again to discuss Protium and he brought up the subject of respiratory education and suggested that the representative contact a local respiratory nurse consultant.

The length of the meeting and the indisputable outcomes would be highly unlikely to have occurred if the meeting had been antagonistic or overtly confrontational.

Altana submitted that the meeting notes also clearly stated that:

1 The complainant agreed that provided that a GP had used BDP and then wanted to use Alvesco, he would be happy with the situation and would 'not come down on any practices doing so'.

2 The complainant was specifically asked if he would give his endorsement to using his name when seeing GPs and practice nurses and discussing Alvesco for use after BDP. He agreed.

3 The complainant agreed that patients who were poor compliers, those who had oral side effects, those fearful of inhaled corticosteroids and those who would benefit from the convenience of once daily therapy were all patients on whom he would be happy to see Alvesco used. (Patient profiles in sales materials.)

4 The complainant was not happy for Alvesco to be used as first line therapy ahead of BDP as it was against the formulary guideline and the BTS guidelines. (the complainant's statement about Alvesco not included as first line therapy ahead of BDP in the formulary guideline was correct but his statement about Alvesco in the BTS guidelines was incorrect. According to the BTS guidelines and the Alvesco summary of product characteristics (SPC), Alvesco was one of the inhaled steroids that could be prescribed as a first choice preventer in step 2 therapy).

5 Neither the complainant nor the GP were prepared to write a newsletter to support the use of Alvesco.

6 The complainant did not support any position other than Alvesco being used after BDP at step 2.

7 The complainant knew of inappropriate use of combination therapy locally at step 1 and step 2 which was outside the BTS guidelines for asthma management.

One of the representatives at the meeting agreed that the meeting report sent by the other representative accurately reflected the content and agreements from the meeting with the complainant. This representative was surprised by the complaint because the meeting was handled professionally and the positioning of Alvesco during the meeting was for step 2 therapy after BDP, which gained the complainant's endorsement and agreement for his name to be used in sales calls for this specific product usage.

The representative who sent the report recalled asking the complainant to write an endorsement for Alvesco but refuted the allegation that she 'repeatedly asked' as alleged in the complaint. She was surprised at the complaint as the meeting was 'good-humoured' and she was confident that no issues relating to Alvesco were left unresolved.

Altana noted that the complainant alleged that an unnamed nurse informed him that a GP representative from Altana had told her that he endorsed Alvesco as an alternative to other steroids and to step 3 of the BTS Guidelines.

Altana submitted that it had no more information on this meeting. The company did not have the nurse's name and it was therefore impossible for it to be certain that it had obtained the correct electronic meeting notes that were created. Although there was a short list of meetings that this representative undertook with nurses in the area between 2 June and 9 June, Altana was not able to use the electronic record to give it highly relevant information, which would have helped create a more robust version of events.

However, on interview, the representative was extremely surprised to learn of the complaint, as he had not deviated from the agreed product messages or the communication from one of the representatives at the meeting with the complainant in any of the potential meetings from which the complaint arose. He was consistent with the primary care sales materials used (provided). For further clarity during the interview, he was asked to state his understanding of the Alvesco positioning that had been endorsed by the complainant; he responded in line with both the Altana Alvesco positioning and the positioning supported by the complainant – that Alvesco could be used once BDP had not been successful and before resorting to combination therapy.

Altana submitted that the behaviour of its representatives had been of the highest order, promoting a product in line with the marketing authorization, the BTS guidelines, current medical practice and within the tight confines of the agreement with the complainant to use his name in support for a specific product positioning. Therefore Altana did not consider that it had breached Clauses 2, 9.1, 11.3 or 15.2 of the Code.

The briefing notes and sales materials provided in its response unequivocally confirmed that Alvesco was positioned as step 2 therapy, in line with the BTS guidelines and current medical therapy. Whilst the complainant did not specifically cite any one particular piece of promotional material for censure Altana was certain that all of its materials were robust and complied with the Code. Therefore Altana did not consider that Clauses 7.2, 7.4 or 7.6 had been breached.

In summary, whilst Altana deeply regretted that a misunderstanding occurred during a meeting between its representative and a nurse it could not be held responsible given the high standards of both the promotional positioning by the representative and the promotional materials and the agreement with the complainant to use his name during the call to support the positioning of the product.

FURTHER COMMENTS FROM THE COMPLAINANT

The complainant stated that he and his colleague were astonished by Altana's notes of the meeting as this was certainly not their recollection of how the

meeting progressed and frankly they found it difficult to provide enough compelling information to allow a breach to be ruled. Nonetheless they would try to provide their account of the meeting, point out the inaccuracies as they saw them, in Altana's account of the meeting and provide, where possible, reason why their account might be a more acceptable version of events. Taking Altana's points in order:

1 Altana stated that the complainant would not reprimand any practice for using Alvesco provided it had used BDP first.

This was accurate. The PCT's formulary positioned BDP as the first choice inhaled steroid. Provided that clinicians followed the formulary the complainant was not concerned with product choice beyond the first line selection.

2 Altana stated that permission was given for names to be used when discussing Alvesco for use after BDP.

Indeed permission was given for the Altana representatives to state that they had met with the complainant and his colleague during promotional activity for Alvesco, however the placing of the product was not as described here (see later).

3 Altana stated that agreement was reached that Alvesco could be used in patients who were poor compliers, had oral side effects, who were fearful of steroids or who would benefit from a once daily product.

The complainant actually stated that he could not stop Altana marketing its product in this way despite the fact that he and his colleague disagreed with it. There was no evidence to support greater compliance with Alvesco compared to other steroids, it was still an inhaled steroid and once daily dosing had not been shown to improve outcomes over products with a greater frequency of administration. These factors made many of Altana's arguments irrelevant. The conversation therefore focussed upon oral side effects, which despite the complainant's concerns were, according to nursing colleagues, very rare. As such the complainant and his colleague stated that they would be happy with the product being used in the niche of patients for whom oral side effects might affect continued compliance but no more.

4 Altana stated that the complainant and his colleague were not happy to place Alvesco as first line steroid choice ahead of BDP.

This was accurate. The complainant and his colleague stated that using the STEP model (safety, tolerability, efficacy, price) to assess the place of Alvesco compared to treatment with BDP, Alvesco was a black triangle medicine and therefore safety could not be assured to the same extent as BDP. It was perhaps as well tolerated and efficacious from the trial data but was more expensive. Based on the current data therefore it must be placed after BDP.

Altana additionally stated that Alvesco was named at step 2 of the BTS guidelines.

This was not disputed, however it was not placed between step 2 and 3 (see later). Patients who were uncontrolled at step 2 of the BTS guidelines had therapy added, not steroid changed.

5 Altana stated that neither the complainant nor his colleague were prepared to write a newsletter in support of Alvesco.

This was accurate. The only question to be raised here though was if they had been happy placing Alvesco where Altana stated that they were, why then would they refuse to write this in a newsletter?

6 Altana stated that the complainant and his colleague did not support any position for Alvesco other than step 2 after BDP.

This statement was vague and perhaps open to interpretation. The complainant and his colleague stated at the meeting and reiterated above that they placed Alvesco at step 2 of the BTS guidelines for patients who were well controlled but suffered oral side effects that might affect continued compliance. This statement could also be interpreted to mean that Alvesco could be used after BDP at step 2 before moving to step 3. This interpretation was inaccurate. The role of the complainant and his colleague within the PCT was to advise clinicians on appropriate medicine choice, not to override nationally recognised guidelines for disease treatment. The complainant and his colleague most certainly would never suggest delaying stepping up any patient who was poorly controlled at the current step of the BTS guidelines and there was no reason not to step up using the guidelines unless control was poor.

7 Altana stated that the complainant and his colleague were aware of inappropriate use of combination products locally at step 1 and step 2.

This was partly accurate. The complainant and his colleague were aware of patients who were at step 1 or who were newly diagnosed being treated with combination products (step 3) without correctly progressing through the BTS management steps.

In summary the complainant stated that he and his colleague recalled that they placed Alvesco at step 2 of the BTS guidelines and suggested that it might be used only in patients who got oral side effects from the first line choice, BDP. Furthermore, they disagreed with Altana that Alvesco could be used in patients who were uncontrolled at step 2, before moving to step 3, as it was not their place to amend the BTS guidelines for local use.

Despite this placing of Alvesco it seemed obvious from Altana's response that information was relayed to the representatives that Alvesco had been endorsed by the complainant and his colleague as an alternative to other steroids and to step 3 of the BTS guidelines. It would be noted from the above that they most certainly did not place Alvesco as an alternative to step 3 and stated that it was an alternative to BDP at step 2 only where oral side effects were a problem.

The complainant and his colleague stated that to the best of their knowledge, the above represented a true account of the meeting.

PANEL RULING

The Panel noted that the parties' accounts differed; it was difficult in such cases to know exactly what had transpired. A judgement had to be made on the

available evidence bearing in mind that extreme dissatisfaction was usually necessary on the part of an individual before he was moved to actually submit a complaint.

The Panel considered that it was beholden upon representatives to be abundantly clear when using the names of health professionals to endorse a promotional message. The circumstances were complicated in that the complainant had met two Altana representatives to discuss Alvesco and its place in therapy. As a result of that discussion the representatives had presumably briefed another Altana representative who had in turn discussed the outcome of the meeting, at which he was not present, with a practice nurse. It was a remark made to the practice nurse which had prompted the complaint.

The complaint focussed on when Alvesco should be used within the BTS guidelines. Step 2 of the guidelines involved the 'as required' use of a short-acting B_2 agonist plus the regular use of inhaled corticosteroids, BDP or equivalent. If asthma worsened then patients progressed to step 3 and a long-acting B_2 agonist was added to the existing corticosteroid therapy. The complainant had given permission for representatives to state that they had discussed the use of Alvesco with him but he had not endorsed their placement of Alvesco in therapy, ie as an alternative to BDP in patients uncontrolled at step 2 of the BTS guidelines instead of progressing to step 3. In the complainant's view, Alvesco should only be used at step 2 of the BTS guidelines in the small number of patients who were uncontrolled with BDP therapy (the PCT's first choice inhaled steroid) because compliance was compromised by oral side effects.

Altana's response stated that the representative who had spoken to the practice nurse had understood that the complainant had endorsed the use of Alvesco once BDP had not been successful and before resorting to combination therapy. This was not so.

The promotional literature for Alvesco placed the product as an alternative to BDP at step 2 of the BTS guidelines in patients uncontrolled on BDP without any reference to poor compliance. The BTS guidelines, however, did not indicate that patients uncontrolled at step 2 on one inhaled steroid should try an alternative inhaled steroid; patients in whom asthma was uncontrolled should progress to step 3. The Panel noted that Altana had referred to the 'tight confines of the agreement with the complainant'. In the Panel's view, however, the promotional literature positioned Alvesco for a wide range of patients.

The Panel considered it unlikely that the complainant, head of prescribing at a PCT, would endorse a course of action which was not referred to in the BTS guidelines and this was supported by the complainant's comments. The complainant's name had been used, with his permission, by a representative during the course of promoting Alvesco. The promotional literature positioned Alvesco in a way which was not referred to in the BTS guidelines, ie as an alternative for use in any patient uncontrolled on BDP. The Panel thus considered that, on the balance of probability, the practice nurse had been led to believe that the complainant endorsed Altana's positioning of Alvesco which was not so. The Panel considered that the representatives had failed to maintain a high standard of ethical conduct and had failed to comply with all relevant requirements of the Code. Formal permission had not been obtained in relation to the quotation used by the representative with the practice nurse, ie the misquotation. Breaches of Clauses 7.2, 7.4, 9.1, 11.3 and 15.2 were ruled. The Panel ruled no breach of Clause 7.6 as that clause related to references to published studies.

The Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 of the Code which was used as a sign of particular censure.

APPEAL BY ALTANA

Altana had serious concerns about the decisions of the Panel, having regard to the balance of the evidence available to it. For example, the whole complaint was based on a piece of unattributed hearsay from an unidentified individual.

Secondly, Altana was equally concerned to learn of the serious breaches of the complaints procedure in this case. These were not just technical irregularities: they significantly disadvantaged Altana and it was clear that they materially affected the outcome of the Panel's deliberations.

Altana strongly supported the ABPI and was happy to be subject to the rules and procedures for complaint handling. However, the Authority clearly had a duty to deal with complaints under the procedure in a fair manner. Regrettably, in this instance, Altana believed strongly that the complaints procedure had been dealt with in a manner that was grossly unfair to the company.

Altana submitted that the complaint relied entirely upon the content of a meeting between an Altana representative and an unnamed nurse in the local area on an unspecified date. There was no dissatisfaction with the conduct of two other Altana representatives at a meeting with the complainant.

Altana noted that the complainant had stated that he 'learned' of the meeting between 'a nurse' and an Altana representative and that he was 'incensed' to learn what was allegedly said by the nurse. The alleged content of this meeting formed the basis of his complaint. The complainant did not name his source (other than as a nurse in a GP surgery in a local area) nor crucially did he indicate whether this was reported directly to him by the nurse or whether via one or more other persons. He gave no details about the time or the place of the meeting.

Altana submitted that there were two obvious issues which applied to a complaint of this nature. Firstly without knowing the basic details of the meeting the company could not introduce the contemporaneous meeting notes made by the representative and entered into a database (as per company policy) as a reasonable counterbalance to this unsupported 'hearsay' provided by the complainant. This was unfair and put Altana at an extreme disadvantage. Secondly, the complaint was based on what the

complainant learnt had been said by an unidentified person. This was highly unsatisfactory. No indication was given how he learnt about what had been said, nor who told him. The story might have come through any number of intermediaries. In most tribunals such uncorroborated hearsay evidence was treated with extreme caution and not given the same weight as more direct evidence.

Altana submitted that the representative indicated that in meetings with nurses in the local area during the possible timeframe for the 'undisclosed' meeting he did not deviate from the prescribed Altana position that Alvesco was for 'step 2 asthma as an alternative to BDP, if management using BDP had been unsuccessful'.

Altana submitted that in cases such as this where, through lack of available evidence, one could not reasonably discern the content of a meeting, then the Panel should base its ruling on the hard evidence submitted. These were the Alvesco promotional materials and the SPC used by the representative during promotional calls. These had been reviewed by the Panel. Altana submitted that the promotional materials were consistent with the SPC for Alvesco, the Code and the BTS guidelines.

Altana noted the Panel stated that 'A judgement had to be made on the available evidence bearing in mind that extreme dissatisfaction was usually necessary on the part of an individual before he was moved to actually submit a complaint'. However when the 'extreme dissatisfaction' was based upon unsupported 'hearsay' from an undisclosed third party it was surely inappropriate to allow such tenuous sentiment to form any part of the consideration, especially when it appeared to weigh so heavily in favour of the complainant.

Altana submitted that given the paucity of confirmed evidence of a material breach of the Code at the Panel level (other than the literature submitted by Altana), then the Panel's ruling should be reversed. Not only was the Panel's ruling based on poor evidential foundations, but the position was exacerbated by the manner in which the complaint had been handled.

Altana was also deeply concerned that the Panel had prejudiced the outcome of this case by not conducting its investigation according to documented procedures. The Panel had a duty to provide a fair and balanced process to all parties during its work. There were three serious breaches of the Constitution and Procedure as follows:

1 Following receipt of the complaint, Altana supplied a formal response to the Authority. This response (which included confidential materials) was shown in its entirety to the complainant. There was no provision for this under Paragraph 6.1 of the Constitution and Procedure. This allowed the complainant to refine his complaint and expand upon it using the contemporaneous notes written by Altana employees as the template for this adaptation.

2 Where materials viewed by the respondent were considered to be confidential, there was a procedure for determining whether or not they ought to be provided to the complainant. There was no indication that such a procedure was ever followed in this case.

3 More seriously, however, the complainant's comments upon Altana's response were not shown to Altana prior to the Panel making a ruling. This was a clear breach of Paragraph 6.1 of the Constitution and Procedure and seriously prejudiced the outcome of the case. As had been noted in the introduction above, Altana was denied the opportunity to respond to the expanded allegations. On any basis, this was grossly unfair.

Altana submitted that the unsatisfactory nature of the evidence on which the original complaint was based was therefore compounded by the manner in which the procedures were not followed

In summary, Altana submitted that; there was a lack of substantiated evidence about the contents of the meeting between an Altana representative with an unnamed nurse in the local area. The evidence relied upon by the complainant was unsatisfactory and based on unsourced and uncorroborated hearsay; these evidential failings had been exacerbated by significant breaches of procedure by the Panel when handling the complaint, which had caused substantial unfairness and seriously prejudiced the outcome. Accordingly, Altana submitted that this judgment must be overturned in its entirety.

COMMENTS FROM THE COMPLAINANT

The complainant noted that Altana appealed on two fronts, firstly on the evidence and secondly that procedures were not followed by the Panel. Accordingly, the complainant restricted his response to countering the evidential areas.

The complainant noted that Altana had re-stated its position for Alvesco, which was for 'step 2 asthma as an alternative to BDP, if management using BDP had been unsuccessful'. Additionally, Altana did not deny that the name of the PCT, and the complainant's in particular, were used during this promotional activity.

The complainant stated that his complaint was based upon the fact that Altana was using his name in combination with a product positioning statement with which he entirely disagreed. Altana's placement was not in keeping with the current BTS guidelines and the complainant would never endorse a product recommendation that was outside such a well recognised national guideline.

The complainant noted that the Panel ruled breaches in Clauses 7.2, 7.4, 9.1, 11.3 and 15.2. Clause 11.3 related to using quotations with formal permission, the complainant had not given Altana permission to use his name or the name of the PCT in the endorsement or promotion of Alvesco but merely to state that they had met.

The complainant noted that Clauses 7.2 and 7.4 related to promotional claims being accurate and capable of substantiation. Altana disputed the content of his meeting with Altana and about his endorsement of Alvesco were inaccurate and could not be formally substantiated. Altana's account of the meeting was at odds with the account previously submitted by the complainant. Nonetheless, the complainant confirmed that it was his extreme dissatisfaction when he learned that he was being

quoted in support of a product placement he would never endorse, that prompted him to complain.

The complainant noted that the final two breaches (Clauses 9.1 and 15.2) related to maintenance of high standards overall and for representatives in particular. Given the information above he contended that the original rulings were appropriate on all counts, formal permission was not obtained; information used was misleading and could not be substantiated and high standards were not maintained. As such the original rulings should be sustained.

Finally, the complainant noted that much of Altana's appeal was based upon the unknown identity of the practice nurse who met with the Altana representative and the mode of communication of the content of this meeting to him. The complainant confirmed that the nurse in question met with the Altana GP representative at the end of June 2006. She telephoned the complainant directly to ask for his confirmation, or otherwise, of the content of this meeting.

The complainant provided a copy of a letter from the nurse in question giving her account of the meeting and the telephone call immediately after, that would corroborate his version of events. The complainant trusted that this letter would confirm that the 'unnamed nurse' existed and moreover that the meeting described in his complaint occurred.

In summary, the complainant appreciated fully the difficulties in reaching a decision when presented with two conflicting accounts of the same meeting. The complainant submitted that if he had met with representatives from Altana and was in agreement with the positioning of its product he would grant permission to promote it in combination with his name and that of the PCT. The very fact that in this instance the complainant had felt compelled to complain and devote several hours to submitting his complaint and responding to this appeal must give some inclination to the level of dissatisfaction he felt in regard to the conduct of the Altana representatives. As a direct consequence of this incident the complainant categorically told all representatives with whom he met that they could not use his name or the name of the PCT in any activities, promotional or otherwise. The representatives were told this at the beginning of the meeting and given the opportunity to leave if it was not acceptable to them. This was now PCT policy.

APPEAL BOARD RULING

The Appeal Board noted that the complainant had alleged that, following a meeting with two Altana representatives, he had been misquoted by a third. The complainant had stated that during the meeting with the Altana representatives he had repeatedly been asked to endorse Alvesco after BDP as an alternative to other steroids and to step 3 of the BTS guidelines. The complainant had submitted that this request had been repeatedly refused. However, the complainant had found out that another Altana representative had subsequently used his name to endorse this product positioning when discussing Alvesco with a practice nurse. It appeared that the complainant had not met with the representative who had talked to the practice nurse and so any information that that representative had must have come from those who met with the complainant.

The Appeal Board noted that one of the representatives who had met with the complainant had emailed an account of that meeting to, *inter alia*, the representative who had subsequently visited the practice nurse. It was noted in the email that the meeting with the complainant had lasted an hour and a half during which time he had 'finally came round to agreeing that as long as a GP had tried BDP first of all and wanted to then use Alvesco as their next step particularly instead of using a combination then he was happy with that'. It was also noted in the email that the complainant was not willing to put something about Alvesco in a newsletter. The email later advised the reader 'to really spread the word across [local] GPs and [practice nurses] that our positioning of 'after BDP and before combinations' is one that [the complainant] and the PCT supports and endorses. [The complainant] eventually stated that those patients who are poor compliers or potentially poor compliers, those who have oral side effects, those who are fearful of [inhaled corticosteroids], those who would benefit from the convenience of OD (all the patient types we talked to him about) are all patients that [he] is happy for Alvesco to be used on. If Alvesco is used rather than a combination then he is very happy with that. He confirmed he would not come down on any GP who uses Alvesco after BDP especially if they have a rationale for doing so'. The email concluded by ' … we can really blitz [certain areas] and drive the business forward'.

The Appeal Board considered that the email showed that the representative had had to work extremely hard to get any agreement out of the complainant. Agreements gained in such circumstances should be treated with caution. The Appeal Board considered that following such a protracted discussion the representative should have written to the complainant so that both parties could confirm their understanding of what had been agreed. It was beholden upon representatives to be abundantly clear when using the names of health professionals to endorse a promotional message. In circumstances where companies sought to gain the endorsement of public bodies ie PCTs and the like, for their products, the Appeal Board considered that they would be well advised to confirm formal agreement before making such endorsement known.

On the evidence before it, the Appeal Board was satisfied on the balance of probabilities that the complainant's views about the positioning of Alvesco had been misrepresented. The Appeal Board upheld the Panel's rulings of breaches of Clauses 7.2, 7.4, 9.1, 11.3 and 15.2 of the Code. The appeal was thus unsuccessful.

Complaint received **9 June 2006**

Case completed **25 September 2006**

CASE AUTH/1848/6/06

MEDIA/DIRECTOR v JANSSEN-CILAG

Payments offered to journalists

An article in PR Week headed '[a public relations company] in NICE apology for media cash carrot', criticised the activities of the PR company in relation to Eprex (epoetin alfa), a Janssen-Cilag product. In accordance with custom and practice the matter was taken up as a complaint under the Code.

The article stated that ahead of a National Institute for Health and Clinical Excellence (NICE) appeal hearing, a public relations (PR) company emailed reporters to offer them £200 if they wished to attend the hearing. The appeal concerned NICE's rejection of the use of erythropoietins for chemotherapy-induced anaemia.

The Panel noted that there was a contractual agreement between Janssen-Cilag (via Johnson & Johnson) and the PR company. Janssen-Cilag had submitted that the PR company's actions in this case had gone beyond that agreement. In the Panel's view, however, companies were responsible for the actions or omissions of their agents, when acting on their behalf, even if such were contrary to the agreement which existed between the two. If this were not so then it would be possible for agents to undertake any activity beyond the scope of contractual agreements, on behalf of a company, which the company could not do itself, and so avoid the restrictions of the Code.

Although Janssen-Cilag knew nothing of it, the PR company whilst in effect acting for Janssen-Cilag had offered to pay journalists to attend a meeting. The Panel considered that Janssen-Cilag was responsible under the Code. Janssen-Cilag had been let down by its agent. The Panel considered that high standards had not been maintained. Breaches of the Code were ruled including a breach of Clause 2 as the Panel considered that the offer to pay journalists to attend a meeting brought discredit upon, and reduced confidence in, the pharmaceutical industry.

Upon appeal by Janssen-Cilag the Appeal Board noted that the agreement between the PR company and Janssen-Cilag in the UK derived from a global agreement originating from Johnson & Johnson in the US. The Appeal Board considered, however, that in the UK there was insufficient clarity locally on both sides of the PR company's responsibilities under the Code. The Appeal Board noted that Janssen-Cilag had run compliance training for the agency and had had conversations about the Code with the agency. However it considered that verbal agreements and assumptions concerning the PR company's detailed knowledge of the Code were insufficient. A formal requirement that all materials be provided to Janssen-Cilag prior to use might have prevented the problem. The Appeal Board considered that Janssen-Cilag had not actively managed its PR agency or taken all reasonable steps to ensure its agent did not breach the Code.

The Appeal Board considered that Janssen-Cilag was, despite being unaware, responsible for the PR company offering to pay journalists to attend a meeting. The Appeal Board considered that high standards had not been maintained and that the offer to pay journalists to attend a NICE meeting bought discredit upon and reduced confidence in the pharmaceutical industry. The Appeal Board upheld the Panel's ruling's of breaches of the Code including the ruling of a breach of Clause 2.

An article in PR Week, 9 June, headed '[a public relations company] in NICE apology for media cash carrot', criticised the activities of a PR company in relation to Eprex (epoetin alfa), a Janssen-Cilag Ltd product. In accordance with custom and practice the matter was taken up as a complaint under the Code.

COMPLAINT

The article stated that ahead of a National Institute for Health and Clinical Excellence (NICE) appeal hearing, a public relations (PR) company sent an email to reporters saying 'As it is possible that the hearing will take up most of the day, and we understand that your time is valuable, we are able to offer £200 (€293) if you wish to attend'. The appeal concerned NICE's rejection of the use of erythropoietins for chemotherapy-induced anaemia.

When writing to Janssen-Cilag, the Authority asked it to respond in relation to Clauses 2, 9.1 and 19 of the Code.

RESPONSE

Janssen-Cilag stated that the article indicated that a PR company had advised that it was working for Ortho Biotech, a division of Janssen-Cilag and part of the Johnson & Johnson group. Eprex had been mentioned for which Janssen-Cilag held the UK marketing authorization.

Janssen-Cilag knew that under the Code pharmaceutical companies were responsible for activities undertaken by their agents. It contended, however, on this occasion that Janssen-Cilag was not in breach of the Code.

Janssen-Cilag explained that the global PR company was retained by Johnson & Johnson (and wholly owned subsidiary companies such as Janssen-Cilag) to work on, *inter alia*, projects related to Eprex. As part of this work, the PR company had assisted Janssen-Cilag to manage issues related to the negative opinion by NICE of the use of epoietins for chemotherapy-induced anaemia. Janssen-Cilag, among others, had appealed this decision; the appeal was scheduled for hearing on Friday, 2 June.

A contractual agreement, 'General Agreement', had existed between Johnson & Johnson and the PR company since January 1999. Within the terms of this General Agreement, Johnson & Johnson included the corporation, its affiliates, subsidiaries, offices and franchises including international affiliates, subsidiaries, offices and franchises. The PR company

included its offices, subsidiaries and affiliates including international offices, subsidiaries and affiliates. Thus within the terms of this contractual framework, activities undertaken between the PR company and Janssen-Cilag within the UK were bound by the terms of this General Agreement.

Within the General Agreement was a further document, the 'Work Order Agreement', which constituted the mandatory model for all project assignments between the PR company and Johnson & Johnson.

Prior to the NICE appeal on 2 June, Janssen-Cilag found out through a news wire report that a PR agency had offered journalists cash to attend the NICE erythropoietin appeal. The report stated that the PR company had emailed journalists telling them that 'as it is possible that the hearing will take up most of the day, and we understand that your time is valuable, we are able to offer £200 if you wish to attend'.

This financial incentive to attend was made known to NICE and its chairman publicly condemned it and in a broader media statement added that 'it is disappointing that a PR firm finds it necessary to offer financial incentives for journalists to attend NICE public appeal hearings'.

Immediately Janssen-Cilag became aware of this news report, commentary was made in respect of the following:

1 that offering cash incentives to attend public hearings was entirely inappropriate,

2 that whilst acknowledging a PR company worked on the company's behalf, that Ortho Biotech was not aware of, nor did it sanction the offering of payments.

Following the press reports, the chief executive of the PR company in the UK emailed a retraction to the journalists who had been offered a payment to attend the NICE appeal hearing stating:

1 that the matter was a serious misinterpretation of the PR company policy,

2 stressing that the action took place without the knowledge of its client, Ortho Biotech and that such activity would not have received its sanction,

3 noting that NICE appeal hearings had been freely open to the press and public since October 2004.

The chief executive of the PR company in the UK contacted the chairman of NICE directly and apologised. Additionally, a senior executive from Johnson & Johnson in Europe also contacted the chairman expressing concern that such activity had taken place and apologising. The chairman indicated the matter was closed.

The PR company accepted responsibility for its actions, blaming human error, and re-affirming publicly that its client (Ortho Biotech/Janssen-Cilag) was not aware nor would have sanctioned such activities.

In respect of Clause 9.1, Janssen-Cilag asserted that with regard to its own actions high standards were maintained. The PR company publicly stated that Janssen-Cilag was unaware of its offer to pay journalists and that Janssen-Cilag would not have sanctioned such payment. These comments were made on the basis of the agreement between Janssen-Cilag as a subsidiary company of Johnson & Johnson, and the General Agreement which existed between the PR company and Johnson & Johnson:

1 Within the General Agreement and in particular the provision of services within that document it explicitly stated that '[the PR company] covenants that it will abide by all applicable laws and regulations in the exercise of any work it may do for the Client'.

2 The work order agreement (previously stated as the mandatory model for all project assignments between the PR company and Client [Johnson & Johnson Company]) specifically outlined a description of activities undertaken in preparation for the NICE appeal and demonstrated due diligence by Janssen-Cilag in respect of contractual work expected to be carried out by the PR company.

Additionally, as a matter of practice, Janssen-Cilag required all of its contractors to participate in a company run training session so they were familiar with the company's code of ethics and guidelines as well as local laws and regulations. The PR company staff had undertaken such training. Therefore Janssen-Cilag expected agents or contractors operating on its behalf to comply fully with the appropriate laws and regulations, and failure to do so was considered a serious breach of contractual obligation.

Janssen-Cilag therefore contended that with respect to the contractual arrangements which allowed the PR company to act as agent for Janssen-Cilag, it demonstrated a high degree of integrity. The actions leading to this complaint were the errant actions of an individual employee of the PR company. This in no way detracted from the due diligence undertaken by Janssen-Cilag. It therefore denied a breach of Clause 9.1.

With regard to Clause 2, Janssen-Cilag reiterated the points above in relation to Clause 9.1. The company further noted that the article in question clearly stated that the PR company had blamed human error for what it described as a total breach of policy. Additionally, the UK chief executive for the PR company also stated that the offer to pay journalists was not something the client knew about and was a mistake by an individual; again clearly stating that this was a result of a failure of one person to follow company procedure which had resulted in a serious breach of policy.

Janssen-Cilag submitted that this had been an isolated (albeit serious) breach of the PR company's policy and procedure. In the news article in question, the author centred the blame on the PR company rather than Ortho Biotech/Janssen-Cilag, as indeed did the chairman of NICE who stated 'it is disappointing that a PR firm finds it necessary to offer financial incentives for journalists to attend NICE public appeal hearings'. The discredit therefore was not aimed at the pharmaceutical industry; if it was aimed anywhere it was at the PR industry.

The Code gave examples of activities that were likely to be in breach of Clause 2; these included the conduct of company employees/agents that fell short of competent care and multiple/cumulative breaches of a similar and serious nature within a short period of time. Within this framework, accepting that although the incident was serious and that the PR company was indeed Janssen-Cilag's agent, Janssen-Cilag submitted that the incident was isolated and reiterated the strong contractual arrangements it had with the PR company to ensure compliance with laws and regulations. Further Janssen-Cilag also reiterated the PR company's own admission that the incident occurred due to the actions of an individual acting in breach of company policy.

While admitting that journalists had been offered a payment, which was indeed a serious breach of policy, by way of the arguments expounded above, Janssen-Cilag sought to mitigate culpability and thus denied a breach of Clause 2.

With regard to Clause 19 Janssen-Cilag appreciated that NICE appeals were open to journalists and indeed the general public and had already stated that it considered it inappropriate that journalists were offered a payment to attend. As previously stated, Janssen-Cilag was not aware of the offer and hence could not answer specifically with respect to Clause 19 or any of its sub clauses. Again Janssen-Cilag argued that such actions were outside of the policy framework and contractual obligation that the PR company had to Janssen-Cilag, and hence again denied breach of Clause 19.

PANEL RULING

The Panel noted that there was a contractual agreement between Janssen-Cilag (via Johnson & Johnson) and a PR company. Janssen-Cilag had submitted that the PR company's actions in this case had gone beyond that agreement. In the Panel's view, however, companies were responsible for the actions or omissions of their agents, when acting on their behalf, even if such acts or omissions were contrary to the agreement which existed between the two. If this were not so then it would be possible for agents to undertake any activity beyond the scope of contractual agreements, on behalf of a company, which the company could not do itself, and so avoid the restrictions of the Code.

The supplementary information to Clause 20.2 stated, *inter alia*, that meetings organized for or attended by journalists must comply with Clause 19. The supplementary information to Clause 19.1 stated that delegates must not be offered compensation merely for their time spent at meetings. Although Janssen-Cilag was unaware of the specific activity, the PR company whilst in effect acting for Janssen-Cilag had offered to pay journalists to attend a meeting. The Panel considered that Janssen-Cilag was responsible under the Code. Janssen-Cilag had been let down by its agent. The Panel ruled a breach of Clause 19.1 of the Code. This ruling was accepted by Janssen-Cilag. The Panel considered that high standards had not been maintained. A breach of Clause 9.1 was ruled.

The Panel considered that the offer to pay journalists to attend a meeting brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 of the Code was ruled.

APPEAL BY JANSSEN-CILAG

Janssen-Cilag appealed the Panel's rulings of breaches of Clauses 2 and 9.1 of the Code. In particular, the company considered that it had acted entirely properly in respect of contractual arrangements with the PR company, and failed to understand how, because of the unauthorised action of an employee from the PR company, it had been found to be in breach of Clause 2 of the Code.

Janssen-Cilag submitted that the complaint had arisen from the inexplicable and unforeseeable actions of one errant individual within the PR company. The agency had confirmed in writing that the company had not requested, nor was aware, of the individual's actions. Furthermore, that individual had acted in clear contravention of both Janssen-Cilag policies and those of the PR company.

Janssen-Cilag understood that the Panel had based its ruling on Clause 1.2 of the Code where the definition of promotion included any action undertaken by a pharmaceutical company, or with its authority, which promoted the prescription, supply, sale or administration of its medicines. This had been interpreted to mean that companies were responsible for PR agencies acting on their authority.

Janssen-Cilag submitted that it was clear and logical that companies should usually be accountable for the actions of PR agencies acting on their authority. Without this provision, companies could avoid compliance with the Code by merely instructing PR agencies to undertake tasks for them. However, a company should not necessarily be accountable for the actions of its PR or advertising agency when it was clear that neither the company, nor indeed the relevant agency, intended the agency to act in the way that it did. Janssen-Cilag noted previous relevant cases, Case AUTH/1087/10/00 and Case AUTH/1028/6/00 in which it was accepted that there were circumstances where an advertising agency might be at fault and not the pharmaceutical company, which had taken reasonable steps to comply with the Code.

Janssen-Cilag submitted that the same rationale applied now. In the current case, Janssen-Cilag took all reasonable steps to avoid a breach of the Code and to control the actions of its PR agency. There was a contract in place in which the PR agency covenanted to abide by all applicable laws and regulations in the exercise of any work it did for the company. Janssen-Cilag had even taken the additional precautionary step of performing due diligence in respect of the agency's policies.

Janssen-Cilag submitted that the employee who offered to pay journalists had acted contrary to the PR company's policies. There could be no suggestion that he/she had acted on the authority of Janssen-Cilag or the PR agency. The employee's action had been described very specifically by the company as errant. The employee's actions were thus unforeseeable and unpredictable, and there were no

steps that it could have taken to prevent such inexplicable action being taken by a maverick employee of a third party.

Janssen-Cilag submitted that it had acted honourably and openly at every stage of this situation. The action taken by the company, and the PR agency, immediately upon becoming aware of the situation, was swift and strong. The PR agency explained the situation to NICE, which declared the matter closed. It was hard to reconcile this with the Panel's ruling that Janssen-Cilag's conduct had brought discredit upon, and reduced confidence in, the pharmaceutical industry.

Janssen-Cilag submitted that with respect to high standards, should a contract stipulate that relevant codes of practice were adhered to, then it expected its agents to adhere to them. Specifically for the future no payments should be offered to journalists to attend a meeting, however this was already covered in respect of reference to Clauses 19 and 20.2 and the supplementary information. Short of stating every conceivable scenario in advance within a contract Janssen-Cilag failed to understand how it had not maintained high standards (Clause 9.1).

Notwithstanding the above Janssen-Cilag also failed to understand what further reasonable steps it could take to prevent completely unexpected actions of an errant individual acting contrary to his/her own company's policies and in breach of the contractual obligation to it. Janssen-Cilag therefore could not give a meaningful undertaking that similar breaches of the Code would not occur at some future time despite of its due diligence. Such actions were entirely out of its, or indeed any other pharmaceutical company's, control.

COMMENTS FROM THE JOURNALIST

The journalist made no comment.

APPEAL BOARD RULING

The Appeal Board noted that there was a contractual agreement between Janssen-Cilag (via Johnson & Johnson in the US) and a PR company. Janssen-Cilag submitted that the PR company's actions had gone beyond that agreement. The Appeal Board considered that as the agreement between the PR company and Janssen-Cilag in the UK derived from a global agreement, there was insufficient clarity locally on both sides of a PR company's responsibilities under the UK Code. The Appeal Board noted that Janssen-Cilag had run compliance training for the agency and had had conversations about the Code with the agency. However it considered that verbal agreements and assumptions concerning the PR company's detailed knowledge of the Code were insufficient. A formal requirement that all materials be provided to Janssen-Cilag prior to use might have prevented the problem. The Appeal Board considered that Janssen-Cilag had not actively managed its PR agency or taken all reasonable steps to ensure its agent did not breach the Code.

The Appeal Board noted that Janssen-Cilag accepted the Panel's ruling of a breach of Clause 19.1 of the Code. It considered that Janssen-Cilag was, despite being unaware, responsible for a PR company offering to pay journalists to attend a meeting. The Appeal Board considered that high standards had not been maintained and it upheld the Panel's ruling of a breach of Clause 9.1 of the Code. The Appeal Board considered that the offer to pay journalists to attend a NICE meeting bought discredit upon, and reduced confidence in, the pharmaceutical industry. The Appeal Board upheld the Panel's ruling of a breach of Clause 2.

Proceedings commenced **20 June 2006**

Case completed **25 September 2006**

MEDIA/DIRECTOR v ASTRAZENECA

Disclosure of patient group involvement

An article in The Financial Times of 20 June claimed that two leading pharmaceutical companies, one of them AstraZeneca, were delaying disclosure of their funding of patient groups. In accordance with established practice the criticism was treated as a complaint under the Code of Practice.

The article stated that the companies were delaying disclosure of patient groups they funded for up to 18 months after the new Code called for publication of the data. The companies were quoted as stating that they believed that they did not have to reveal the list of patient groups they supported until their annual reports were released in Spring 2007.

The Panel noted that the supplementary information to the Code stated, *inter alia*, that:

'Any involvement a pharmaceutical company has with a patient organisation must be declared and transparent. Companies must make public by means of information on their websites or in their annual report a list of all patient organisations to which they provide financial support. This might include sponsoring materials and meetings.'

The two methods of disclosure provided for in the supplementary information were alternatives. A company could disclose the requisite information either on its website or in its annual report. Clearly the timeframe for first disclosure would be different in each case.

If a company disclosed the information on its website it would have to keep the information as up-to-date as possible. That is to say that the website would have to provide up-to-date information at all times. On the other hand, if a company disclosed the information in its annual report it would of necessity be retrospective as each annual report would cover a year ending some time earlier. That was an inevitable consequence of the wording of the supplementary information.

As far as the introduction of the requirement was concerned, the Panel considered that by 1 May 2006, the date when the transitional provisions in the new Code expired, a website providing the information would have to fully disclose all involvements with patient organisations which had been entered into on or after 1 January 2006, when the new Code became operative, or which had been entered into prior to that date but were still ongoing at that time.

If a company had decided to disclose the information in its annual report, the Panel considered that the information would have to appear for the first time in the first annual report which covered any period commencing on 1 January 2006. If a company's annual report was on a calendar year basis, this would be the annual report for 2006 which would be published in 2007. If a company's annual report was not on a calendar year basis it would be its annual report for 2005/2006. As with disclosure on a website, the information to be published in the first instance would be all involvements with patient organisations which had been entered into on or after 1 January 2006, or which had been entered into previously but were still ongoing at that date.

The Panel considered that some companies might initially decide to publish retrospective information about their involvement with patient organisations in their annual report but subsequently decide to publish up-to-date information on their website. It would thus be fundamentally unfair to rule such companies in breach of the Code for publishing data on their websites later than 1 May 2006 but sooner than would have been the case if they had waited for their annual report to be published.

In view of its interpretation of the requirement, the Panel considered that AstraZeneca's actions were not unacceptable. No breach the Code was ruled.

During its consideration of this case the Panel noted that companies were required to comply with both the spirit and the letter of the Code. In that regard, the Panel considered that companies which published retrospective details of their involvement with patient organizations in their annual reports must, nonetheless, be prepared to make available up-to-date information about such activities at any time in response to enquiries.

An article in The Financial Times of 20 June claimed that two leading pharmaceutical companies, one of them AstraZeneca UK Limited, were delaying disclosure of patient groups funded by them. In accordance with established practice the criticisms were treated as a complaint under the Code of Practice.

COMPLAINT

The article stated that the companies were delaying disclosure of patient groups they funded for up to 18 months after the new Code called for publication of the data. The companies were quoted as stating that they believed that they did not have to reveal the list of patient groups they supported until their annual reports were released in Spring 2007.

When writing to AstraZeneca the Authority asked it to respond in relation to Clause 20.3 of the Code and its supplementary information.

RESPONSE

AstraZeneca stated that it took corporate governance and compliance with both the letter and the spirit of the Code very seriously and as such had been working since late 2005 to ensure compliance with the 2006 Code.

AstraZeneca explained that an appropriate website design was identified in early 2006 and had been developed subsequently. Care had been taken to ensure listing of appropriate information within the site, within an easy to access format, to ensure compliance with the relevant elements of the Code.

The original planned release date was 1 August.

The website list of patient groups went 'live' on 20 June in response to the article in The Financial Times and consultation with the Authority.

AstraZeneca stated that it operated a number of different business arms within the UK. Its UK marketing company was based in Luton and was responsible for all the sales and marketing activities that took place with respect to UK health professionals. Some of AstraZeneca's global marketing teams were based in Cheshire, as were some of its research and development teams. Across the UK it also had a number of other research and science sites, such as those in Edinburgh, Loughborough and Brixham, and a number of pharmaceutical manufacturing and distribution sites. AstraZeneca's international corporate offices were based in London. All these businesses interacted with their local communities and customers in a wide range of activities.

Since January, as well as identifying its own relevant interactions, the UK marketing company had liaised with the global teams around the implications of the new Code requirements to ensure that it was provided with accurate details on any global activities with UK patient groups.

Early in 2006, the UK marketing company established a process to ensure that it did not make any payments to UK patient groups until a transparency agreement had been signed. This agreement detailed the principles on which the two organisations would work together and included the need to comply with all aspects of the Code. The transparency agreement included consent to publish details on the AstraZeneca website, as it would be inappropriate to list organisations without their permission. Therefore no publications could be made until the transparency agreements had been signed. No financial support was released to any patient group until the agreement was signed. On 23 February 2006 the first transparency agreement was signed.

Three examples of signed transparency agreements were provided and all were available for scrutiny.

The process supporting the transparency agreements had evolved during the early part of 2006 to ensure its effectiveness and robustness and now included a certified template for the agreement; early versions were certified individually. Emails pertaining to the new process were provided as was a copy of the certified template.

As at 3 July, 18 transparency agreements had been signed and the relevant patient groups were now listed at www.astrazeneca.co.uk/responsibility/patient-groups.asp.

AstraZeneca had a comprehensive sponsorship policy, which was last revised in June 2005. This required all sponsorship applicants (including patient groups) to supply written details of specific projects requiring financial or other support and to sign an undertaking that the project was in keeping with the Code. Two nominated registered signatories, one of whom must be a physician, then approved the details of the project.

All projects over £5,000 (including more complex projects) were also formally reviewed by a sponsorship panel which comprised the legal director, the head of medical specialist care, the company compliance lead, the head of meetings management, the UK marketing company financial controller and an experienced senior physician.

AstraZeneca considered that The Financial Times had misrepresented the company's position with respect to compliance with Clause 20.3. Details of the written interaction with the journalist were provided.

With regards to the allegations made in the articles concerning the timing of the publication of patient group relationships, AstraZeneca stated:

- The supplementary information to Clause 20.3 clearly stated that a company must provide a list of patient groups either within the annual report or on a website. Thus, it could be considered acceptable for pharmaceutical companies to provide a list of those organisations supported in 2006 in their 2006 annual report – which would be published during 2007.
- There was no specific requirement in the Code to publish a list of those organisations historically supported by the company during 2005 or earlier.
- AstraZeneca believed this interpretation was in line with the Authority's own interpretation of the Authority's Constitution and Procedure Paragraph 13.6, which required all *prima facie* cases to be listed on the PMCPA website – this was updated periodically rather than daily (provided was a print out from the website on 27 June) and only listed cases since 1 January 2006).

As requested by the Authority, a full list of patient organisations which had received support from AstraZeneca in 2006 was provided. Currently only the list of names was made public. Copies of the signed transparency agreements would shortly appear on the AstraZeneca website next to the name of the patient group. At this stage AstraZeneca did not publicly declare the details of the specific interactions with each group, however these activities were of course available to the Authority on request.

In summary, as of 1 May 2006, AstraZeneca had not published on a website a list of all patient organisations due to its interpretation of the Code. However, it had undertaken a wide range of activities to ensure proper compliance with the Code in a reasonable and timely fashion, as detailed above. Finally, The Financial Times misrepresented the company's position opposite this issue.

AstraZeneca denied any breach of Clause 20.3 of the Code.

PANEL RULING

The Panel noted that the supplementary information to Clause 20.3 of the Code stated, *inter alia*, that:

'Any involvement a pharmaceutical company has with a patient organisation must be declared and transparent. Companies must make public by means of information on their websites or in their annual

report a list of all patient organisations to which they provide financial support. This might include sponsoring materials and meetings.'

The two methods of disclosure provided for in the supplementary information to Clause 20.3 were alternatives. That is to say that a company could disclose the requisite information either on its website or in its annual report. Clearly the timeframe for first disclosure would be different in each case.

If a company disclosed the information on its website it would have to keep the information as up-to-date as possible. That is to say that the website would have to provide up-to-date information at all times. On the other hand, if a company disclosed the information in its annual report it would of necessity be retrospective as each annual report would cover a year ending some time earlier. That was an inevitable consequence of the wording of the supplementary information.

As far as the introduction of the requirement was concerned, the Panel considered that by 1 May 2006, the date when the transitional provisions in the new Code expired, a website providing the information would have to fully disclose all involvements with patient organisations which had been entered into on or after 1 January 2006, when the new Code became operative, or which had been entered into prior to that date but were still ongoing at that time.

If a company had decided to disclose the information in its annual report, the Panel considered that the information would have to appear for the first time in the first annual report which covered any period commencing on 1 January 2006. If a company's annual report was on a calendar year basis, this would be the annual report for 2006 which would be published in 2007. If a company's annual report was not on a calendar year basis it would be its annual report for 2005/2006. As with disclosure on a website, the information to be published in the first instance would be all involvements with patient organisations which had been entered into on or after 1 January 2006, or which had been entered into previously but were still ongoing at that date.

The Panel considered that some companies might initially decide to publish retrospective information about their involvement with patient organisations in their annual report but subsequently decide to publish up-to-date information on their website. It would thus be fundamentally unfair to rule such companies in breach of the Code for publishing data on their websites later than 1 May 2006 but sooner than would have been the case if they had waited for their annual report to be published.

In view of its interpretation of the requirement, the Panel considered that AstraZeneca's actions were not unacceptable. No breach of Clause 20.3 was ruled.

During its consideration of this case the Panel noted that companies were required to comply with both the spirit and the letter of the Code. In that regard, the Panel considered that companies which published retrospective details of their involvement with patient organizations in their annual reports must, nonetheless, be prepared to make available up-to-date information about such activities at any time in response to enquiries.

Proceedings commenced **20 June 2006**

Case completed **22 August 2006**

MEDIA/DIRECTOR v NOVARTIS

Disclosure of patient group involvement

An article in The Financial Times of 20 June claimed that two leading pharmaceutical companies, one of them Novartis, were delaying disclosure of their funding of patient groups. In accordance with established practice the criticism was treated as a complaint under the Code.

The article stated that the companies were delaying disclosure of patient groups they funded for up to 18 months after the new Code called for publication of the data. The companies were quoted as stating that they believed that they did not have to reveal the list of patient groups they supported until their annual reports were released in Spring 2007.

The Panel noted that the supplementary information of the Code stated, *inter alia*, that:

'Any involvement a pharmaceutical company has with a patient organisation must be declared and transparent. Companies must make public by means of information on their websites or in their annual report a list of all patient organisations to which they provide financial support. This might include sponsoring materials and meetings.'

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If a company had decided to disclose the information in its annual report, the Panel considered that the information would have to appear for the first time in the first annual report which covered any period commencing on 1 January 2006. If a company's annual report was on a calendar year basis, this would be the annual report for 2006 which would be published in 2007. If a company's annual report was not on a calendar year basis it would be its annual report for 2005/2006. As with disclosure on a website, the information to be published in the first instance would be all involvements with patient organisations which had been entered into on or after 1 January 2006, or which had been entered into previously but were still ongoing at that date.

In view of its interpretation of the requirement, the Panel considered that Novartis was entitled to defer disclosure until such time as it published an annual report covering from 1 January 2006 on. No breach of the Code was ruled.

During its consideration of this case the Panel noted that companies were required to comply with both the spirit and the letter of the Code. In that regard, the Panel considered that companies which published retrospective details of their involvement with patient organizations in their annual reports must, nonetheless, be prepared to make available up-to-date information about such activities at any time in response to enquiries.

An article in The Financial Times of 20 June claimed that two leading pharmaceutical companies, one of them Novartis Pharmaceuticals UK Ltd, were delaying disclosure of patient groups funded by them. In accordance with established practice the criticisms were treated as a complaint under the Code.

COMPLAINT

The article stated that the companies were delaying disclosure of patient groups they funded for up to 18 months after a new Code called for publication of the data. The companies were quoted as stating that they believed that they did not have to reveal the list of patient groups they supported until their annual reports were released in Spring 2007.

When writing to Novartis the Authority asked it to respond in relation to Clause 20.3 of the Code and its supplementary information.

RESPONSE

Novartis questioned the Authority's decision to interpret the Financial Times article as a complaint against the company; it appeared to Novartis that the article was more a criticism of the ABPI and the current lack of clarity around the Code than a specific criticism of any of the companies mentioned. Novartis trusted that this would be taken into consideration in the assessment of its response.

The issue raised by the journalist was about the interpretation of the supplementary information to Clause 20.3 of the 2006 Code that 'Companies must make public by means of information on their websites or in their annual report a list of all patient organisations to which they provide financial support'. This wording did not specify that the information had to appear on the company's web site by 1 May as suggested in the Financial Times article, but implied that companies could choose to include this information in accordance with their publication schedule for their annual reports. As the Authority would be aware, companies' annual reports were published in the subsequent year to the generation of the financial data. Companies choosing this route to publicise information on their patient organisations interactions as permitted by the Code would only be able to do so annually and retrospectively.

Although the article referred specifically to Novartis and AstraZeneca, Novartis considered that the lack of

clarity around this area of the Code was shared by the industry as a whole. Indeed Novartis noted that this confusion was shared by the ABPI. An article on the PMLive.com web site (provided) in response to the Financial Times article quoted Richard Ley, Head of Media Relations at the ABPI, as stating 'The Code of Practice is very clear in that companies have to make public on their website or in their annual review their involvement with patient groups. However for those companies that choose to reveal this in their annual report alone this could mean April 2007'.

Novartis stated that there had been no intention on its part to delay disclosure of this information; it had always intended to provide a comprehensive listing of the year's interactions in its annual report. Novartis believed that this would better serve the intention of this new requirement of the Code than including incomplete or out of date information on the company's website as suggested by the article in The Financial Times.

It appeared that the Authority's request to Novartis to explain which patient organisations the company supported, and how much support was made public, in Novartis' response to this complaint, implied that its interpretation of the Code had already been ruled as incorrect. This directly conflicted with Richard Ley's statement which had publicly confirmed Novartis' own interpretation of the Code in this context. Novartis noted that providing this information to the complainant would result in the selective disclosure of the company's interactions with patient groups. Novartis preferred not to include this information in the response to this complaint but to await the formal consideration of the case by the Panel and make such information fully public on the company's website if that was the ruling. Novartis hoped that whatever the ruling the Authority made would recognise this shared industry confusion and would publish clear guidance to all companies, including those not contacted for the article in The Financial Times.

Novartis was committed to complying with the Code and it hoped that this information would serve to clarify the company's position in relation to this issue.

PANEL RULING

The Panel noted that the supplementary information to Clause 20.3 of the Code stated, *inter alia*, that:

'Any involvement a pharmaceutical company has with a patient organisation must be declared and transparent. Companies must make public by means of information on their websites or in their annual report a list of all patient organisations to which they provide financial support. This might include sponsoring materials and meetings.'

As regards the timing and method of making this information public, the Panel noted that the ABPI was reported as having given its own view on the matter. The interpretation of the Code was for the Authority and it was the practice of the Authority to qualify any guidance it gave. If any doubt existed over the meaning of a requirement, it could be definitively resolved only by the Code of Practice Appeal Board and so far there had been no cases in this area as the requirement was new.

The Panel rejected Novartis' assertion that the Authority's initial letter on the matter implied that Novartis' interpretation of the Code had already been ruled as incorrect. The Panel had not previously considered the matter and had now come to it for the first time.

The two methods of disclosure provided for in the supplementary information to Clause 20.3 were alternatives. That is to say that a company could disclose the requisite information either on its website or in its annual report. Clearly the timeframe for disclosure would be different in each case.

If a company disclosed the information on its website it would have to keep the information as up-to-date as possible. That is to say that the website would have to provide up-to-date information at all times. On the other hand, if a company disclosed the information in its annual report, it would of necessity be retrospective as each annual report would cover a year ending some time earlier. That was an inevitable consequence of the wording of the supplementary information.

As far as the introduction of the requirement was concerned, the Panel considered that by 1 May 2006, the date when the transitional provisions in the new Code expired, a website providing the information would have to fully disclose all involvements with patient organisations which had been entered into on or after 1 January 2006, when the new Code became operative, or which had been entered into prior to that date but were still ongoing at that time.

If a company had decided to disclose the information in its annual report, the Panel considered that the information would have to appear for the first time in the first annual report which covered any period commencing on 1 January 2006. If a company's annual report was on a calendar year basis, this would be the annual report for 2006 which would be published in 2007. If a company's annual report was not on a calendar year basis it would be its annual report for 2005/2006. As with disclosure on a website, the information to be published in the first instance would be all involvements with patient organisations which had been entered into on or after 1 January 2006, or which had been entered into previously but were still ongoing at that date.

In view of its interpretation of the requirement, the Panel considered that Novartis was entitled to defer disclosure until such time as it published an annual report covering from 1 January 2006 on. No breach of Clause 20.3 was ruled.

During its consideration of this case the Panel noted that companies were required to comply with both the spirit and the letter of the Code. In that regard, the Panel considered that companies which published retrospective details of their involvement with patient organizations in their annual reports must, nonetheless, be prepared to make available up-to-date information about such activities at any time in response to enquiries.

Proceedings commenced 20 June 2006

Case completed 22 August 2006

CASE AUTH/1851/6/06

ROCHE v NOVARTIS

Promotion of Myfortic

Roche complained about the promotion of Myfortic (mycophenolate sodium) by Novartis. Roche supplied CellCept (mycophenolate mofetil).

Roche was concerned that a review article (Budde *et al* 2004), which was freely available from the Novartis stand at a UK conference, referred to ongoing or planned clinical trials of Myfortic and Cellcept in which the products were used in ways which were not consistent with their summaries of product characteristics (SPCs). Roche alleged that as the article discussed off-licence indications for both products, its use in a promotional setting was in breach of the Code.

The Panel noted that as Budde *et al* had been available at the Novartis promotional stand and used proactively for a promotional purpose it had to comply with the Code. The supplementary information to the Code stated that the legitimate exchange of medical and scientific information during the development of a medicine was not prohibited provided that any such information or activity did not constitute promotion. The Panel considered that distribution of the paper from Novartis' promotional stand was not in accordance with this supplementary information; on balance the distribution of the paper from a promotional stand was inconsistent with the SPC. A breach of the Code was ruled.

The Panel considered there was a difference between proactive provision of a paper and a clinical trial register whereby information about clinical research could be accessed by interested parties from such a website.

Roche stated that an advertisement published in Transplant International was subject to the Code because the registered office for the publisher (Blackwell Publishing Ltd) was in the UK. The advertisement was alleged to contain a number of misleading claims for Myfortic, some of which had previously been withdrawn by Novartis following inter-company discussions.

The Panel noted that the supplementary information to the Code, Journals with an International Distribution, stated that the Code applied to the advertising of medicines in professional journals which were produced in the UK and/or intended for a UK audience. International journals produced in English in the UK were subject to the Code even if only a small proportion of their circulation was to a UK audience.

Transplant International was the journal of the European Society for Organ Transplantation and the European Liver and Intestine Transplant Association and was intended for an international readership. It was clearly an international journal with an editorial office, editor-in-chief and co-editor-in-chief all based in Vienna. It was published by Blackwell Munksgaard, Germany, it was printed in, and distributed from, Singapore.

The principal UK connection was that the head office of the publisher, Blackwell Publishing, was located in Oxford. The Panel noted that Blackwell Publishing had informed Novartis that, in legal terms, the journal must be considered as being produced in the UK.

The Panel, however, had to base its decision on the wording of the Code and its supplementary information. The Panel considered that in view of the locations in which the activities associated with the journal's publication took place, it could not be regarded as having been produced in the UK. The Panel's opinion was that the word 'produced' in the supplementary information related to factors such as where an international journal was compiled and edited and where it was physically produced etc, rather than the location of the publisher's head office. Further, the journal was not intended specifically for a UK audience but for an international one. It did not come within the scope of the UK Code. The Panel accordingly ruled that there could have been no breach of the Code.

Roche Products Limited complained about the promotion of Myfortic (mycophenolate sodium) by Novartis Pharmaceuticals UK Ltd. The items at issue were a review article and a journal advertisement (ref myf1001D). Roche supplied CellCept (mycophenolate mofetil).

1 Review article 'Review of the immunosuppressant enteric-coated mycophenolate sodium', Budde *et al*, 2004

COMPLAINT

Roche stated that this article was freely available from the Novartis trade display at the British Society for Transplantation meeting, held in Edinburgh on 29-31 March. Roche's specific concerns related to the section entitled 'Future directions' which provided details of ongoing or planned clinical trials investigating the following uses of Myfortic:

- withdrawal or avoidance of steroids;
- in combination with currently licensed immunosuppressants tacrolimus or sirolimus;
- in combination with the investigational compounds everolimus or FTY 720.

Furthermore, references were made to the use of mycophenolate mofetil (MMF) and tacrolimus in steroid-sparing or steroid-free regimens.

None of these uses were consistent with the recommendations in the respective summaries of product characteristics (SPCs) for Myfortic and CellCept. As the article discussed off-licence indications for both products, its use in a promotional setting such as a trade display was in breach of Clause 3.2 of the Code.

RESPONSE

Novartis noted that Roche had alleged that the inclusion of a brief description of the design of

Myfortic clinical trials at the end of an independent review article provided on the stand at the British Society for Transplantation meeting held in March of this year was in breach of Clause 3.2 of the Code. Novartis disagreed for two reasons. Firstly, the section of the article to which Roche referred was clearly entitled 'Future directions' and was distinctly separate from the section entitled 'Clinical safety and tolerability' and secondly, no claim for the efficacy, safety or tolerability of any unlicensed use was made in association with this listing.

The ABPI had made laudable efforts to increase the transparency of clinical trial activity, with the establishment of an ABPI Clinical Trial Register in 2003. Novartis was an early contributor to this register and the ABPI website currently contained links to Novartis trial listings. It was difficult to see how the bland listing of ongoing trials in an independent review paper breached Clause 3.2 of the Code when a similar listing on a public website was both encouraged and endorsed by the ABPI as part of a commitment to increased transparency regarding industry led research. With the greater availability of such information to prospective authors it was to be expected that many more would legitimately include summaries of ongoing and proposed research in their publications as Budde *et al* had done.

PANEL RULING

The Panel noted that Budde *et al* had been available at the Novartis promotional stand. It was being used proactively for a promotional purpose and thus had to comply with the Code. The Panel noted the supplementary information to Clause 3.1 of the Code that the legitimate exchange of medical and scientific information during the development of a medicine was not prohibited provided that any such information or activity did not constitute promotion which was prohibited under this or any other clause. The Panel considered that distribution of the paper from the Novartis' promotional stand was not in accordance with this supplementary information.

The Panel considered there was a difference between proactive provision of a paper and a clinical trial register whereby information about clinical research could be accessed by interested parties from such a website.

The Panel noted that the section at issue in Budde *et al* was headed 'Future directions' and referred to ongoing clinical studies. Reference was made to different patient populations and treatment regimes including withdrawal or avoidance of steroids. Some of the results were said to be expected in 2005. No outcomes were reported. The Panel considered that on balance the distribution of the paper from a promotional stand was inconsistent with the SPC. Thus a breach of Clause 3.2 of the Code was ruled.

2 Journal advertisement

COMPLAINT

Roche stated that an advertisement published in the May edition of Transplant International was subject to the Code because the registered office for the publisher (Blackwell Publishing Ltd) was in the UK.

The advertisement contained a number of misleading claims for Myfortic, some of which had previously been withdrawn by Novartis following inter-company discussions in September 2004 and January 2005. These included:

- 'advanced, enteric-coated formulation …'; this claim was alleged to be in breach of Clauses 7.2 and 7.4;
- 'designed to avoid MPA-related upper GI adverse events'; the claim 'designed to protect the upper GI tract' was alleged to be in breach of Clauses 7.2 and 7.4;
- 'The next step'; this claim was alleged to be in breach of Clauses 7.2 and 7.4.

The advertisement also contained a number of other claims that were alleged to be inappropriate and misleading:

- 'my protection' and subsequent 'patient quote'; this claim suggested clinical superiority of Myfortic in respect to CellCept: Roche stated that randomised head-to-head comparisons of CellCept and Myfortic had shown no statistically significant differences in terms of efficacy or safety or endpoints; therefore this claim was misleading and alleged to be in breach of Clause 7.3;
- '… designed to avoid MPA-related upper GI adverse events* with the goal of minimizing the need for dose reductions'; the presentation of this claim was misleading, as it was not made clear to the reader that there was no statistical difference in upper GI adverse events conferred by Myfortic. A breach of Clause 7.2 was alleged as the fact that there was no statistically significant difference in upper GI adverse events was qualified in a footnote, thereby breaching Clause 7 (general supplementary information).

RESPONSE

Novartis noted that the advertisement was not produced or placed in Transplant International by the UK company. The advertisement was designed for an international audience and had been placed in an international journal and, as such, Novartis did not believe that it was subject to the Code. The supplementary information to Clause 1.1 stated that 'The Code applies to the advertising of medicines in professional journals which are produced in the UK and/or intended for a UK audience'.

Transplant International was the journal of the European Society for Organ Transplantation and the European Liver and Intestine Transplant Association, and was intended for an international audience.

The editorial office, the editor-in-chief and co-editor-in-chief of the journal were all based in Vienna. The journal was published by Blackwell Munksgaard, Germany, and it was printed in and distributed from Singapore (communication from Blackwell publishing). It was not therefore produced in the UK or intended for a specifically UK audience.

It was possible that Roche had misinterpreted the statement 'Transplant International is published by Blackwell Publishing, 9600 Garsington Rd, Oxford, UK' to mean that the journal was produced in the UK and/or was intended for a UK audience. Blackwell Publishing was a global publisher, with its head office in Oxford. It published 805 journals worldwide and had offices in the US, UK, Australia, China, Denmark, Germany, Singapore and Japan.

Novartis did not believe that the listing of a UK head office representing a global publisher was an appropriate basis for defining production or intended readership. Many other Blackwell journals, for example the American Journal of Transplantation (AJT) could, by the same reasoning be classed as 'produced in the UK and/or intended for a UK audience' and therefore all advertisements carried would need to include UK prescribing information.

Following receipt of the response further comments were received from Novartis regarding new information received from Blackwell Publishing which appeared to contradict the information previously received from Blackwell's used as the basis for Novartis' original response.

Subsequent communication from Blackwell's confirmed the accuracy of the geographical information provided but it now suggested after consultation with its legal department that the journal in question, in legal terms, must be considered as being 'produced' in the UK.

Novartis continued to believe that applicability of the Code must relate to more than an individual publishers' legal definition of 'production' when by all practical criteria this was an international journal because of its intended auidence and geographical site of editing, production and distribution.

In practical terms, it would seem extremely problematic to define all 805 journals produced by Blackwell's, including titles such as the American Journal of Transplantation, as being produced in the UK. This would require them, by the wording of Clause 1.1, to adhere to the UK Code. Novartis suggested that to date international companies worked in good faith, and on the same assumption as Novartis, in placing non-UK advertisments in certain Blackwell Journals.

INITIAL CONSIDERATION BY PANEL

The Panel gave preliminary consideration to the matter and provisionally decided that the advertisement was published in a journal which was subject to the Code. As Novartis had thus far, only responded as to whether or not the advertisment was subject to the Code it now needed to respond to the specific allegations.

Novartis was asked to respond to the allegations.

FURTHER RESPONSE FROM NOVARTIS

Novartis was surprised and disappointed by the Panel's preliminary view that advertisments appearing in Transplant International were subject to the Code. Novartis continued to believe that the respective sites of publication, editing, printing and distribution of a journal, together with it purpose and readership, should be considered in addition to the location of the publisher's global head office when defining the location of 'production' of a journal.

With regard to the specific allegations made by Roche, the claims were not used in any promotional copy employed by the UK company and the advertisement in question was not placed in Transplant International by Novartis Pharmaceuticals UK Limited. The advertisements were placed by the parent company, Novartis Pharma AG, in the reasonable belief that this was an international publication with an international readership, not subject to the UK Code or having a specifically UK audience.

Novartis in the UK reached an intercompany agreement with Roche to stop using the claims detailed in Roche's letter of 19 June to Novartis. The two additional claims referred to in Roche's complaint, represented no more than an extension of the claims previously withdrawn in the UK.

Novartis had honoured its agreement with Roche and would continue to do so for UK materials. It did not seek to defend any specific allegations.

PANEL RULING

The Panel noted that the supplementary information to Clause 1.1 of the Code, Journals with an International Distribution, stated that the Code applied to the advertising of medicines in professional journals which were produced in the UK and/or intended for a UK audience. International journals produced in English in the UK were subject to the Code even if only a small proportion of their circulation was to a UK audience.

Transplant International was the journal of the European Society for Organ Transplantation and the European Liver and Intestine Transplant Association and was intended for an international readership. It was clearly an international journal. The Panel noted that the journal's editorial office, editor-in-chief and co-editor-in-chief were all based in Vienna. It was published by Blackwell Munksgaard, Germany, and it was printed in, and distributed from, Singapore.

The principal connection between the journal and the UK was that the head office of the publisher, Blackwell Publishing, was located in Oxford. The Panel noted that Blackwell Publishing had informed Novartis that, in legal terms, the journal must be considered as being produced in the UK.

The Panel, however, had to base its decisions on the wording of the Code and its supplementary information. The Panel considered that in view of the locations in which the activities associated with the journal's publication took place, it could not be regarded as having been produced in the UK. The Panel was of the opinion that the reference to 'produced' in the supplementary information related to factors such as where an international journal was compiled and edited and where it was physically produced etc, rather than the location of the publisher's head office. Further, the journal was not intended specifically for a UK audience but for an

international one. It did not come within the scope of the UK Code. The Panel accordingly ruled that there could have been no breach of the Code.

The advertisement in Transplant International would be covered by a code of practice and it was a question of which applied. As the advertisement had been placed by Novartis Switzerland, the Swiss, Austrian and German codes might apply.

Complaint received **22 June 2006**

Case completed **1 September 2006**

CASE AUTH/1852/6/06 *NO BREACH OF THE CODE*

GENERAL PRACTITIONER v PFIZER

Alleged disguised promotion of Lipitor

A general practitioner alleged that Pfizer's electronic response, which appeared in the BMJ's 'Rapid Responses', was disguised promotion of Lipitor (atorvastatin). Pfizer's response had been prompted by an editorial in the BMJ entitled 'Switching statins'. The subtitle of the editorial read 'Using generic simvastatin as first line could save £2bn over five years in England'.

The complainant stated that, as far as he knew, BMJ 'Rapid Responses' were not 'peer reviewed' and as such any information provided by a pharmaceutical company in support of its products could be said to be promotional. Given that the response referred to atorvastatin and made claims in support of it, surely it required prescribing information and advice about the need to report adverse events? Also this forum was not restricted to health professionals and was open to the public.

The complainant did not consider that the response constituted a genuine medical information letter from Pfizer's medical information department to a specific enquiry regarding the issue of switching.

The Panel noted that the term promotion in the Code did not include replies made in response to individual enquiries from members of the health professions or appropriate administrative staff or in response to specific communications from them whether of enquiry or comment, including letters published in professional journals, but only if they related solely to the subject matter of the letter or enquiry, were accurate and did not mislead and were not promotional in nature.

The Panel did not consider that Pfizer's response to the editorial was promotional in nature; it provided information on Lipitor in a scientific, factual style. The response did not go beyond the topic of switching statins and included reasons as to why Pfizer disagreed with the proposal to change all patients taking 10mg and 20mg of atorvastatin to 40mg simvastatin.

The response was signed by Pfizer's medical director and would be read in that context. There was no allegation that Pfizer's response was misleading or inaccurate. The Panel considered that the response met the requirements of the Code. The response was not disguised promotion nor was it promotion that required prescribing information or a reference to reporting adverse events as alleged. Thus the Panel ruled no breach of the Code.

A general practitioner complained about the response from the medical director of Pfizer Limited to an editorial in the BMJ on 10 June entitled 'Switching statins' (Moon and Bogle 2006). The subtitle of the editorial read 'Using generic simvastatin as first line could save £2bn over five years in England'.

COMPLAINT

The complainant stated that, as far as he knew, the BMJ's 'Rapid Responses' were not 'peer reviewed' in any strict sense and as such any information provided by a pharmaceutical company in support of its products could be said to be a promotional activity. Given that this article referred to atorvastatin (Pfizer's product Lipitor) and made claims in support of it surely it required prescribing information and advice about the need to report adverse events? Also this forum was not restricted to health professionals and was open to the public and any other interested parties such as consumer journalists.

The complainant did not consider that Pfizer's response constituted a genuine medical information letter from the company's medical information department to a specific enquiry regarding the particular issue of switching. Indeed if this was of concern, Pfizer's medical director could have issued a 'Dear Doctor' letter as had often been done in the recent past or indeed subjected the views expressed in the response to the rigours of a formal peer review process. This was disguised promotion of Lipitor albeit not a 'blatant advertisement' which was prohibited by the BMJ's Rapid Responses guidelines. Surely if this was allowed, without the necessary requirements laid out in the Code for all promotional materials, what was there to advise the unsuspecting reader of what was in fact a genuine peer-to-peer discourse and simple promotion in the guise of an electronic blog?

When writing to Pfizer, the Authority asked it to respond in relation to Clauses 4.1, 4.10 and 10.1 of the Code.

RESPONSE

Pfizer noted that the complainant accused it of disguised promotion in sending a fully referenced

scientifically balanced response to correct the errors of fact in the BMJ's editorial. Pfizer strongly disagreed with the suggestion that the response was promotional.

The Code definition of promotion (Clause 1.2) specifically excluded 'replies made in response to … specific communications from them [health professionals] , including letters published in professional journals, but only if they relate solely to the subject matter of the letter of enquiry, are accurate and do not mislead and are not promotional in nature'. There seemed to be no difference in principle between responding to a letter and responding to an article.

The complainant's suggestion that this was not a medical information letter in response to an enquiry was correct in that there was no such enquiry, however the lack of an enquiry did not render the rebuttal of scientific error any the less important or appropriate. A medical information letter would not have been the appropriate manner in which to respond. Medical information letters were issued in response to a specific request or enquiry by a health professional and were therefore particular to that enquiry.

If a health professional requested information about switching from atorvastatin to simvastatin or *vice versa*, or to clarify the literature misquoted by Moon and Bogle, Pfizer's response would be likely to draw on the same references used to support the BMJ response.

The complainant seemed to misunderstand the basis of the letters page of the BMJ. Neither this, nor any other journal letters page was peer reviewed in the same way as original articles. The editor of the BMJ selected, and sometimes also edited letters for publication in the journal's letters page. The journal required that all letters submitted were first posted to its website and publication in the printed journal was by selection from letters posted there.

Pfizer submitted its response to correct the misrepresentation of the literature on statins (not just atorvastatin) by Moon and Bogle. The response was scientifically balanced, and correctly reported the literature it quoted. Clauses 4.1, 4.10 and 10.1 did not apply. Promotional material requirements such as adverse event reporting statements and prescribing information were therefore not applicable.

The complainant suggested that a 'Dear Doctor letter' should have been sent, but also misunderstood the purpose of such a communication. A 'Dear Doctor letter' was issued by a marketing authorisation holder, following approval of the content by the Medicines and Healthcare products Regulatory Agency (MHRA), to communicate something specific about the safety profile of a medicine. The editorial by Moon and Bogle was not concerned with safety information on atorvastatin.

To deal with the complaint of open access to the webpage a discussion took place with the BMJ. It was clear that the BMJ regarded the rapid responses webpage as part of the journal and not separate from it. The BMJ had not had any other complaint about a pharmaceutical company scientific response submitted to the journal. The BMJ positively welcomed Pfizer's response, and did not regard it as promotional; had this been the case it would not have been selected for publication in the paper journal. The BMJ's view was that the response, like others from the scientific staff in industry, encouraged appropriate debate on items of scientific interest and it would invite the authors of the original article to respond to Pfizer's response. Fulfilling the requirement for total transparency on the potential conflict of interest as an industry employee, the journal saw this as welcome input to an important dialogue that it wished to encourage.

In summary, Pfizer disagreed with the suggestion that its response was promotional, and regretted that a health professional should apparently aim to stifle a legitimate response from senior medical staff of a company. The response sought to correct the erroneous representation of the published literature on a whole class of medicines, not just Lipitor.

It would seem to be quite strange if anyone could make whatever erroneous remarks they chose about any medicine as long as they were outside the industry, and the scientific and medical response from the industry were then to be disallowed. Pfizer hoped the Authority would therefore agree that submitting its response to the BMJ was an appropriate element of scientific debate and was not promotional.

PANEL RULING

The Panel noted that Clause 1.2 stated that the term promotion did not include replies made in response to individual enquiries from members of the health professions or appropriate administrative staff or in response to specific communications from them whether of enquiry or comment, including letters published in professional journals, but only if they related solely to the subject matter of the letter or enquiry, were accurate and did not mislead and were not promotional in nature.

The Panel did not consider that Pfizer's response to Moon and Bogle's editorial 'Switching statins' was promotional in nature; it provided information on Pfizer's product Lipitor in a scientific, factual style. The response did not go beyond the topic of switching statins and included reasons as to why Pfizer disagreed with Moon and Bogle's proposal to change all patients taking 10mg and 20mg of atorvastatin to 40mg simvastatin.

The response was signed by Pfizer's medical director and would be read in that context. There was no allegation that Pfizer's response was misleading or inaccurate. The Panel considered that the response met the requirements of Clause 1.2 of the Code. The response was not disguised promotion nor was it promotion that required prescribing information or a reference to reporting adverse events as alleged. Thus the Panel ruled no breach of Clauses 4.1, 4.10 and 10.1 of the Code.

Complaint received **26 June 2006**

Case completed **21 August 2006**

CASE AUTH/1853/6/06

ANONYMOUS HOSPITAL CONSULTANT v ASTRAZENECA

Symbicort journal advertisement

An anonymous hospital consultant complained about a journal advertisement for Symbicort (budesonide/formoterol), issued by AstraZeneca. The advertisement was headed 'Improving survival in COPD' and consisted of two columns of text. At the top of the right hand column, and thus immediately below the heading, was a diagram showing that treating 100 patients with Symbicort for 1 year vs formoterol alone could prevent 47 exacerbations. The prescribing information for Symbicort was provided at the bottom of the page.

The complainant was concerned that AstraZeneca appeared to be claiming that Symbicort improved survival in COPD without any evidence other than a study with an alternative medicine.

The Panel noted AstraZeneca's submission that there were data to show a link between frequent exacerbations and increased mortality and that combination therapy of the same type as Seretide as a class, was associated with reduced mortality. The Panel considered, however, that the advertisment implied that Symbicort in particular had been shown to improve survival in COPD and this was not so. The claim was misleading and could not be substantiated. The Panel ruled a breach of the Code.

An anonymous hospital consultant with an interest in respiratory diseases complained about a journal advertisement (ref SYM 06 18758) for Symbicort (budesonide/formoterol), issued by AstraZeneca UK Limited and published in the BMJ.

The advertisement was headed 'Improving survival in COPD' and consisted of two columns of text. At the top of the right hand column, and thus immediately below the heading, was a diagram showing that treating 100 patients with Symbicort for one year vs formoterol alone could prevent 47 exacerbations. The prescribing information for Symbicort was provided at the bottom of the page.

COMPLAINT

The complainant stated that AstraZeneca appeared to be claiming that Symbicort improved survival in COPD without any evidence other than a study with an alternative medicine.

Was this permitted? The complainant would be grateful if it was investigated as it was typical of pharmaceutical company activity where a class action was claimed for efficacy but never for safety.

When writing to AstraZeneca the Authority asked it to respond in relation to Clauses 7.2 and 7.4 of the Code of Practice.

RESPONSE

AstraZeneca accepted in hindsight that the juxtaposition of the advertisement's title 'Improving Survival in COPD' to the diagram indicating the data for Symbicort on exacerbation reduction could be potentially misconstrued as Symbicort having demonstrated a direct effect on mortality which was not what it had intended. AstraZeneca accepted a breach of Clause 7.2. However, the company denied a breach of Clause 7.4 since the data presented was valid and capable of substantiation.

The advertisement described how the inhaled corticosteroid and long-acting beta 2 agonist (ICS/LABA) class had several beneficial effects including reducing severe COPD exacerbations and overall COPD mortality.

The introduction stressed the serious clinical consequences of COPD and the burden it placed on the health service. In fact, COPD was the only major disease in the developed countries for which mortality was increasing. Of particular relevance was the prediction that it would become the third leading cause of death by 2020.

The strong link between frequent exacerbations and increased mortality was well established (as described in the first section of the article). The study cited in the advertisement (Soler-Cataluna *et al* 2005) demonstrated that, over a 5-year period, patients with 3 or more exacerbations per year had a four times greater risk of dying compared with those with no exacerbations. More frequent exacerbations were also associated with a greater deterioration in lung function, which in turn left patients more vulnerable to further exacerbations. And lastly, more frequent exacerbations were associated with greater reductions in quality of life, which in turn was an independent predictor of mortality.

Taking all this together, reducing the frequency of COPD exacerbations was a clear treatment goal that in turn reduced the decline in lung function, improved quality of life, and (of most relevance to the advertisement) decreased mortality associated with COPD. Thus, a key goal in COPD management was the prevention of exacerbations as reflected in COPD treatment guidelines.

The second section 'Managing exacerbations with combination treatment' emphasised the efficacy of Symbicort at reducing the frequency of exacerbations and improving health-related quality of life in comparison to LABA monotherapy in two Symbicort pivotal trials. This added to the substantial body of evidence that ICS/LABA combination therapy reduced COPD exacerbations and improved quality of life. This evidence formed the basis of both international (GOLD) and national (NICE and BTS) evidence-based treatment guidelines regarding the use of ICS/LABA to reduce the exacerbation rate in patients with severe COPD.

There were also extensive data relating to a class effect in reducing mortality. Firstly, ICS monotherapy reduced mortality in the majority of observational studies. ICS was the component of the ICS/LABA combination that was thought to have the greatest effect in this regard. Secondly, ICS/LABA combination therapy itself reduced mortality in both retrospective observational studies and in a recently published post-hoc pooled analysis of the two previously mentioned Symbicort COPD pivotal trials. This pooled data showed that treatment for severe COPD patients treated with budesonide added to formoterol (Symbicort) or terbutaline alone; a short acting bronchodilator (SABA) reduced the risk of mortality compared with patients treated with only a LABA (formoterol) and/or SABA (terbutaline). The results showed fewer deaths in the combined budesonide and budesonide plus formoterol (Symbicort) group compared with the bronchodilator group (p=0.037). This represented a 44% reduction in all-cause mortality over one year for patients treated with budesonide-containing therapy. This new data from the same author of the TORCH study corroborated the findings of the TORCH study and whilst these abstracts were not published when the advertisement was published, the data was available on request. Thus in consideration of this pool of clinical data, it was justifiable to claim that ICS/LABA as a class was associated with a reduction in mortality.

Finally the complainant was concerned that AstraZeneca was claiming a class effect without consideration for safety. In fact combination ICS/LABA products had a good risk benefit profile as indicated in the available evidence for these products in patients with COPD. There were no specific safety issues other than those noted in the prescribing information for Symbicort. The prescribing information was included in the advertisement along with all the relevant safety information.

PANEL RULING

The Panel noted AstraZeneca's submission that there were data to show a link between frequent exacerbations and increased mortality and that ICS/LABA as a class was associated with a reduction in mortality. The Panel considered, however, that the advertisment implied that Symbicort in particular had been shown to improve survival in COPD and this was not so. The claim was misleading and could not be substantiated. The Panel ruled breaches of Clauses 7.2 and 7.4 of the Code.

Complaint received **27 June 2006**

Case completed **18 August 2006**

PRINCIPAL HOSPITAL PHARMACIST/DIRECTOR v SERVIER

Alleged breach of undertaking

A principal hospital pharmacist alleged that a journal advertisement for Coversyl (perindopril) issued by Servier had been used again despite it having previously been ruled to be in breach of the Code in Case AUTH/1756/9/05.

As the complaint involved an alleged breach of undertaking, it was taken up by the Director as it was the responsibility of the Authority itself to ensure compliance with undertakings.

The Panel noted that, at first glance, the advertisement now at issue looked very similar to that considered in Case AUTH/1756/9/05. There were, however, important differences. The claim previously ruled in breach of the Code had implied that Coversyl monotherapy could reduce the risk of a cardiovascular event. The claim now at issue, however, clearly stated that a reduction in cardiovascular events was seen when Coversyl was used as part of a blood pressure lowering regimen in patients who needed more than one agent to reach blood pressure targets. The Panel thus considered that the advertisement had been revised such that there was no breach of the undertaking previously given. The Panel therefore ruled no breach of the Code.

A principal hospital pharmacist complained about a journal advertisement (ref 06COAD339) for Coversyl (perindopril) issued by Servier Laboratories Ltd, alleging that it had previously been ruled to be in breach of the Code.

As the complainant alleged a breach of undertaking, the complaint was taken up by the Director as it was the responsibility of the Authority itself to ensure compliance with undertakings.

COMPLAINT

The complainant noted that he had previously complained about an identical advertisement and a breach of the Code was ruled (Case AUTH/1756/9/05). The complainant understood that Servier would be required to withdraw the advertisement forthwith.

The complainant was appalled to see that Servier had again used the same misleading advertisement. He considered that this required the most severe censure possible as the company clearly regarded his complaint and the Authority with contempt.

When writing to Servier, the Authority asked it to respond in relation to Clauses 2, 9.1 and 22 of the Code of Practice.

RESPONSE

Servier stated that it treated all complaints, whether from health professionals, industry or directly from the Authority, extremely seriously. It respected the rulings made by the Panel or the Appeal Board and strove to ensure that, when ruled in breach of the Code, it complied with the undertaking and gave assurance that it would take all possible steps to avoid similar breaches of the Code occurring in the future.

In Case AUTH/1756/9/05 it was alleged that a claim in large type face that 'The preliminary results of ASCOT, in addition to EUROPA and PROGRESS, prove that BP [blood pressure] lowering with Coversyl 4-8mg can reduce the risk of a CV [cardiovascular] event' was misleading. It was further stated that 'The PROGRESS study included a patient group who received a combination of perindopril and a diuretic and there was a significant reduction in stroke incidence compared with placebo. However, since there was no arm of the study in which patients received a diuretic alone, it was not possible to ascertain whether it was the diuretic or the drug combination which was responsible for the apparent therapeutic benefit'. In its ruling the Panel considered that the advertisement implied that all three studies, ASCOT, EUROPA and PROGRESS proved that blood pressure lowering with Coversyl (alone) could reduce the risk of a CV event. With regard to PROGRESS, this was not so. The Panel considered that the claim was misleading as alleged and ruled a breach of Clause 7.2 of the Code. In summary, the Panel ruled that the claim in question was misleading because it implied that in the PROGRESS study Coversyl alone reduced the risk of a CV event by lowering blood pressure.

In line with the undertaking signed in October 2005, all Coversyl advertising containing the claim in question was immediately withdrawn from use.

Servier noted that the claims in the Coversyl advertisement found in breach of the Code in October 2005 were very different from the current campaign including the advertisement/claim in question. Key differences included: complete change of copy under the main strapline; removal of mention of EUROPA study from copy; change of strapline; removal of ASCOT, EUROPA and PROGRESS trial logos and removal of claim below Coversyl product logo.

The main strapline 'Coversyl (perindopril) can …… effectively reduce BP and deliver 24-hour BP control' was in line with the Coversyl licensed indication and supporting references.

The copy below the main strapline, that had been completely and carefully reworded, clearly took into account the issue highlighted in Case AUTH/1756/9/05, that was the implication that in the PROGRESS study Coversyl alone reduced the risk of a CV event by lowering blood pressure.

The copy in the current Coversyl advertisement stated 'For patients who need more than one agent to reach BP targets, ASCOT and PROGRESS, two landmark clinical studies, demonstrated that using COVERSYL, as part of a BP lowering regimen achieved clinically relevant reductions in BP, which reduced major

cardiovascular events'. By making it clear at the beginning and re-emphasising again in the middle of the copy that with ASCOT and PROGRESS it was Coversyl in combination that reduced BP which in turn reduced major cardiovascular events, Servier considered that it had fully addressed the issue in Case AUTH/1756/9/05. This, along with the other changes to the Coversyl advertising detailed above, completely removed any implication that in the PROGRESS study treatment with Coversyl alone reduced the risk of a CV event by lowering blood pressure.

Therefore, Servier denied that it had breached its undertaking; the company had maintained high standards and had not bought discredit to, and reduced confidence in, the industry.

PANEL RULING

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

The Panel noted that, at first glance, the advertisement now at issue looked very similar to that considered in Case AUTH/1756/9/05. There were, however, important differences. The claim previously ruled in breach of the Code had implied that Coversyl monotherapy could reduce the risk of a CV event. The claim now at issue, however, clearly stated that a reduction in CV events was seen when Coversyl was used *as part* of a BP lowering regimen in patients who needed *more than one agent* to reach BP targets. The Panel thus considered that the advertisement had been revised such that there was no breach of the undertaking previously given. The Panel therefore ruled no breach of Clause 22. It thus followed that there was no breach of Clauses 9.1 and 2.

Complaint received **27 June 2006**

Case completed **16 August 2006**

CASE AUTH/1856/6/06 *NO BREACH OF THE CODE*

MEDIA/DIRECTOR v ASTRAZENECA

Criticism of a meeting

An article in The Guardian headed 'Drug firms a danger to health – report' with the subheading 'International research exposes flaws in £33bn marketing budget' criticised, *inter alia*, AstraZeneca. In accordance with established practice, the matter was taken up by the Director as a complaint under the Code.

The article at issue stated: 'The British company AstraZeneca, for instance, has been criticised by regulatory bodies; it allegedly organised an event to promote its drug Crestor which included tickets for a musical, and provided flights and hotels for doctors to attend a conference on bipolar disease on the French Riviera. AstraZeneca says all employees must now pass an exam on its code of conduct'.

The Panel noted that AstraZeneca in the UK had sponsored doctors to attend a meeting in Cannes. The arrangements for the meeting, insofar as they affected the UK company's involvement, were, therefore, subject to the UK Code. Meetings organised by pharmaceutical companies which involved UK health professionals at venues outside the UK were not necessarily unacceptable. There had, however, to be valid and cogent reasons for holding meetings at such venues. As with meetings held in the UK, in determining whether such a meeting was acceptable, consideration had also to be given to the educational programme, overall cost, facilities offered by the venue, nature of the audience, hospitality provided and the like. As with any meeting it should be the programme that attracted delegates and not the associated hospitality or venue.

The meeting held in Cannes was an international congress organised by AstraZeneca global. The meeting was attended by over 1,000 international delegates. AstraZeneca in the UK had sponsored a hundred senior UK psychiatrists to attend. The invitation, which also included the agenda, showed that the meeting started in the late afternoon of a Tuesday and finished, after a full day and a half of presentations and poster sessions, at lunchtime on a Thursday. The faculty was international.

The Panel considered that the arrangements for the meeting were not unacceptable. Delegates were drawn from around the world, as was the faculty, and the meeting had a high scientific content. Although the cost per delegate was on the limits of acceptability, the Panel did not consider that the hospitality offered would be viewed as the primary inducement to attend the meeting. No breach of the Code was ruled.

An article in The Guardian of 26 June headed 'Drug firms a danger to health – report' with the subheading 'International research exposes flaws in £33bn marketing budget' criticised, *inter alia*, AstraZeneca UK Limited. In accordance with established practice, the matter was taken up by the Director as a complaint under the Code of Practice.

COMPLAINT

The article at issue referred to a report compiled by Consumers International which examined marketing practices and self regulation. The article stated: 'The

British company AstraZeneca, for instance, has been criticised by regulatory bodies; it allegedly organised an event to promote its drug Crestor which included tickets for a musical, and provided flights and hotels for doctors to attend a conference on bipolar disease on the French Riviera. AstraZeneca says all employees must now pass an exam on its code of conduct'.

When writing to AstraZeneca the Authority asked it to respond in relation to Clause 19.1 of the Code.

RESPONSE

AstraZeneca stated that it took corporate governance and compliance with both the letter and the spirit of the Code very seriously and as such had been working since late 2005 to ensure compliance with the 2006 Code. Both the events referred to in the article, and the report upon which it was based ('Branding the cure' by Consumers International), related to activities within other (non-UK markets) during 2003.

AstraZeneca stated that, in compiling its report, Consumers International sought to bring its concerns about the global activities of pharmaceutical companies to the attention of consumers. Its research into pharmaceutical promotional activities appeared to have been conducted largely via the internet and all the references provided in the report related to investigations published by the relevant national regulatory bodies or previous media articles.

AstraZeneca stated that it had a comprehensive external meetings policy, which was last revised in June 2005. This required all meetings to be reviewed for compliance with the Code and for all details to be recorded. The policy clearly outlined the educational content expected from each type of meeting and also specified the type of venue, subsistence costs and honoraria rates. As the associated costs of the meeting increased, so did the seniority of the manager required to review and approve it.

AstraZeneca noted that the article in The Guardian did not state that the event as reported related to the activities of overseas AstraZeneca marketing companies and had already been reviewed by the relevant regulatory authorities.

The Consumers International report also referred to a meeting on bipolar disorder held in Cannes. The report stated that the Dutch marketing company was 'put on probation' by the authorities but AstraZeneca believed that the report was wrong in this regard as there was no corresponding report on the Dutch regulatory authority's website.

AstraZeneca had contacted Consumers International for clarification, as the specific reference was not provided in the report itself. The reply from Consumers International was provided.

The reference was to an international event run by the global business and held in Cannes in November 2003. This was a scientific meeting attended by over 1,000 psychiatrists from a wide range of countries. The specific case referred to in the Consumers International report was made against the Canadian marketing company.

Specifically, the Canadian marketing company was found in breach of its local code because it had not contracted with Canadian physicians appropriately about the need to share their learning on their return to Canada – a pre-requisite for such support.

AstraZeneca in the UK took 100 senior psychiatrists to this meeting. The company believed the agenda and logistics were within the spirit and the letter of the 2003 Code. It provided copies of the certified materials.

In the financial breakdown a line appeared stating 'entertainment'. This referred to subsistence costs allocated to each AstraZeneca employee. This allowed AstraZeneca staff to offer appropriate refreshments to delegates and equated to £8 per delegate per day. In 2003, this was the terminology used. Since then AstraZeneca had reworded its forms to reflect more appropriate wording.

Cannes was deemed an acceptable venue for an international meeting of this size owing to the conference facilities that were available, allowing AstraZeneca to accommodate the 1,000 delegates who attended this particular event.

AstraZeneca believed therefore that there was no *prima facie* case and denied any breach of Clause 19.1.

In summary, AstraZeneca submitted that the event, as reported by the Consumers International article and subsequently by The Guardian, did not relate to the UK marketing company, therefore there was no *prima facie* case and AstraZeneca denied any breach of Clause 19.1.

PANEL RULING

The Panel noted that AstraZeneca in the UK had sponsored doctors to attend a meeting in Cannes. The arrangements for the meeting, insofar as they affected the UK company's involvement, were, therefore, subject to the UK Code. As the meeting had taken place in November 2003 the requirements of the 2003 edition of the Code applied. The supplementary information to Clause 19.1 of the 2003 Code stated that meetings organised by pharmaceutical companies which involved UK health professionals at venues outside the UK were not necessarily unacceptable. There had, however, to be valid and cogent reasons for holding meetings at such venues. As with meetings held in the UK, in determining whether such a meeting was acceptable or not, consideration had also to be given to the educational programme, overall cost, facilities offered by the venue, nature of the audience, hospitality provided and the like. As with any meeting it should be the programme that attracted delegates and not the associated hospitality or venue.

The Panel noted that the meeting held in Cannes was an international congress organised by AstraZeneca global. The meeting was attended by over 1,000 delegates from all over the world. AstraZeneca in the UK had sponsored 100 senior UK psychiatrists to attend. The invitation, which also included the agenda, showed that the meeting started in the late afternoon of Tuesday, 11 November and finished, after a full day and a half of presentations and poster

sessions, at lunchtime on Thursday, 13 November. The faculty was international. The cost of attendance for each UK delegate was £1,414.

The Panel considered that the arrangements for the meeting were not unacceptable. Delegates were drawn from around the world, as was the faculty, and the meeting had a high scientific content. Although the cost per delegate was on the limits of acceptability, the Panel did not consider that the hospitality offered would be viewed as the primary inducement to attend the meeting. No breach of Clause 19.1 of the 2003 Code was ruled.

Proceedings commenced 29 June 2006

Case completed 29 August 2006

CASE AUTH/1858/6/06 *NO BREACH OF THE CODE*

PHARMACIST v PFIZER

Newspaper article about the use of statins

A pharmacist complained about an article in The Times entitled 'Savings on heart drugs attacked as 'bad medicine''. The complainant noted that the article was about the increasing use of generic, cheaper statins which would mean less effective care for some patients. Clearly the journalist was unaware of the Heart Protection Study 2002, a double-blind, randomized, controlled trial involving over 20,000 patients in the UK. This trial used simvastatin 40mg and showed significant reductions in primary end points with numbers needed to treat of 19. The complainant thus questioned whether a doctor who prescribed simvastatin 40mg could be described as practising 'bad medicine'?

The complainant noted Pfizer's statement 'Not only does this represent bad medicine and a further assault on clinicians' freedom to prescribe the most appropriate medicine for their patients…'. The complainant asked where atorvastatin had an evidence base of a similar quality to that of simvastatin? The pharmaceutical industry would do well to promote evidence based clinical practice rather than the chasing of surrogate markers.

With regard to surrogate markers, Pfizer also stated 'On 40mg of simvastatin, a normal dose, only 33 per cent of people would reach this target (4mmol/litre). Lipitor (atorvastatin) is more potent'. The complainant agreed that thanks to the practice of evidence based medicine simvastatin 40mg was a 'normal dose'. The tone of the article was that tougher cholesterol lowering targets should be aimed at. The complainant noted the CURVES study compared the cholesterol lowering benefits of various statins. The percentage LDL-C reduction for atorvastatin 10mg 'normal dose' was 38% but those physicians who used simvastatin 40mg would only see a reduction of 41% in LDL-C!

The complainant submitted that if he wished to achieve these new tougher targets then he should prescribe simvastatin 40mg rather than atorvastatin 10mg. This contradicted Pfizer's comments. Yes, atorvastatin was more potent per milligram but not when comparing simvastatin (normal dose) with atorvastatin (normal dose).

The Panel noted that complaints about articles in the press were considered with regard to the information supplied by the pharmaceutical company to the journalist etc and not on the content of the article itself.

The Panel noted that the article in The Times reported on new guidelines which urged prescribers to write at least 60% of their statin prescriptions for simvastatin or pravastatin (excluding combination products). The article stated that Pfizer had referred to this change as 'bad medicine'; immediately before this quotation The Times article stated 'Pfizer, the drug company that makes Lipitor, the statin likely to lose market share as a result of any enforced change says that the policy risks reversing recent advances in the management of heart disease'.

Material supplied by Pfizer to the journalist stated 'The new targets will rank [PCTs] compliance on a league table based on a target of 60% use of older less effective generic statins. To reach this [60%] target clinicians may be forced to switch patients currently well controlled on newer, more effective stains to less effective generics, purely on the grounds of cost. In fact they may even be forced to attain levels of generic usage above 60% in order to avoid their PCT appearing 'bottom of the table'. Not only does this represent bad medicine and a further assault on clinicians' freedom to prescribe the most appropriate medicine for their patients, but it could also slow progress towards the government's own goal of significantly reducing deaths caused by coronary heart disease by 2010'. The Panel considered that in the briefing material it was clear that Pfizer considered that prescribing a medicine including switching well controlled patients in order to reach or exceed prescription cost targets rather than meeting the clinical needs of a patient, was 'bad medicine'; not that prescribing simvastatin or pravastatin *per se* was bad medicine compared with atorvastatin. The Panel did not consider that Pfizer's statement was misleading. No breach of the Code was ruled.

The Panel noted the complainant's submission that the normal doses of simvastatin and atorvastatin were 40mg and 10mg respectively. The summary of product characteristics (SPC) for Zocor (simvastatin) stated that in cardiovascular prevention the usual dose of Zocor was 20-40mg/day; for treatment of hypercholesterolaemia the usual starting dose was

10-20mg/day. The Lipitor (atorvastatin) SPC stated a dose of 10mg/day for prevention of cardiovascular disease; this was also the dose which controlled the majority of patients with hypercholesterolaemia.

The Panel noted the complainant's comments about the CURVES study in that the percentage LDL-C reduction for atorvastatin 10mg was 38% compared with 41% with simvastatin 40mg. Pfizer, however, had referred to the percentage of patients likely to reach the new target of total cholesterol of 4mmol/litre when it had referred to only 33% of patients hitting target with 40mg simvastatin. (Although not discussed, the comparative data for atorvastatin showed that with milligram equivalent doses more patients would be likely to achieve a target total cholesterol of <4mmol/litre with atorvastatin thus justifying the use of 'only' when referring to simvastatin). The Panel considered that the complainant had compared the doses of atorvastatin and simvastatin used to prevent cardiovascular disease (10mg and 40mg respectively) whereas Pfizer had referred to the lipid lowering ability of the two medicines whereby, milligram for milligram, more patients were likely to achieve the target of <4mmol/litre with atorvastatin than simvastatin. In that regard the information given to The Times by Pfizer was not misleading. No breaches of the Code were ruled.

A pharmacist complained about an article entitled 'Savings on heart drugs attacked as 'bad medicine'', The Times, 22 June. The article contained quotations from, *inter alia*, Pfizer.

COMPLAINT

The complainant noted that the article was about the increasing use of generic, cheaper statins which would mean less effective care for some patients. Clearly the journalist was unaware of the Heart Protection Study 2002 which was described as one of the most significant studies in recent years. This was a double-blind, randomized, controlled trial involving over 20,000 patients in the UK. This trial used simvastatin 40mg and showed significant reductions in primary end points with numbers needed to treat of 19. So was a doctor who prescribed simvastatin 40mg practising 'bad medicine'? No, just gold standard evidence based medicine.

The complainant noted that Pfizer had stated 'Not only does this represent bad medicine and a further assault on clinicians' freedom to prescribe the most appropriate medicine for their patients…'. Could Pfizer show the complainant where atorvastatin had an evidence base of a similar quality to that of simvastatin? The pharmaceutical industry would do well to promote evidence based clinical practice rather than the chasing of surrogate markers.

With regard to surrogate markers, Pfizer had also stated 'On 40mg of simvastatin, a normal dose, only 33 per cent of people would reach this target (4mmol/litre). Lipitor (atorvastatin) is more potent'.

The complainant agreed with Pfizer that thanks to the practice of evidence based medicine simvastatin 40mg was a 'normal dose'. The tone of the article was that tougher cholesterol lowering targets should be aimed at. The complainant noted the CURVES study compared the cholesterol lowering benefits of various statins. The percentage LDL-C reduction for atorvastatin 10mg 'normal dose' was 38% but those physicians who used simvastatin 40mg would only see a reduction of 41% in LDL-C!

The complainant alleged that if he wished to achieve these new tougher targets from the Joint British Societies then he should prescribe simvastatin 40mg rather than atorvastatin 10mg. This contradicted Pfizer comments. Yes, atorvastatin was more potent per milligram but not when comparing simvastatin (normal dose) with atorvastatin (normal dose).

The complainant noted that many primary care trusts had encouraged the use of simvastatin while it was on patent and more expensive than Lipitor.

The complainant found the use of articles like the one at issue annoying, and he noted that only that morning a fellow health professional had had to deal with a patient clutching the article believing they were receiving 'bad medicine'. The complainant considered that bad journalism was more appropriate.

When writing to Pfizer the Authority asked it to respond in relation to the requirements of Clauses 7.2 and 7.3.

RESPONSE

Pfizer submitted that the article related to the announcement by the Department of Health of new productivity measures with specific reference to the prescribing metric. The complainant interpreted the quote attributed to Pfizer as referring to simvastatin within the article. Pfizer submitted that the position remained that the target itself was at fault and this statement was not a reference to simvastatin.

Pfizer submitted that the quotation attributed to it paraphrased what was discussed during an interview. The point made was that simvastatin 40mg and atorvastatin 10mg per day achieved similar reductions in LDL cholesterol. With the greater dose range for atorvastatin, it was possible to treat more patients to the new lower target for cholesterol than with simvastatin. The word 'potency' was used by the journalist as synonymous with efficacy which was not how it was briefed by Pfizer.

Pfizer did not believe there were breaches of Clauses 7.2 or 7.3 of the Code as the information it provided both orally and in writing was accurate, balanced and not misleading.

Pfizer submitted that during its review it had, however, identified that material sent to the journalist was not appropriately reviewed and certified in breach of Clause 14.3 of the Code. Pfizer submitted that it had reemphasised and clarified its approval process for its employees involved with the media and undertook that this would not happen again.

In response to a request for further information, Pfizer supplied copies of the references given to The Times.

In an interview with the journalist Pfizer highlighted that not all patients would achieve the current Joint

British Society's guidelines on cholesterol reduction, to target total cholesterol of 4mmol/litre with simvastatin 40mg. This was based on two pieces of information: the average total cholesterol of UK patients, naïve to treatment, was 6.4mmol/litre and information presented in the CURVES study. The average reduction in total cholesterol seen with simvastatin 40mg would achieve target in 33% of patients. Discussion also covered that across the dose range atorvastatin could lower total cholesterol to a greater extent than simvastatin.

Modelling using the data from the CURVES study (mean percentage total cholesterol reductions at each dose with standard deviations) in a statin naïve population gave the following figures for treating to total cholesterol < 4mmol/litre atorvastatin: 10mg, 27%; 20mg, 45%; 40mg, 63% and 80mg, 70%. The figures for simvastatin were: 10mg, 13%; 20mg, 21%; 40mg, 33% and 80mg, 52%. The percentage of patients achieving target with simvastatin 40mg was discussed but no direct data regarding atorvastatin were given.

PANEL RULING

The Panel noted that complaints about articles in the press were considered with regard to the information supplied by the pharmaceutical company to the journalist etc and not on the content of the article itself.

The Panel noted that the article in The Times reported on new guidelines which urged prescribers to write at least 60% of their statin prescriptions for simvastatin or pravastatin (excluding combination products) The guidelines calculated the savings from all PCTs moving to a minimum value of 60% and the rationale in the prescribing metric was given as 'selection of drugs with low acquisition cost in line with NICE guidance'. The article in The Times stated that Pfizer referred to this change as 'bad medicine'. Immediately before the quotation from Pfizer, the article stated 'Pfizer, the drug company that makes Lipitor, the statin likely to lose market share as a result of any enforced change says that the policy risks reversing recent advances in the management of heart disease'.

Pfizer's briefing material supplied to the journalist showed that, in full, Pfizer had stated 'The new targets will rank [PCTs] compliance on a league table based on a target of 60% use of older less effective generic statins. To reach this [60%] target clinicians may be forced to switch patients currently well controlled on newer, more effective stains to less effective generics, purely on the grounds of cost. In fact they may even be forced to attain levels of generic usage above 60% in order to avoid their PCT appearing 'bottom of the table'. Not only does this represent bad medicine and a further assault on clinicians' freedom to prescribe the most appropriate medicine for their patients, but it could also slow progress towards the government's own goal of significantly reducing deaths caused by coronary heart disease by 2010'. The Panel considered that in the briefing material it was clear that Pfizer considered that prescribing a medicine including switching well controlled patients in order to reach or exceed prescription cost targets rather than meeting the clinical needs of a patient, was 'bad medicine'; not that prescribing simvastatin or pravastatin *per se* was bad medicine compared with atorvastatin. The Panel did not consider that Pfizer's statement was misleading. No breach of Clause 7.2 was ruled.

The Panel noted the complainant's submission that the normal doses of simvastatin and atorvastatin were 40mg and 10mg respectively. The summary of product characteristics (SPC) for Zocor (simvastatin) stated that in cardiovascular prevention the usual dose of Zocor was 20-40mg/day; for treatment of hypercholesterolaemia the usual starting dose was 10-20mg/day. The Lipitor (atorvastatin) SPC stated a dose of 10mg/day for prevention of cardiovascular disease; this was also the dose which controlled the majority of patients with hypercholesterolaemia.

The Panel noted the complainant's comments about the CURVES study in that the percentage LDL-C reduction for atorvastatin 10mg was 38% compared with 41% with simvastatin 40mg. Pfizer, however, had referred to the percentage of patients likely to reach the new target of total cholesterol of 4mmol/litre when it had referred to only 33% of patients hitting target with 40mg simvastatin. (Although not discussed, the comparative data for atorvastatin showed that with milligram equivalent doses more patients would be likely to achieve a target total cholesterol of <4mmol/litre with atorvastatin thus justifying the use of 'only' when referring to simvastatin). The Panel considered that the complainant had compared the doses of atorvastatin and simvastatin used to prevent cardiovascular disease (10mg and 40mg respectively) whereas Pfizer had referred to the lipid lowering ability of the two medicines whereby, milligram for milligram, more patients were likely to achieve the target of <4mmol/litre with atorvastatin than simvastatin. In that regard the information given to The Times by Pfizer was not misleading. No breach of Clauses 7.2 and 7.3 was ruled.

Complaint received **26 June 2006**

Case completed **14 September 2006**

ANONYMOUS GENERAL PRACTITIONER v PROFILE PHARMA

Promotion of Promixin

An anonymous general practitioner queried whether Profile's provision of I-neb nebulisers with Promixin (colistimethate sodium) was an inducement to prescribe. The nebuliser was operated by a disc which was provided in boxes of Promixin vials. The complainant noted that Promixin was much more expensive than comparable presentations of colistimethate sodium and asked if this was the way in which Profile was able to offer nebulisers on free loan.

The complainant further alleged that claims made by Profile representatives ie that 1MIU of Promixin via the I-neb was as effective as 2 MIU of colistimethate sodium via other nebulisers, could not be proven.

The Panel noted that built into the price of each 30 vial pack of Promixin was an element for the provision of the I-neb system and the continued supply of associated disposables. The Panel considered that the I-neb was not on long-term loan; it was supplied as part of a package deal with the purchase of Promixin. Package deals, whereby the purchaser of a particular medicine received other associated benefits, such as apparatus for administration, were permissible under the Code provided that the transaction as a whole was fair and reasonable and the associated benefits were relevant to the medicine involved. The Panel considered that the package deal offered with Promixin was not unreasonable. No breach of the Code was ruled.

The Panel noted the allegation that claims made by representatives about the lung deposition of Promixin could not be proven ie that 1 MIU of Promixin via the I-neb was as effective as 2 MIU colistimethate sodium via other nebulisers. The product support pack explained that the I-neb had a very low residual volume (0.1ml) which allowed for smaller volumes of medicine to be place in the medication chamber. Profile produced data to show the 1 MIU/1ml delivered by the I-neb would achieve a lung dose similar to that achieved by 2 MIU/4ml delivered by a conventional nebuliser. Given that the complainant was anonymous, the Panel had no way of knowing exactly what representatives had said, nor was it possible to ask the complainant to comment on the company's response prior to a ruling being made. Profile submitted that it did not promote to GPs. The Panel considered that on the material before it there was no evidence that representatives had made misleading claims. No breach of the Code was ruled.

An anonymous complainant, writing as 'an overspent and annoyed GP', complained about the promotion of Promixin (colistimethate sodium) by Profile Pharma Ltd. Promixin was powder to be reconstituted and used as a nebuliser solution in the treatment of lung infections in patients with cystic fibrosis.

COMPLAINT

The complainant was concerned that Profile's I-neb nebuliser was offered to cystic fibrosis patients on a 'free loan' basis. The device only operated when a disc containing a microchip was inserted. The disc was supplied in a box of Promixin vials. Patients were told that the only way to get a disc was to get a repeat prescription for Promixin. Did this imply that no other colistimethate sodium vial could be used with the device? If so, was this not an inducement to prescribe? The complainant provided an article from the Pharmaceutical Services Negotiating Committee (PSNC) website which commented on the use of Promixin.

The complainant noted that there were significant budgetary implications for both primary and secondary care when prescribing Promixin: Promixin 1 MIU vial cost £4.60 vs colistimethate sodium 1 MIU which cost £1.68. Was this huge differential in price the way in which Profile was able to offer nebulisers on free loan?

The complainant alleged that claims made by Profile representatives about the lung deposition of Promixin could not be proven, ie that 1 MIU of Promixin via the I-neb was as effective as 2 MIU of colistimethate sodium via other nebulisers.

When writing to Profile, the Authority asked it to respond in relation to Clauses 7.2, 7.3, 15.2 and 18.1 of the Code.

RESPONSE

Profile explained that I-neb was supplied by Respironics UK and offered on a long-term loan basis to patients; not as a 'free loan' as stated by the complainant. It was acknowledged that the higher cost for the medicine paid for the long-term loan of the nebuliser.

Promixin could be used with any conventional nebuliser suitable for delivery of antibiotic solutions but boxes of 30 Promixin vials included a disc which enabled the product to be used with an I-neb device.

The I-neb device could be used with other products intended for nebulisation by means of a disc which was supplied with the nebuliser. If patients/health workers did not wish to use the long-term loan option, but still wanted to obtain an I-neb they could purchase one and appropriate discs would be supplied.

The article referred to by the complainant was factually incorrect and Profile thanked the complainant for bringing it to its attention. The Promixin summary of product characteristics (SPC) clearly stated that 'Promixin may be reconstituted with Water for Injections (WFI) to produce a hypotonic solution or a 50:50 mixture of WFI and 0.9% saline to produce an isotonic solution. When reconstituted, Promixin may be used with any conventional nebuliser suitable for delivery of antibiotic solutions'.

Profile noted that the complaint had been received from a GP. Profile did not promote to GPs.

The need to use 1 MIU in an I-neb to obtain an equivalent dose to 2 MIU delivered through a conventional nebuliser was related to the concentration of the solutions placed in the nebulisers, and not related to lung deposition. This point had previously been covered in correspondence with the Medicines and Healthcare products Regulatory Agency (MHRA) which agreed with Profile's stance on the issue.

Promixin was supplied as a sterile dry powder for nebulisation. It could be administered via conventional nebulisers or via the I-neb nebuliser system. Promixin was prescribed and supplied separately to the nebuliser system and this was in common with other pharmaceutical products intended for nebulisation. As there was a wide variation between the different types of nebuliser available, Promixin might need to be reconstituted to different volumes dependent upon the manufacturers' instructions for the specific nebuliser being used.

Profile explained that the delivery of drugs from nebulisers was highly variable due to the large variation in nebuliser technology and the variable efficiency of nebulisers. The I-neb system, utilising adaptive aerosol delivery (AAD) technology was developed to address this problem. Conventional air-stream nebulisers required a minimum volume in the nebulisation chamber to operate and so a fill volume would be recommended by the manufacturer of the nebuliser and part of this would be nebulised until the residual volume was left in the chamber. Conventional nebulisers generated an aerosol continuously even while the patient was exhaling so a lot of aerosolised medicine was wasted to the atmosphere. The I-neb was designed to deliver medicine during inhalation only, reducing the amount of medicine wasted to the atmosphere. Hence a significantly lower fill volume was required in order to achieve a lung dose equivalent to that of a conventional nebuliser. The residual volume of the I-neb was low and such efficiencies made it possible to use smaller fill volumes of a higher concentration to deliver approximately the same amount to the lungs. Such efficiencies also resulted in rapid dose delivery with associated improvement in compliance. Based on these data the I-neb delivered an approximately equivalent dose to a conventional nebuliser but required only half the amount of dose due to reduced wastage and higher concentration.

Profile conceded that Promixin was more expensive than other brands of colistimethate sodium. This was to allow for the long-term loan of the I-neb system and the continued supply of the associated disposable items. Due to the efficiency of the I-neb, the cost of the 1 MIU and 2 MIU Promixin doses were the same when using this nebuliser. The product monograph openly discussed the differences in cost.

PANEL RULING

The Panel noted from the Promixin SPC that the product was supplied in packs of 30 vials each of which contained a disc to enable use with the I-neb system. Built into the price of each 30 vial pack (£138) was an element for the provision of the I-neb system and the continued supply of the associated disposable items. The Panel considered that the I-neb was not on long-term loan; it was supplied as part of a package deal with the purchase of Promixin. The supplementary information to Clause 18.1 stated that Clause 18.1 did not prevent the offer of package deals whereby the purchaser of a particular medicine received with it other associated benefits, such as apparatus for administration, provided that the transaction as a whole was fair and reasonable and the associated benefits were relevant to the medicine involved. In the Panel's view the provision of an I-neb was clearly relevant to the use of Promixin. The section on 'Costs' in the product monograph clearly stated that the cost of Promixin included the provision of the I-neb system.

The Panel noted that Promixin could be used with other nebulisers – although as the cost of the product included provision of the I-neb system to use another delivery device would seem illogical. Alternatively the I-neb system could be bought as a separate item and used to nebulise products other than Promixin. The Panel noted that the article from the PSNC website had wrongly stated that Promixin could only be used with a Prodose nebuliser.

The Panel considered that the package deal offered with Promixin was not unreasonable. No breach of Clause 18.1 of the Code was ruled.

The Panel noted that the complainant had alleged that claims made by representatives about the lung deposition of Promixin could not be proven ie that 1 MIU of Promixin via the I-neb was as effective as 2 MIU colistimethate sodium via other nebulisers. The product support pack contained a sheet which explained the I-neb system. It was stated that the I-neb had a very low residual volume (0.1ml) which allowed for smaller volumes of medicine to be placed in the medication chamber. The fill volume was only 1ml. This enabled less medicine to be used to deliver the same dose to patients. Profile produced data to show that 1 MIU/1ml delivered by the I-neb would achieve a lung dose similar to that achieved by 2 MIU/4ml delivered by a conventional nebuliser. Given that the complainant was anonymous, the Panel had no way of knowing exactly what representatives had said, nor was it possible to ask the complainant to comment on the company's response prior to a ruling being made. Profile submitted that it did not promote to GPs. The Panel considered that on the material before it there was no evidence that representatives had made misleading claims. No breach of Clauses 7.2, 7.3 and 15.2 of the Code was ruled.

Complaint received **3 July 2006**

Case completed **8 August 2006**

ANONYMOUS v FERRING

Sponsorship of a sporting venue

An anonymous complaint was received about sponsorship by Ferring at a polo ground. Photographs showed Ferring's logo displayed on a low wall around the polo field.

In view of the clinicians present at the meeting and the amount of sponsorship paid for this advertising, the complainant thought the Authority would be interested as he believed that the 2006 Code prohibited sponsorship of sporting events by companies such as Ferring.

The Panel noted that the complainant had only provided very limited details. He had not stated when the photographs of the polo match had been taken but given his reference to the 2006 Code the Panel assumed that it must have been sometime after 1 May 2006 when the polo season started. According to Ferring, its corporate sponsorship of the polo club had expired in September 2005 although it appeared that the boards bearing the company logo may have stayed in place after that date. The complainant referred to 'clinicians present at the meeting' but gave no details of the meeting or who had sponsored it. Ferring stated that it had last used the ground for a meeting of health professionals in September 2003.

The Panel noted that the complaint was about the placement of boards bearing Ferring's company logo around the polo field, not about a meeting *per se*. The boards did not contain any promotional claims or refer to any medicines or therapy area. The Panel ruled no breach of the Code.

An anonymous complainant complained about signs denoting sponsorship by Ferring Pharmaceuticals Ltd at a polo ground.

COMPLAINT

The complainant enclosed two photographs which he stated had been taken at a polo match in the midlands. The photographs showed Ferring's logo displayed on a low wall around the field.

In view of the clinicians present at the meeting and the amount of sponsorship paid for this advertising, the complainant thought the Authority would be interested as he believed that the 2006 Code prohibited sponsorship of sporting events by such companies as Ferring. The complainant did not fully appreciate the changes which had been made but in fairness to all considered he must bring it to the Authority's attention.

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

RESPONSE

Ferring noted that the complaint concerned a sign bearing its company logo at a polo club. The sign had appeared at the ground between May 2003 and September 2005, during which time Ferring was a corporate patron of the club.

Under the agreement, Ferring paid a fixed sum to the polo club in return for the following benefits during the polo season (1 May to 30 September): access for Ferring staff to watch polo matches; access to the club facilities for meetings; 40 inclusive buffet lunches per season; two advertising hoardings at the ground and the right to hire additional facilities, such as a marquee at reduced cost.

The ground was centrally placed and offered good access for meetings. During the term of the agreement Ferring used the facilities at the polo club on a number of occasions for internal management meetings. On one occasion only, the facilities were used for an advisory board meeting which took place on the morning of Saturday, 27 September 2003. This meeting was to discuss a new therapeutic indication with a small group of seven specialist clinicians. The meeting had a full agenda starting at 8.30am and ending at 1pm, at which time a buffet lunch was provided. All participants left the polo club by 2pm.

Ferring had not invited any other health professional to the polo club for any reason, and accordingly it had no knowledge or involvement in the meeting attended by the complainant.

With regard to the Ferring company logo, which the complainant had photographed, Ferring stated that it believed that the sign had been removed when the agreement ended on 30 September 2005. Since receiving this complaint Ferring had contacted the club and asked it to remove the sign immediately as the agreement had expired over nine months ago.

Ferring noted that the sign was non-promotional as it simply consisted of the company logo. There was no promotional strapline or any reference to a medicine or therapeutic area.

Ferring did not consider that there had been any breach of the Code.

PANEL RULING

The Panel noted that the complainant had only provided very limited details. He had not stated when the photographs of the polo match had been taken but given his reference to the 2006 Code the Panel assumed that it must have been sometime after 1 May 2006 when the polo season started. According to Ferring its corporate sponsorship of the polo club had expired in September 2005 although it appeared that the boards bearing the company logo may have stayed in place after that date. The complainant referred to 'clinicians present at the meeting' but gave no details of the meeting or who had sponsored it. Ferring stated that it had last used the ground for a meeting of health professionals in September 2003.

The Panel noted that the Code stated that meetings organized for doctors, other health professionals

and/or for administrative staff which were wholly or mainly of a social or sporting nature were unacceptable. The Code did not prohibit corporate sponsorship of sports teams and/or grounds and nor did the Code prohibit the use of sports venues *per se* for meetings provided that, *inter alia*, the venue was appropriate and conducive to the main purpose of the meeting and that the overall impression given by the arrangements was not unacceptable in relation to the requirements of Clause 19.1 of the Code. Companies must ensure that no sporting event took place at the venue immediately before, during or immediately after the meeting. Advice on the use of sporting venues for meetings had been published in the May 2006 Code of Practice Review.

The Panel noted that the complaint was about the placement of boards bearing Ferring's company logo around the polo field, not about a meeting *per se*. The boards did not contain any promotional claims or refer to any medicines or therapy area. The Panel ruled no breach of Clauses 2, 9.1 and 19.1 of the Code.

Complaint received	**3 July 2006**
Case completed	**31 July 2006**

CASE AUTH/1863/7/06 *NO BREACH OF THE CODE*

MEDIA/DIRECTOR v SANOFI-AVENTIS

Patient organisation meeting

An article in The Observer newspaper entitled 'Cancer drug firm's PR trip sparks a row' criticised the activities of Sanofi-Aventis. In accordance with established practice the matter was taken up by the Director as a complaint under the Code. The article stated that a row had broken out over a trip described as 'educational' to Budapest and Paris by the heads of most of Britain's cancer charities. Sanofi-Aventis had arranged for policymakers and patients' representatives to enjoy a weekend away while they got the chance to hear about new cancer medicines, many of which were not yet offered by the NHS.

The article stated that a leaked draft of the itinerary described the meeting as a 'parliamentary and stakeholder working group'. It began with a flight to Budapest for the opening of the European Association of Cancer Research (EACR) conference. There was 'optional attendance' at the lectures and an exhibition, followed by dinner. Participants were also to visit a hospital in Paris to see the 'gold standard' treatment received by French patients in contrast with that experienced by NHS patients. The most senior cancer official within the Department of Health (DoH) was attending, paid for by the government, and two MPs were going, courtesy of a firm of political lobbyists. However, the chairman of the all-party parliamentary group on cancer declined the invitation stating, 'I didn't want to go because it was funded by a drugs company. There are other ways of finding out how other countries' cancer plans work without taking a weekend in Budapest and Paris. If I want to learn more about a particular cancer therapy, I can talk to doctors here who know about it. I really feel that these charities should pay for themselves – or if they can't, the company should hold the meeting in London'.

One insider who saw the draft itinerary was reported as saying, 'This kind of trip gives the company a chance to point out that other countries are spending more on new cancer drugs than the NHS. What it does is give charities the ammunition to go back to the UK and say, well the French are prescribing this new drug, so why is it being denied to our patients?'

In the article the charity bosses defended their roles, one of whom stated 'We've fully discussed this trip with our trustees and the board, and felt it was of value. If we paid, then it would come out of the charity's fund for research, which would be very wrong'.

The article reported growing concern about how 'Big Pharma' was influencing patients' groups and noted that The Lancet had called for greater transparency from the charities over where their sponsorship money came from.

The Panel noted from Sanofi-Aventis' submission that the reason for visiting France was to learn about the differences between the UK and French cancer plans and to see why there was such a difference in survival rates between the two countries.

The initial invitation sent on 12 April stated that the study group would attend the EACR conference in Budapest and then meet with key decision makers involved in the development of the French Cancer Plan. The group would include parliamentarians, patient group representatives, DoH officials and clinical leaders. It would explore best practice in cancer prevention, research and treatment.

A draft agenda had been sent to all invitees on 20 June. This stated that the group would attend the opening ceremony of the EACR conference followed by 'optional attendance at lectures, poster sessions and exhibition'. The final agenda stated that there was a choice of sessions at the EACR conference not that attendance was optional. According to the draft agenda the working group was to fly to Budapest early on 1 July. Delegates were to attend the opening ceremony of the EACR conference. An evening seminar with EACR was followed by a working dinner to discuss 'Advances in Cancer: making it a reality in the NHS'. On 2 July delegates were to attend the plenary lecture at the EACR conference at 9am and subsequently arrived in Paris at around 3pm with free time until dinner at 8pm with pan-European cancer groups to discuss improvement in survival rates, preventing cancer,

tackling health inequalities, increasing spending on cancer and access to new cancer treatments. On 3 July there would be a visit to a cancer clinic/unit (yet to be confirmed), lunch with a representative from the French Cancer Research Association to discuss what the UK could learn from France with regard to making and maintaining progress and a seminar and discussion in the afternoon to learn more about the French approach. The working group was due to arrive back in London later that evening.

The final agenda differed with regard to the description of attendance at the EACR conference as noted above, a seminar with an adviser to the French health minister was arranged for 6pm on 2 July and there was no mention of free time although there was a little spare time between arriving in Paris at 3.20pm and the 6pm seminar. The tour of the cancer department the next day was confirmed. The attendees included MPs, advisers, patient groups in the cancer area and DoH officials.

The Panel considered that both the draft and the final agenda were very full with little free time given the number of meetings and working meals. The prime reason for attending the meeting would be educational including meeting experts and discussing differences between France and the UK.

The Panel noted that the EACR conference provided a valid and cogent reason for travelling to Budapest. It would be much more difficult to hold the meetings and discussion about the French arrangements in the UK. The relevant resource or expertise was in France thus there were valid and cogent reasons to travel there.

With regard to the comments made by an 'insider' in the article, the Panel did not consider that the Code prevented companies discussing spending on cancer medicines and if other countries prescribed medicines which were licensed for use in the UK but were not prescribed in the UK it was not necessarily a breach of the Code to make this known.

With regard to the concerns in the article about pharmaceutical companies' relationships with patients' groups, the Panel noted that the supplementary information to the Code stated that any involvement a pharmaceutical company had with a patient organisation must be declared and transparent. Companies must make public by means of information on their websites or in their annual report a list of all patient organisations to which they provided financial support. This might include sponsoring materials and meetings. There was no specific criticism of Sanofi-Aventis in this regard.

The Panel considered that the meeting had a clear educational purpose such as to justify the hospitality. The hotels were described as standard business hotels. Most of the meals were working discussions. The hospitality was secondary to the education. The cost of attending the meeting at £1,508 per person was not unreasonable given there were two European destinations and the registration fee for EACR conference was £310.

Overall the Panel considered that the arrangments were not unreasonable. No breach of the Code was ruled.

An article entitled 'Cancer drug firm's PR trip sparks a row' which appeared in The Observer newspaper of 2 July 2006 criticised a Sanofi-Aventis organised trip to Budapest and Paris, Saturday 1 July to Monday 3 July, for the heads of most of Britain's cancer charities.

COMPLAINT

The author of the article stated that a row had broken out over a trip described as 'educational' to Budapest and Paris by the heads of most of Britain's cancer charities that had been funded by a major drugs company.

The article reported that Sanofi-Aventis had arranged for policymakers and patients' representatives to enjoy a weekend away while they got the chance to hear about new cancer medicines, many of which were not yet offered by the NHS.

A draft of the itinerary, leaked to The Observer, described the meeting as a 'parliamentary and stakeholder working group'. It began with a flight to Budapest and incorporated the opening of the European Association of Cancer Research (EACR) conference. There was 'optional attendance' at the lectures and an exhibition, followed by a dinner. Participants were also going to a hospital in Paris where they were seeing the 'gold standard' treatment received by French patients in contrast with that experienced by NHS patients.

The most senior cancer official within the Department of Health (DoH) was attending, although her costs were being met by the government, and two MPs were going on the trip, courtesy of a Westminster firm of political lobbyists. However, the chairman of the all-party parliamentary group on cancer, declined the invitation stating, 'I didn't want to go because it was funded by a drugs company. There are other ways of finding out how other countries' cancer plans work without taking a weekend in Budapest and Paris. If I want to learn more about a particular cancer therapy, I can talk to doctors here who know about it. I really feel that these charities should pay for themselves – or if they can't, the company should hold the meeting in London'.

One insider who saw the draft itinerary was reported as saying, 'This kind of trip gives the company a chance to point out that other countries are spending more on new cancer drugs than the NHS. What it does is give charities the ammunition to go back to the UK and say, well the French are prescribing this new drug, so why is it being denied to our patients?'

In the article the charity bosses defended their roles one of whom stated: 'We've fully discussed this trip with our trustees and the board, and felt it was of value. If we paid, then it would come out of the charity's fund for research, which would be very wrong'.

The article reported that there was growing concern about how 'Big Pharma' was influencing patients' groups. The medical journal The Lancet had called

for greater transparency from the charities over where their sponsorship money came from.

The communications director for Sanofi-Aventis, said, 'This is a purely educational trip. It enables the MPs and the patients' groups representatives to look at best practice that is happening; I can't see the harm in this'.

When writing to Sanofi-Aventis, the Authority asked it to respond in relation to Clauses 2, 9.1 and 19.1 of the Code and its supplementary information as well as the supplementary information to Clause 20.2 of the Code which stated that meetings for member of public, journalists and patient organisations must comply with Clause 19.

RESPONSE

Sanofi-Aventis submitted that the trip was educational, organised in the context of the annual congress of the EACR, in Budapest. The EACR supported research in cancer through scientific meetings and fellowships and independently arranged its annual meeting at locations which it selected; it received no sponsorship from Sanofi-Aventis UK. The agenda for the Budapest conference covered all areas of cancer research, including epidemiology, cell and tumour biology, signalling pathways, tumour immunology, oncogenomics, apoptosis and medicine related research.

Sanofi-Aventis submitted that the UK delegates then travelled to Paris, in order to learn from senior French policy markers about the French Cancer Plan, both in theory and practice. The location was prompted by the 'Karolinska Report' (A pan-European comparison regarding patient access to cancer medicines originating from the Karolinska Institutet, Stockholm, Sweden, September 2005) which reviewed cancer care across Europe and identified France as demonstrating best practice – in direct contrast to the UK. On this basis, Sanofi-Aventis considered that there was a need in the UK to enhance awareness and understanding of current and future best practice in cancer prevention, research, and treatment amongst stakeholders. The Sanofi-Aventis programme was entirely non-promotional and encompassed a wide range of topics including epidemiology, genetics, new treatment modalities, organisation of cancer services and commissioning. There was no promotion of the company's products or services. A detailed agenda was provided.

Attendees

Sanofi-Aventis submitted that 58 delegates were invited on the basis of their experience or interest in oncology research and management of cancer services; 13 initially accepted but two withdrew at the last minute leaving 11 delegates. They were not approached as potential prescribers, and indeed the majority were not health professionals with prescribing powers or influence. Sanofi-Aventis was represented by three of its staff; no sales personnel were involved.

The initial part of the trip incorporated the official EACR meeting for the afternoon of 1 July and early morning of 2 July, plus two Sanofi-Aventis organised meetings. The first meeting concerned research in cancer and was led by EACR officials. The second meeting was with prominent UK researchers (all of whom were attending the EACR independently) during the evening of 1 July.

With regard to the statement in the Observer article that there was 'optional attendance' at the [EACR] lectures followed by a dinner', Sanofi-Aventis submitted that an initial draft of the programme, clearly marked as such, indicated that there were options available for the first part of the EACR meeting on the afternoon of 1 July; however, this was never intended to imply that the options extended beyond the EACR itself. The ambiguity of wording was subsequently recognised and it was altered accordingly before the final programme was distributed.

Sanofi-Aventis submitted that the latter part of the trip involved direct contact with senior French policymakers and patient group representatives, and a visit to a major Paris hospital in order to gain a practical view of the French approach to management of cancer services. As detailed in the agenda, the first meeting in France on 2 July was a seminar with an adviser to the French Health Minister. The second meeting on 2 July was a pan-European patient group discussion with Europa Uomo and Europa Colon.

Sanofi-Aventis submitted that on 3 July the first meeting was held at the Georges Pompidou European Hospital, where a presentation on the hospital was given. Following a front-line tour of the specialist cancer department, presentations on the implementation of the French Cancer Plan were delivered by local experts at the hospital.

In the afternoon of 3 July two further meetings were held. One was with the Association pour la Recherche sur le Cancer and the Europa Donna. The second meeting was a seminar with the Institut National du Cancer. Other speakers were also French Cancer Plan policy experts.

Sanofi-Aventis submitted that the total cost per delegate was £1,508; this included transport, accommodation and subsistence at £845 per person and an EACR registration fee of £310. A detailed breakdown of all of the costs associated with the meeting was provided. Further evidence of the modest nature of the costs incurred was also provided in the delegates' expenses claims. One flight was economy class, and the other was a budget air-line. The Eurostar journey returning to London was in standard class, and all group transfers were by bus.

Hotels with standard business facilities were used in both locations and both these and the restaurants to which delegates were taken were of a standard appropriate to the delegates without being lavish or luxurious. Sanofi-Aventis noted that most of the meals taken during the trip were working discussions, and the programme did not include any leisure component or free time.

In support of the utility and appropriate nature of this trip, correspondence from delegates and aggregated feedback on the content quality and relevance of the meeting was provided.

The invitation, agenda and programme for this trip, including detailed arrangements for travel and

hospitality, were reviewed, approved and certified as required by the Code and the company's standard operating procedure.

Compliance with the ABPI Code

Sanofi-Aventis submitted that, in light of the details provided above, there had been no breach of the Code in either letter or spirit. The hospitality was associated with an educational and scientific meeting, secondary to the main purpose of the meeting, in proportion to the occasion and cost what the recipients would reasonably pay themselves (Clause 19.1). The arrangements and programme were the same for health professionals, policy-makers and patient organisation representatives, and complied with Clause 19 (Clause 20.2).

Sanofi-Aventis submitted that the programme and arrangements recognised the commitment and professionalism of the delegates; there was no social programme and the scientific and educational content extended throughout the available time. The delegates were senior managers, patient group representatives, MPs, policymakers and clinical oncologists and researchers who were prominent and highly involved in the subjects covered.

Sanofi-Aventis submitted that high standards were therefore maintained (Clause 9.1) and that no aspect of the meeting had brought discredit upon, or reduced confidence in, the pharmaceutical industry (Clause 2).

Sanofi-Aventis provided additional information including the draft programme (sent on 20 June), and a list of all those invitees who received it. A working document which pre-dated the draft programme (dated 15 June), and was sent to a single recipient was also provided.

PANEL RULING

The Panel noted that Clause 20.3 of the Code stated, *inter alia*, that the requirements of Clause 19, which covered meetings for health professionals and appropriate administrative staff, also applied to pharmaceutical companies supporting patient organisation meetings. The supplementary information to this clause stated that meetings organised for or attended by members of the public, journalists and patient organisations must comply with Clause 19 of the Code.

Clause 19.1 stated that companies must not provide hospitality to members of the health professions and appropriate administrative staff except in association with scientific meetings, promotional meetings, scientific congresses and other such meetings. Meetings must be held in appropriate venues conducive to the main purpose of the event. Hospitality must be strictly limited to the main purpose of the event and must be secondary to the purpose of the meeting ie subsistence only. The level of subsistence offered must be appropriate and not out of proportion to the occasion. The costs involved must not exceed that level which the recipients would normally adopt when paying for themselves.

The supplementary information stated the provision of hospitality was limited to refreshments/subsistence (meals and drinks), accommodation, genuine registration fees and the payment of reasonable travel costs which a company might provide to sponsor a delegate to attend a meeting.

With any meeting, certain basic principles applied:

- The meeting must have a clear educational content
- The venue must be appropriate and conducive to the main purpose of the meeting; lavish or deluxe venues must not be used and companies should avoid using venues that were renowned for their entertainment facilities
- The subsistence associated with the meeting must be secondary to the nature of the meeting, must be appropriate and not out of proportion to the occasion.

Meetings orgainsed by pharmaceutical compaines which involved UK health professionals at venues outside the UK were not necessarily unacceptable. There had to be valid and cogent reasons for holding meetings at such venues. These were that most of the invitees were from outside the UK and, given their countries of origin, it made greater logistical sense to hold the meeting outside the UK or given the location of the relevant resource or expertise that was the object or subject matter of the meeting, it made greater logistical sense to hold the meeting outside the UK. As with meetings held in the UK, in determining whether such a meeting was acceptable or not, consideration must also be given to the educational programme, overall cost, facilities offered by the venue, nature of the audience, subsistence provided and the like. As with any meeting it should be the programme that attracted delegates and not the associated hospitality or venue.

The Panel noted that the Karolinska Report did not conclude that France demonstrated best practice as submitted by Sanofi-Aventis. With regard to adoption of the newest cancer medicines made available between 1999 and 2004, France was described as an average adopter of new cancer medicines for breast cancer, colorectal cancer, lung cancer, non Hodgkin's lymphoma and supportive care. Austria, Spain and Switzerland were the top three countries in this regard. The UK was below average. The one year and five year survival rates for all tumour types in France was 81% and 61% respectively. Only Sweden was better (81% and 62%). The relevant data for the UK was 67% and 48%.

The Panel noted from Sanofi-Aventis' submission that both the UK and France had a cancer plan and the reason for visiting France was to learn about the differences in the plans and to see why there was such a difference in survival rates between the two countries. Sweden did not have a national cancer plan.

The initial invitation sent on 12 April stated that the study group would attend the EACR conference in Budapest followed by a series of meetings with key decision makers who had been involved in the development of the French Cancer Plan. The group would include parliamentarians, patient group representatives, DoH officials and clinical leaders. It would explore best practice in cancer prevention, research and treatment.

A draft agenda had been sent to all invitees on 20 June. This stated that the group would attend the opening ceremony of the EACR conference followed by 'optional attendance at lectures, poster sessions and exhibition'. The final agenda stated that there was a choice of sessions at the EACR conference not that attendance was optional. According to the draft agenda the working group was to fly to Budapest early on 1 July. Delegates were to attend the opening ceremony of the EACR conference and welcome reception. An evening seminar with EACR was arranged with officials of the EACR speaking. This was followed by a working dinner with UK researchers attending the EACR conference to discuss 'Advances in Cancer: making it a reality in the NHS'. The draft agenda listed four speakers at this dinner. On 2 July delegates were to attend the plenary lecture at the EACR conference at 9am and subsequently arrived in Paris at around 3pm with free time until dinner at 8pm with pan-European cancer groups to discuss improvement in survival rates, preventing cancer, tackling health inequalities, increasing spending on cancer and access to new cancer treatments. On 3 July there would be a visit to a cancer clinic/unit (yet to be confirmed), lunch with a representative from the French Cancer Research Association to discuss what the UK could learn from France with regard to making and maintaining progress and a seminar and discussion in the afternoon to learn more about the French approach. The working group was due to arrive back in London later that evening.

The final agenda differed with regard to the description of attendance at the EACR conference as noted above, a seminar with an adviser to the French health minister was arranged for 6pm on 2 July and there was no mention of free time although there was a little spare time between arriving in Paris at 3.20pm and the 6pm seminar. The tour of the cancer department the next day was confirmed. The attendees included MPs, advisers, patient groups in the cancer area and DoH officials.

The Panel considered that both the draft and the final agenda were very full with little free time given the number of meetings and working meals. The prime reason for attending the meeting would be educational including meeting experts and discussing differences between France and the UK.

The Panel considered that it was not necessarily inappropriate for a pharmaceutical company to fund an educational meeting provided the requirements of the Code were met. Of course there were other ways of finding out about how other countries' cancer plans worked but given the location of the experts it was not unreasonable to travel outside the UK. The EACR conference was in Budapest which provided a valid and cogent reason for travelling to Budapest. It would be much more difficult to hold the meetings and discussion about the French arrangements in the UK. The relevant resource or expertise was in France thus there were valid and cogent reasons to travel there.

With regard to the comments made by an 'insider' in the article, the Panel did not consider that the Code prevented companies discussing spending on cancer medicines and if other countries prescribed medicines which were licensed for use in the UK but were not prescribed in the UK it was not necessarily a breach of the Code to make this known.

With regard to the concerns in the article about pharmaceutical companies' relationships with patients' groups, the Panel noted that the supplementary information to Clause 20.3 stated that any involvement a pharmaceutical company had with a patient organisation must be declared and transparent. Companies must make public by means of information on their websites or in their annual report a list of all patient organisations to which they provided financial support. This might include sponsoring materials and meetings. There was no specific criticism of Sanofi-Aventis in this regard.

The Panel considered that the meeting had a clear educational purpose such as to justify the hospitality. The hotels were described as standard business hotels. Most of the meals were working discussions. The hospitality was secondary to the education. The cost of attending the meeting at £1,508 per person was not unreasonable given there were two European destinations and the registration fee for EACR conference was £310.

Overall the Panel considered that the arrangments were not unreasonable. No breach of Clause 19.1 of the Code was ruled. The Panel considered that there was also no breach of Clause 9.1 of the Code and ruled accordingly. Given its rulings above the Panel ruled no breach of Clause 2 of the Code.

Proceedings commenced 4 July 2006

Case completed 26 September 2006

MEMBER OF THE PUBLIC v LILLY

Erectile dysfunction television advertisement

A member of the public complained about a Lilly television advertisement for erectile dysfunction (ED). The complainant questioned whether such an advertisement was allowed under the Code.

The complainant stated that he was not a doctor, nor did he work in healthcare, but it was obvious from the Lilly Icos logo on the advertisement and the campaign website that Lilly was peddling its ED treatment on UK national television.

The complainant thought that the Code was supposed to prevent advertising to the public and if the Code was defined so vaguely that things like this were allowed, then it was time for another re-write.

The Panel noted that the Code prohibited the advertising of prescription only medicines to the public. It permitted information about them to be made available to the public provided such information was factual and presented in a balanced way. It must not raise unfounded hopes of successful treatment or be misleading with respect to the safety of the product. Statements must not be made for the purpose of encouraging a member of the public to ask their health professional to prescribe a specific prescription only medicine. Supplementary information stated that a company might conduct a disease awareness campaign provided the purpose was to encourage members of the public to seek treatment for their symptoms while in no way promoting the use of a specific medicine.

The Panel noted that there were two television advertisements, both of which referred to the incidence of erectile problems and that they could be a sign of underlying illness. Both stated that there were over ten treatments available but these treatments were neither named nor described. The advertisements concluded by referring viewers to a website or a telephone number for more information.

The website provided more information including a booklet 'Man matters'. The advertisements, the website and the booklet clearly indicated that the materials were sponsored by Lilly. The booklet mentioned treatments and named the medicines taken orally without attaching significance to any of them. Some of the features of the different oral treatments were mentioned without identifying the medicine. Various other available treatments were mentioned. The website did not name the oral treatments but gave the generic name of one of the other medicines for treatment which was available as three different products.

The Panel did not consider either that the television advertisements constituted advertisements for prescription only medicines or that they failed to meet the requirements of the Code. The information provided was factual and would not lead to a member of the public to ask their health professional to prescribe a specific prescription only medicine. The material might lead a member of the public to ask about treatment but not about any specific treatment. No breach of the Code was ruled.

A member of the public complained about a television advertisement for erectile dysfunction (ED) by Eli Lilly and Company Limited.

COMPLAINT

The complainant noted that the advertisement appeared on Sky Channel One at lunch time on either 26 or 27 June. The complainant questioned whether such an advertisement was allowed under the Code.

The complainant stated that he was not a doctor, nor did he work in healthcare, but it was obvious from the Lilly Icos logo on the advertisement and the campaign website that Lilly was peddling its ED treatment on UK national television.

The complainant thought that the Code was supposed to prevent advertising to the public and if the Code was defined so vaguely that things like this were allowed, then it was time for another re-write.

The complainant alleged that it was an absolute disgrace and irresponsible. A bit like self regulation, really.

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

RESPONSE

Lilly submitted that the advertisement at issue was part of a campaign designed to raise awareness of ED. The advertisement was aimed at female partners of men with ED, and provided balanced, accurate and factual information, including how common the condition was, how it might be a marker of another underlying medical condition such as hypertension or diabetes, and that there were several different treatments available. It did not mention specific treatments by name, and therefore did not constitute advertising to the general public. The campaign encouraged women to talk to their partner about his ED and encourage him to talk to his doctor, not just about the range of different treatment options, but because he could have an underlying illness.

This advertisement offered women two ways of finding out more information on ED; they could either telephone to request a booklet or visit the 'Lovelifematters' website. These sources of information also gave balanced, factual and accurate information on ED.

Lilly submitted that both the Code and the Medicines and Healthcare products Regulatory Agency's (MHRA's) Blue Guide allowed for the provision of information on diseases, and non-promotional information on prescription only medicines to be provided to the general public, although as noted

above the television advertisement mentioned no treatments by name. Sponsorship of the advertisement by Lilly ICOS was declared, as required by the Code and the MHRA guidelines.

Lilly submitted that as it had complied with the Code and the Blue Guide with regard to disease awareness campaigns, it had not brought discredit upon the pharmaceutical industry, the material was of high standard and sponsorship was clearly declared. The television advertisement did not advertise any medicine to the general public nor did it encourage members of the public to ask their health professional to prescribe a specific prescription only medicine. Therefore Lilly did not believe that the advertisement breached Clauses 2, 9.1, 20.1 or 20.2 of the Code.

PANEL RULING

The Panel noted that Clause 20.1 prohibited the advertising of prescription only medicines to the public. Clause 20.2 permitted information to be made available to the public about prescription only medicines provided such information was factual and presented in a balanced way. It must not raise unfounded hopes of successful treatment or be misleading with respect to the safety of the product. Statements must not be made for the purpose of encouraging a member of the public to ask their health professional to prescribe a specific prescription only medicine. The supplementary information to Clause 20.2 stated that a company might conduct a disease awareness campaign provided the purpose was to encourage members of the public to seek treatment for their symptoms while in no way promoting the use of a specific medicine. Reference was made to the MHRA disease awareness campaign guidelines.

The Panel noted that there were two television advertisements, both of which referred to the incidence of erectile problems and that they could be a sign of underlying illness. Both stated that there were over ten treatments available but these treatments were neither named nor described. The advertisements concluded by referring viewers to a website or a telephone number for more information.

The website provided more information including a booklet 'Man matters'. The advertisements, the website and the booklet clearly indicated that the materials were sponsored by Lilly. The booklet mentioned treatments and named the medicines taken orally without attaching significance to any of them. Some of the features of the different oral treatments were mentioned without identifying the medicine. Various other available treatments were mentioned. The website did not name the oral treatments but gave the generic name of one of the other medicines for treatment which was available as three different products.

The Panel did not consider that the television advertisements constituted advertisements for prescription only medicines. No breach of Clause 20.1 of the Code was ruled.

The Panel did not consider that the television advertisements failed to meet the requirements of Clause 20.2 of the Code. The information provided was factual and would not lead to a member of the public to ask their health professional to prescribe a specific prescription only medicine. The material might lead a member of the public to ask about treatment but not about any specific treatment. No breach of Clause 20.2 was ruled.

Given its rulings above the Panel considered that there could be no breach of Clauses 2 and 9.1 of the Code and ruled accordingly.

Complaint received	**7 July 2006**
Case completed	**24 August 2006**

ANONYMOUS v BRISTOL-MYERS SQUIBB

Arrangements for a meeting

One of those present at a meeting sponsored by Bristol-Myers Squibb complained anonymously about the venue. The meeting was held at a football club in a room overlooking the pitch.

The complainant understood that the newly revised Code specifically excluded the use of sporting venues for meetings and hospitality. The complainant alleged that this was a clear breach of the Code and trusted that this matter would be investigated fully.

The Panel noted that although the meeting had been held at a football ground Bristol-Myers Squibb submitted that no sporting event took place immediately before, during or immediately after the meeting. The venue was chosen because the business meeting facilities it offered would accommodate the 175 delegates. Other venues in the area, according to Bristol-Myers Squibb, would have difficulties accommodating that number of people. The programme was for a scientific/educational meeting.

Overall, the Panel considered that it was not inappropriate for Bristol-Myers Squibb to sponsor the meeting held at the football club and ruled no breach of the Code.

One of those present at an afternoon meeting (12 noon to 5pm) sponsored by Bristol-Myers Squibb Pharmaceuticals Limited complained anonymously about the venue.

COMPLAINT

The complainant noted that on 28 June 2006 a meeting on hypertension and cardiovascular medicine was held a football club, in a room overlooking the pitch.

The complainant understood that the newly revised Code specifically excluded the use of sporting venues for meetings and hospitality. The complainant alleged that this was a clear breach of the Code and trusted that this matter would be investigated fully.

When writing to Bristol-Myers Squibb the Authority asked it to respond in relation to Clause 19.1.

RESPONSE

Bristol-Myers Squibb submitted that the meeting in question was organised by a primary care trust (PCT) as a protected learning time event focussing on cardiovascular risk.

Bristol-Myers Squibb submitted that it was approached by the PCT to assist with funding for the meeting to the amount of £500 in return for a stand outside the meeting, as were a number of other named pharmaceutical companies.

Bristol-Myers Squibb submitted that except for its sponsorship the meeting was independent and the company had no control or influence over the content of the meeting and nor was it involved with the meeting logistics, the selection or payment of speakers or the selection of venue. Bristol-Myers Squibb noted that the 'Sponsorship for Training' document which set out the agreement between the company and the PCT, and thus governed Bristol-Myers Squibb's input, reiterated the absence of control by Bristol-Myers Squibb in the meeting.

Bristol-Myers Squibb understood that no sporting events took place either immediately before, during or immediately after the meeting in question. No entertainment or sport was organised or subsidised by Bristol-Myers Squibb for any of the delegates. As stated above, Bristol-Myers Squibb only paid a sponsorship fee to the PCT to have a stand at the event.

However for completeness, Bristol-Myers Squibb stated that in its view the venue was appropriate for the meeting for the reasons set out below.

Bristol-Myers Squibb noted that the supplementary information to Clause 19.1 of the Code stated that a meeting venue must be appropriate and conducive to the main purpose of the meeting; lavish or deluxe venues must not be used and companies should avoid using venues that were renowned for their entertainment facilities. Further guidance on the appropriate use of sporting venues was provided by the Authority in the May 2006 Code of Practice Review. This guidance stated that when large numbers of delegates were to be invited to a meeting it might be impossible to hold it at a business style hotel. A conference centre within a football stadium or the like might have to be used instead. Companies organising, or sponsoring, meetings at such high profile venues should be satisfied that no other venue was large enough to accommodate the meeting and that the overall impression given by the proposed arrangements would not be unacceptable in relation to the requirements of Clause 19.1. The guidance further stated that it must be the programme that attracted delegates to a meeting, not the venue and required that companies ensured that no sporting events took place at the venue immediately before, during or immediately after the meeting.

Bristol-Myers Squibb submitted that the local area suffered from a dearth of suitable meeting venues for large audiences. 175 delegates attended the meeting and Bristol-Myers Squibb understood that the two local hotels would not have been able to accommodate this number. Consequently, this was the second year running that the PCT had organised a meeting at the venue in question.

Bristol-Myers Squibb confirmed that its stand, as the only part of the meeting for which it was responsible, was certified in accordance with the Code. Furthermore, consistent with its standard operating procedure and as a key element in determining

whether the company would sponsor the meeting, the meeting agenda, its proposed content and level of hospitality were reviewed by its area business manager to ensure compliance with the Code.

Bristol-Myers Squibb submitted that it had no *prima facie* case to answer with respect to Clause 19.1 of the Code. If the Authority ruled that the venue selected by the PCT was inappropriate, Bristol-Myers Squibb agreed not to sponsor such an event at this venue in future.

* * * * *

The Director considered that a *prima facie* case had been established. The involvement of Bristol-Myers Squibb as a sponsor was covered by the Code. The matter needed to be considered by the Panel.

* * * * *

PANEL RULING

The Panel noted that the supplementary information to Clause 19.1 of the Code, Meetings and Hospitality, stated, *inter alia*, that venues for meetings must be appropriate and conducive to the main purpose of the meeting; lavish and deluxe venues must not be used and companies should avoid using venues that were renowned for their entertainment facilities. The impression that was created by the arrangements for any meeting must always be kept in mind. Meetings organised for groups of doctors, other health professionals and/or appropriate administrative staff which were wholly or mainly of a social or sporting nature were unacceptable.

The Panel further noted the advice in the May 2006 Code of Practice Review that when large numbers of delegates were to be invited to a meeting it might be impossible to hold it at a business style hotel. A conference centre within a football stadium or the like might have to be used instead. Companies organising, or sponsoring, meetings at such high profile venues should be satisfied that no other venue was large enough to accommodate the meeting and that the overall impression given by the proposed arrangements would not be unacceptable in relation to the requirements of Clause 19.1. Gratuitous use of sporting or leisure venues was unacceptable. It must be the programme that attracted delegates to a meeting, not the venue. Further, companies must ensure that no sporting events took place at the venue immediately before, during or immediately after the meeting. Venues must not be used so as to knowingly take advantage of any entertainment/sport that had been organised/subsidised by a third party.

The Panel noted that although the meeting had been held at a football ground Bristol-Myers Squibb submitted that no sporting event took place immediately before, during or immediately after the meeting. The venue was chosen because the business meeting facilities it offered would accommodate the 175 delegates. Other venues in the area, according to Bristol-Myers Squibb, would have difficulties accommodating that number of people. The programme was for a scientific/educational meeting.

Overall, the Panel considered that it was not inappropriate for Bristol-Myers Squibb to sponsor the meeting held at the football ground. The arrangements were in accordance with Clause 19.1 of the Code. Thus the Panel ruled no breach of Clause 19.1.

Complaint received **10 July 2006**

Case completed **9 August 2006**

CASE AUTH/1866/7/06

VOLUNTARY ADMISSION BY DAIICHI-SANKYO

Breach of undertaking

Daiichi-Sankyo (formerly Sankyo) voluntarily advised the Authority that an advertisement which had been ruled in breach of the Code in Case AUTH/1787/12/05 had reappeared despite the company giving an undertaking not to use it again.

As the admission related to a breach of undertaking, which was a serious matter, it was treated as a complaint under the Code in accordance with the Authority's Constitution and Procedure. Daiichi-Sankyo provided a detailed explanation as to what had happened.

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

The Panel noted that in Case AUTH/1787/12/05 it had considered that an advertisement for Olmetec was closely similar to a previous one which it had ruled in breach of the Code such that Sankyo had not complied with its undertaking. Breaches of the Code, including a breach of Clause 2, were ruled. In the case now at issue, Case AUTH/1866/7/06, the advertisement considered in Case AUTH/1787/12/05 had been published again. The undertaking in Case AUTH/1787/12/05 was signed on 16 February 2006.

Between signing the undertaking in February and the advertisement at issue being published in error in June, Sankyo had changed its advertising agency. The Panel, however, considered that Sankyo should have quickly traced and withdrawn all versions of the advertisement such that when the new agency took over there were no old advertisements in existence. On signing an undertaking it was beholden upon companies to rapidly ensure that no materials which were in breach of the Code were used again, no matter in what format they were held or by whom. The guidelines on company procedures relating to the Code advised companies to keep written records of action taken to withdraw material.

The Panel noted that in correspondence from Sankyo to its various agencies just prior to the signing of the undertaking, there was no clear instruction that old versions of the Olmetec advertisement should be destroyed or returned to the company. The Panel did not consider that merely telling people not to use material ruled in breach of the Code was sufficient – copies should be destroyed. In that regard the Panel considered that Sankyo had not taken all possible steps to comply with its undertaking. High standards had not been maintained. Breaches of the Code were ruled. The Panel further considered that Sankyo, by not doing all that it could have done to comply with its undertaking had brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

Daiichi-Sankyo UK Ltd voluntarily advised the Authority that an advertisement (OLM 188.1B) which had been ruled in breach of the Code in Case AUTH/1787/12/05 had appeared in the May/June edition of the British Journal of Cardiology. Daiichi-Sankyo had given an undertaking not to use the advertisement after 19 February 2006.

COMPLAINT

As the matter related to a breach of undertaking it was sufficiently serious for it to be taken up and dealt with as a formal complaint under the Code (Paragraph 5.4 of the Constitution and Procedure). Daiichi-Sankyo was asked to respond in relation to Clauses 2, 9.1 and 22 of the Code.

RESPONSE

Daiichi-Sankyo stated that it first knew of the advertisement's appearance on 29 June and it alerted the Authority informally of this on 30 June and had since conducted a thorough investigation to identify how this occurred.

Daiichi-Sankyo submitted that following the ruling in Case AUTH/1787/12/05, it had stopped working with one advertising agency and started working with another. Investigations had thus involved the previous advertising agency, the current advertising agency and the media buyer. The previous agency had produced the advertisement found in breach in Case AUTH/1787/12/05 and was involved in the development of a new advertisement (version 1). This new advertisement was subsequently taken over by the new agency and adapted (version 2). The new advertising agency was not involved with the advertising that had been found in breach in Case AUTH/1787/12/05.

Daiichi-Sankyo submitted that the advertising agency was responsible for the production of promotional material and the media buyer was responsible for placement once approved by the company. The media buyer would thus ask the agency for 'an approved' advertisement in order to hit a publication date and the agency in turn would ask the company for an approved advertisement so that it could provide the necessary artwork to the media buyer in order for this to be sent to a publisher by the required deadline.

Daiichi-Sankyo provided copies of correspondence confirming relevant actions and instructions, including a detailed timetable of events from 1 February, when Sankyo received the Panel's ruling in Case AUTH/1787/12/05 and considered appealing, until 11 July when confirmation was received from the new agency that all advertisements were in the current design.

Daiichi-Sankyo submitted that the breach of undertaking had occurred because of the following:

- A failure by the previous agency and/or the media buyer to adhere to the written confirmation

which was provided to Daiichi-Sankyo by ensuring that all journals were informed to cease use of such materials.

There was a difference in the version of events between the previous advertising agency and the media buyer – the media buyer maintained that the responsibility for telling the journals to destroy old copies lay with the advertising agency but the advertising agency maintained that this was not the case and that it was up to the media buyers to inform the journals.

The only consistent documentation Daiichi-Sankyo had between the two parties which confirmed that the appropriate actions had been carried out was that provided on 13 and 15 February and which confirmed that 19 February was the last date of use and all other items had been cancelled.

- An assumption by the new advertising agency that all advertising material with publishers was in the new campaign design and did not feature the previous claims which had been ruled in breach.
- A failure by the new agency to follow process by dealing directly with the publisher instead of using the media buyer.
- A failure of the new advertising agency to check with Daiichi-Sankyo or the media group that the advertisement being re-run complied with the Code.

Daiichi-Sankyo submitted that as a consequence of its findings it had acted in good faith with respect to its undertaking to comply with the ruling in Case AUTH/1787/12/05.

Daiichi-Sankyo submitted that it had sought, received and acted upon written confirmation from the media buyer and previous agency at the time of the ruling and did not foresee the chain of events thereafter or that there would be a breakdown in communication between the previous advertising agency and media buyer.

Daiichi-Sankyo submitted that written assurances from both parties at the time led it to believe that all had been dealt with effectively and that the advertisement would appear for the last time on 19 February. There was no reason to question the process between media buyer and advertising agency at that time. Daiichi-Sankyo was concerned that the new agency had acted beyond its remit by dealing directly with the publisher.

As a consequence Daiichi-Sankyo intended to reinforce clear roles and responsibility into both agency and media buyer contracts and ensure that this series of events could not happen again. A copy of the proposed process was provided.

In addition Daiichi-Sankyo would insist that its media buyer now provided a copy of the advertisement, or identify by code any advertisements before they were re-run.

Daiichi-Sankyo submitted that despite these advertisements having already been signed off and approved at Daiichi-Sankyo, it would insist that it received notification prior to re-placement of any advertisements and provided the approval for use of such advertisements again.

Daiichi-Sankyo hoped this thorough and rapid investigation and resultant actions demonstrated that due process had been followed and the serious nature with which it viewed this issue. Daiichi-Sankyo sincerely regretted this occurrence but believed that it would not happen again.

In a response to a request for further comment Daiichi-Sankyo noted that it was its own internal procedure which identified the re-publication of the advertisement which had previously been ruled in breach. Furthermore Daiichi-Sankyo's voluntary admission within a day of realising this had happened, followed by a detailed, rapid and subsequent investigation with provision of written documentation submitted to the Authority as a voluntary admission, indicated the seriousness with which it viewed the occurrence. These actions further underlined the serious nature which Daiichi-Sankyo viewed the undertaking previously given and its intention to establish how this occurred and immediately rectify identified issues.

Daiichi-Sankyo submitted that it always intended to treat the breach ruled in Case AUTH/1787/12/05 with respect and to comply with the requirements resulting from the findings.

The undertaking affected all of Daiichi-Sankyo's campaign materials and its established and previously tested process enabled the effective recall and destruction of materials from the entire UK organisation. Furthermore Daiichi-Sankyo was confident that its process for withdrawal of copy was robust and had achieved the required written assurances from its third party clients that ensured compliance with the commitment made to the Authority.

Daiichi-Sankyo submitted that it based its belief in its agencies on a previously successful uneventful withdrawal of advertising copy. Daiichi-Sankyo submitted that therefore the process it had in place was robust and effective and once more used this process to ensure compliance with the undertaking in the expectation of the same successful outcome.

Daiichi-Sankyo submitted that it had told the current advertising agency that the previous advertisement had been withdrawn and had been replaced by 'the man on the platform' campaign. The agency had been authorized to run repeats of 'the man on the platform' execution which was the only currently authorised advertisement. However, the agency did not confirm that the repeat advertisement was the approved copy (man on the platform) when instructing the publisher.

Daiichi-Sankyo submitted that it was very surprised and extremely disappointed when it discovered the re-publication of the previous journal advertisement and it took the immediate action of a voluntary admission.

Following the incident Daiichi-Sankyo submitted that it had implemented, or was in the process of implementing, a number of measures which included:

- Reinforcing clear roles and responsibilities with its advertising agency included in contractual terms and conditions.
- Creation of a standard template letter to be provided by Daiichi-Sankyo in accordance with the roles and responsibilities to agencies in the event of a withdrawal.
- An update to the existing SOP for withdrawal of materials to include the previous two points and the inclusion of an express instruction and confirmation of destruction of all electronic versions to be provided by journals. Furthermore this was to be documented and kept within Daiichi-Sankyo.

Following its detailed review, Daiichi-Sankyo had updated its SOP by providing a written template to the agency to provide to the publishers which would also now include an express instruction for all electronic media to be returned or destroyed from servers. This was a strengthening of the previous process as it was clear that written documentation from the agency had not been forthcoming to support instructions that had been made with regards to electronic media.

Daiichi-Sankyo submitted that while it made every endeavour to comply with its undertaking it was let down by external agencies on this occasion and was therefore accountable for a breach of undertaking (Clause 22). However it submitted that it had maintained the expected high standards throughout (Clause 9.1) and had not brought the industry into disrepute (Clause 2) due to its voluntary admission and prompt, thorough response.

PANEL RULING

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

The Panel noted that in Case AUTH/1787/12/05 it had considered that an advertisement for Olmetec was closely similar to a previous one which it had ruled in breach of the Code such that Sankyo had not complied with its undertaking. Breaches of the Code, including a breach of Clause 2, were ruled. In the case now at issue, Case AUTH/1866/7/06, the advertisement considered in Case AUTH/1787/12/05 had been published again. The undertaking in Case AUTH/1787/12/05 was signed 16 February 2006.

Between signing the undertaking in mid February for Case AUTH/1787/12/05 and the advertisement at issue being published in error in June, Sankyo had changed its advertising agency. The Panel, however, considered that Sankyo should have quickly traced and withdrawn all versions of the advertisement such that when the new advertising agency took over there were no old advertisements in existence. On signing an undertaking the Panel considered that it was beholden upon companies to rapidly ensure that no materials which were in breach of the Code were used again, no matter in what format they were held or by whom. The guidelines on company procedures relating to the Code of Practice stated that companies were advised to keep written records of action taken to withdraw material.

The Panel noted that in correspondence from Sankyo to its various agencies just prior to the signing of the undertaking, there was no clear instruction that old versions of the Olmetec advertisement should be destroyed or returned to the company. The Panel did not consider that merely telling people not to use material ruled in breach of the Code was sufficient – copies should be destroyed. In that regard the Panel considered that Sankyo had not taken all possible steps to comply with its undertaking. High standards had not been maintained. The Panel ruled breaches of Clauses 9.1 and 22 of the Code. The Panel further considered that Sankyo, by not doing all that it could have done to comply with its undertaking had brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

Complaint received **13 July 2006**

Case completed **29 August 2006**

ANONYMOUS EMPLOYEES v ROCHE

Activities at a meeting and call rates

Two Roche employees complained anonymously about the conduct of colleagues at a European meeting and also about call rates for representatives.

The complainants alleged that during the course of a European meeting colleagues took customers to a bar late at night and bought illegal substances.

The Panel noted Roche's submission that there was no truth in the allegation. Given that the complaint was anonymous the Panel could not ask the complainants to comment on the company's response before making a ruling. The Panel considered that it had received no evidence that the conduct of company personnel had breached the Code. No breach of the Code was ruled.

The complainants further alleged that Roche required its representatives to see doctors more than three times a year. The complainants had to see at least four doctors every day and if this was added up on all territories it meant that the complainants had to see some of them 8 times a year. Bonuses were lost if this was not done.

The Panel noted that the supplementary information to Clause 15.4 stated, *inter alia*, that the number of calls made on a doctor or other prescriber by a representative each year should not normally exceed three on average. This did not include attendance at group meetings and the like, a visit requested by the doctor or other prescriber or a visit to follow up a report of an adverse reaction.

The Panel noted Roche's submission that hospital representatives were expected to see two senior target customers each day in one-to-one meetings and this in effect meant that senior target customers would receive 1.6 calls per year. In reality this meant that some would receive one call a year but the majority would receive two. Given that some territories would have more than the average number of senior target customers and that on all territories some would be difficult to see, the Panel considered that, in theory, some representatives at least might find it difficult to achieve the expected daily call rate without have to see some customers more than 3 times a year. The Panel, however, had received no evidence that call rates in practice had breached the Code. Given the anonymity of the complainants, the Panel could not ask them to comment on Roche's response before making a ruling. The Panel considered that on the basis of the material before it there was no evidence that call rates had breached the Code. No breach of the Code was ruled.

Two employees at Roche Products Limited complained anonymously about activities at a recent European meeting and call rate targets for representatives.

1 European meeting

COMPLAINT

The complainants alleged that the behaviour of some colleagues recently had brought the industry into disrepute. At a European meeting, two colleagues had taken some customers to a bar late into the night and bought them illegal substances. Several doctors had commented on this on their return, this was outrageous behaviour and made the complainants look as though the price of the medicines they sold was so that this could go on.

The complainants alleged a breach of Clause 2.

When writing to Roche, in addition to Clause 2 cited by the complainants, the Authority also asked it to respond in relation to the requirements of Clauses 9.1 and 19.1 of the Code.

RESPONSE

Roche categorically denied the allegation. The individuals concerned, and a significant number of other company individuals who had attended the meeting, were all quite definite that these events did not occur. Therefore Roche submitted that there was absolutely no truth in this allegation.

PANEL RULING

The Panel noted the company's submission that there was no truth in the allegation. Given that the complaint was anonymous the Panel had no way of contacting the complainants to ask them to comment on Roche's response prior to a ruling being made. The Panel considered that on the basis of the material before it, there was no evidence that the conduct of company personnel had breached the Code. No breaches of Clauses 2, 9.1 and 19.1 of the Code were ruled.

2 Call rates

COMPLAINT

The complainants alleged that Roche required its representatives to see doctors more than 3 times a year. Roche tried to get the complainants to see at least 4 doctors every day and if this was added up on all the territories it meant the complainants had to see some of them 8 times a year. Bonuses were lost if this was not done and the complainants alleged that they were being financially hurt by not breaching the Code.

The complainants alleged a breach of Clause 2.

When writing to Roche, in addition to Clause 2 cited by the complainants, the Authority also asked it to respond in relation to the requirements of Clauses 9.1 and 15.4 of the Code.

RESPONSE

Roche submitted that the standard rate of 4 calls per day only applied to the hospital sales team.

Roche explained that the minimum performance standards set in order for its hospital sales

representatives to qualify for the multiplier components of its incentive scheme was 4 one-to-one calls per day, 2 of which were to be on senior target customers. The average number of senior target customers per territory was 241 which, based on a 190 day year and the application of minimum standards, led to a frequency of 1.6 calls per customer. This was clearly well below the average of 3 specified in Clause 15.4 of the Code and did not take into account additional calls permitted due to the customer making requests to see a representative.

Roche submitted that on occasions individual managers could ask their teams to deliver more than the minimum standards but this would not take them beyond the limits of the Code and would not result in any loss of bonus for the individuals concerned. Roche noted that no member of the hospital sales team had ever lost their bonus due to failure to meet the minimum standard call rates.

Therefore, in summary, Roche submitted that it was true that it asked for 4 calls per day, but only 2 of these were on senior target customers (the smaller audience) and this could be delivered without being in breach of Clause 15.4. Roche took adherence to the Code very seriously, and moving forward it would continue to take proactive steps to ensure that it remained compliant with the Code regarding calling activity for all of its sales teams.

Roche provided a copy of the 'Roche baseline performance standards for hospital sales representatives' explanatory booklet for 2006 for information.

PANEL RULING

The Panel noted that the supplementary information to Clause 15.4 stated, *inter alia*, that the number of calls made on a doctor or other prescriber by a representative each year should not normally exceed three on average. This did not include attendance at group meetings and the like, a visit requested by the doctor or other prescriber or a visit to follow up a report of an adverse reaction, all of which could be additional to the three visits allowed.

The Panel noted that hospital representatives were expected to see two senior target customers each day in one-to-one meetings. Given the average number of such customers in each territory (241), and based on 190 days a year in the field, this meant that senior target customers would receive 1.6 calls per year. The Panel noted, however, that in reality this meant that some customers would receive one call a year but the majority would receive two. Given that some territories would have more than the average number of senior target customers and that on all territories some senior target customers would be difficult to see, the Panel considered that, in theory, some representatives at least might find it difficult to achieve the one-to-one call rate of 2 per day without having to see some customers more than 3 times a year. The Panel noted, however, that the complainants had not provided any evidence that call rates in practice had breached the Code. The Panel considered that on the basis of the material before it there was no evidence that call rates had breached the Code. No breaches of Clauses 2, 9.1 and 15.4 were ruled.

Complaint received **14 July 2006**

Case completed **10 August 2006**

CASE AUTH/1868/7/06

DOCTOR v JANSSEN-CILAG

Tramacet electronic advertisement

A doctor complained about an electronic advertisement for Tramacet (tramadol hydrochloride 37.5mg and paracetamol 325mg) issued by Janssen-Cilag. The advertisement had appeared on www.doctors.net. Tramacet was indicated for the symptomatic treatment of moderate to severe pain.

The part of the advertisement at issue was a section which compared numbers needed to treat (NNT) for Tramacet, its constituents and other step-two analgesics. The stated NNTs were: Tramacet (75/650) 2.6; co-codamol (60/600) 4.2; paracetamol (600) 4.6; tramadol (100) 4.8; tramadol (75) 5.3 and tramadol (50) 8.3. The lower the NNT the more effective the medicine.

The complainant noted that the advertisement used the Oxford league table of analgesics, comparing analgesics by NNT. This was an established tool and widely quoted in the pain literature. Tramacet had an NNT of 2.6; however the complainant alleged that co-codamol was compared at a dose which was not the most effective (60/600) nor the dose which was most commonly used (60/1000). Had the comparisons been with this higher, more commonly used dose, the NNT of co-codamol would have been 2.2 and would not have shown Tramacet in such a favourable light. Although a relatively minor transgression, this advertisement presented a distorted picture of current analgesics.

The Panel considered that by omitting the NNT data for co-codamol 60/1000 the comparison was misleading as alleged. The Panel ruled breaches of the Code as acknowledged by Janssen-Cilag.

A doctor complained about an electronic advertisement (Code 7007) for Tramacet (tramadol hydrochloride 37.5mg and paracetamol 325mg) issued by Janssen-Cilag Ltd. The advertisement had appeared on www.doctors.net. Tramacet was indicated for the symptomatic treatment of moderate to severe pain.

The part of the advertisement at issue was a section which compared numbers needed to treat (NNT) for Tramacet, its constituents and other step-two analgesics. The stated NNTs were: Tramacet (75/650) 2.6; co-codamol (60/600) 4.2; paracetamol (600) 4.6; tramadol (100) 4.8; tramadol (75) 5.3 and tramadol (50) 8.3. The lower the NNT the more effective the medicine.

COMPLAINT

The complainant noted that the advertisement used the Oxford league table of analgesics, comparing analgesics by NNT. This was an established tool and widely quoted in the pain literature. Tramacet had an NNT of 2.6; however the complainant alleged that co-codamol was compared at a dose which was not the most effective (60/600) nor the dose which was most commonly used (60/1000). Had the comparisons been with this higher, more commonly used dose, the NNT of co-codamol would have been 2.2 and would not have shown Tramacet in such a favourable light. Although a relatively minor transgression, this advertisement presented a distorted picture of current analgesics.

When writing to Janssen-Cilag the Authority asked it to respond in relation to Clauses 7.2 and 7.3 of the Code.

RESPONSE

Janssen-Cilag submitted that comparison between analgesics was common, and the comparison used in the advertisement, the Oxford league table of analgesics, used NNT, which was a widely established tool quoted extensively within the literature. The method of comparison used within the advertisement was therefore accepted as suitable, by both the complainant and Janssen-Cilag.

The focus was on the comparison between Tramacet (37.5 mg tramadol and 325mg paracetamol) and co-codamol 60/600 (codeine phosphate, paracetamol). In the case of 60/600, this represented two tablets of co-codamol at strength 30/300 ie 30mg codeine phosphate and 300mg paracetamol per tablet.

Janssen-Cilag noted the complainant's view that the most effective dose of co-codamol and also the most commonly used dose in the UK was 60/1000 ie two tablets each containing 30mg codeine phosphate combined and 500mg paracetamol. The NNT for co-codamol 60/600 (used in the advertisement) was 4.2 and that for co-codamol 60/1000 was 2.2. Tramacet by comparison was 2.6. The lower the NNT the more effective the analgesic hence the complainant suggested that by not comparing Tramacet with co-codamol 60/1000 but only with 60/600, showed Tramacet in a more favourable light.

Co-codamol 30/500 was available for prescription with the recommendation that one to two tablets might be taken every four hours up to a maximum of eight tablets daily. Tramacet was indicated for the symptomatic treatment of moderate to severe pain, hence the appropriate comparator indications should also be for moderate to severe pain. Under these circumstances, it was most likely that two tablets of co-codamol would be prescribed rather than one, giving a total dose of 60mg codeine phosphate combined with 1000mg paracetamol ie 60/1000 as advised by the complainant.

The comparative dose, ie co-codamol 60/600, had been selected because direct comparative clinical trials of co-codamol at that dose and Tramacet had been published (Mullican and Lacy, 2001). Given, however, that co-codamol 60/1000 was available as a recommended prescription dose then this dose should have been included in the advertisement.

Janssen-Cilag therefore admitted breaches of Clauses 7.2 and 7.3 of the Code in that the comparison was not

based on an evaluation of all of the evidence nor did it reflect that evidence clearly. The comparison was therefore misleading as it did not include the co-codamol 60/1000 data.

After receiving the complaint an immediate review of the electronic advertisement was undertaken in respect of the complainant's comments and upon realising the error, the advertisement was immediately removed from the website that day and was no longer available for health professionals to view. Review of all promotional items currently in use for Tramacet indicated that the advertisement in question was the only promotional item which contained the comparative data which was the subject of this complaint.

Janssen-Cilag apologised for this oversight and gave an undertaking that in future advertisements, where using the NNT comparative criteria, that the comparison with co-codamol 60/1000 would be used with its NNT value of 2.2.

PANEL RULING

The Panel considered that by omitting the NNT data for co-codamol 60/1000 the comparison was misleading as alleged. The Panel ruled breaches of Clauses 7.2 and 7.3 of the Code as acknowledged by Janssen-Cilag.

During its consideration of this case the Panel noted that readers were invited to claim a free stethoscope. The Panel queried whether the offer met the requirements of the supplementary information to Clause 18.2 that promotional aids must cost the donor company no more than £6 excluding VAT and have a similar perceived value to the recipient. The Panel decided to take this matter up with the company as a complaint in accordance with Paragraph 17 of the Constitution and Procedure for the Authority (Case AUTH/1879/7/06).

Complaint received **18 July 2006**

Case completed **30 August 2006**

CASE AUTH/1869/7/06

PRIMARY CARE TRUST CHIEF PHARMACIST v DAIICHI-SANKYO

Olmetec spreadsheets

The chief pharmacist at a primary care trust complained about three spreadsheets left by a representative of Daiichi-Sankyo at a GP practice.

The spreadsheets were headed, in handwriting, 'Cozaar', 'Aprovel' and 'Diovan' and listed various antihypertensives. The costs of 50 patients at each of two doses of Cozaar, Aprovel or Diovan were given on the relevant spreadsheets and all of them stated the costs of Olmetec 10mg for 50 patients and Olmetec 20mg for 50 patients. In addition a box in the top right hand corner of each sheet headed 'cost benefit' calculated the current cost, the Sankyo cost and the reduction in cost for each. A note at the bottom stated that the products listed did not necessarily reflect equivalent efficacy. Olmetec (olmesartan) was Daiichi-Sankyo's product.

The spreadsheets referred to dispensing and wholesaler discounts and included a column headed 'profit per script'. These were filled out for all the medicines mentioned.

The complainant alleged that promoting medicines on the basis of profit was unacceptable although dispensing practices might appreciate such information. In this instance, the practice was a non-dispensing practice and therefore to refer to profit was at best misleading and at worst designed to influence prescribing in the worst possible way by focussing on cost.

The Panel noted that the charts had been provided to the practice manager after a promotional call. Daiichi-Sankyo stated that the practice manager had specifically asked for a cost comparison as he was interested in setting up a practice formulary thus the information provided was in response to an individual enquiry.

The Panel noted that the Code stated, *inter alia*, that replies made in response to individual enquiries from appropriate administrative staff were exempt from the definition of promotion but only if they related solely to the subject matter of the letter or enquiry, were accurate and did not mislead and were not promotional in nature. The relevant supplementary information referred to the exemption applying only to unsolicited enquiries. The Panel did not know if the representative had promoted Olmetec to the practice manager and if such a discussion had referred to cost. If that had been so then the practice manager's request was not unsolicited. In any event the Panel considered that the spreadsheets went beyond what was necessary to answer the enquiry. The inclusion of the drug tariff reimbursement price, dispensing discount, wholesaler discount and profit per script was more information than was needed for a non-dispensing practice. Thus the spreadsheets could not take the benefit of the exemption from promotion given in the Code.

The Panel considered that the representative had in effect produced her own promotional material which had not been certified and nor did it include prescribing information. Focusing on profit in a non-dispensing practice would not influence prescribing as alleged. Nonetheless it was misleading to show to a non-dispensing practice how much profit could be made. A breach of the Code was thus ruled. The Panel considered that the

representative by producing and supplying the spreadsheets to the practice manager had not complied with the Code and thus a further breach of the Code was ruled.

The chief pharmacist at a primary care trust complained about three spreadsheets left by a representative of Daiichi-Sankyo UK Ltd at a GP practice.

Two spreadsheets were for a named surgery and had been headed, in handwriting, 'Cozaar' and 'Aprovel' respectively. The third spreadsheet did not have the printed name of a surgery at the top but had been headed, in handwriting, 'Diovan'. Each spreadsheet listed various antihypertensives. The costs of 50 patients at each of two doses of Cozaar, Aprovel or Diovan were given on the relevant spreadsheets and all of them stated the costs of Olmetec 10mg for 50 patients and Olmetec 20mg for 50 patients. In addition a box in the top right hand corner of each sheet headed 'cost benefit' calculated the current cost, the Sankyo cost and the reduction in cost for each. A note at the bottom stated that the products listed did not necessarily reflect equivalent efficacy. Olmetec (olmesartan) was Daiichi-Sankyo's product.

The spreadsheets referred to dispensing and wholesaler discounts and included a column headed 'profit per script'. These were filled out for all the medicines mentioned.

COMPLAINT

The complainant was very concerned that a Daiichi-Sankyo representative had left the spreadsheets with a GP practice. The spreadsheets compared the prices of different ACE inhibitors, angiotensin receptor blockers and calcium channel blockers. It featured 'profit per scrip'. From the headings which were inadequately obscured, they presumably were meant for another practice.

The complainant alleged that promoting medicines on the basis of profitability was unacceptable although it could be understood why dispensing practices might appreciate such information. In this instance, the practice was a non-dispensing practice and therefore to show prescribers how much profit they could make was at best misleading and at worst designed to influence prescribing in the worst possible way by focussing on cost.

When writing to Daiichi-Sankyo the Authority asked it to respond in relation to Clauses 7.2 and 9.2 of the Code.

RESPONSE

Daiichi-Sankyo noted the complainant alleged that its representative had left the cost spreadsheet with the practice implying that such action was proactive and part of a promotional exercise. This was not so. After a normal promotional call the representative followed up the request that was asked by providing information to the practice manager. This incident therefore constituted the provision of information following a request and was not part of a specific promotional activity. Daiichi-Sankyo referred to Clause 1.2 of the Code where it stated that replies made in response to individual enquiries from members of health professions etc were not included in the Code, provided they were not promotional (see above) and were factual, accurate, informative etc. This was in effect a request for information. It was provided outside the call and therefore was not strictly within the Code.

Daiichi-Sankyo submitted that the practice manager specifically asked the representative for a cost comparison and further information as he was interested in helping set up a practice formulary. The representative provided the information requested by using an interactive spreadsheet she already had. Although this was designed for use with dispensing practices and not to be left with customers, she felt that as this was a 'one off' request it was appropriate to provide it. The representative zeroed out the non-relevant information, ie profit section in the top left hand corner and changed the parameters to 100% non-dispensing to avoid confusion so that the 'profit benefit' column was defunct. The sheets were then printed as a comparator sheet, five times for each of the comparator treatments. The representative posted the information to the customer, including the additional requested information as clinical reprints.

The representative asked the practice manager for surgery specific data to help indicate a more realistic comparative number, however the practice manager stated that it was not possible to provide this information. As a consequence the representative had selected a nominal 100 patients for comparison purposes. The box in the top right hand side of the spreadsheet indicated the potential reduction in cost.

Daiichi-Sankyo noted that a few days later the representative received a brief call from a pharmacist at the local PCT stating that they were not happy with the information that had been provided to the practice manager; the pharmacist was not willing to discuss the incident other than to make it clear that this type of information should not be provided again. The representative apologised and the call was summarily terminated. At the time the representative did not understand why the pharmacist was upset about the information that had been provided as no further detail was provided. The representative emailed the practice manager to apologise for the incident. The practice manager who was unaware that there had been an issue was surprised by the email; he had not separately complained or raised a concern about the incident or the information provided.

The requested information was provided solely for the use of the practice manager. Daiichi-Sankyo did not know how the information was provided to the pharmacist both at the PCT or the complainant.

Daiichi-Sankyo submitted that it was unable to comment on the scope of the Code in relation to a complaint made by a third party recipient of information which was not intended for their use. This was of particular importance as the complaint implied that the representative might have promoted solely, or at least mainly, on the basis of cost. The company strongly refuted this accusation. The provision of the relevant data was in a follow-up

action by post and was generated following a legitimate promotional product call for which the representative had been fully trained. As stated above the request was outside the formal promotional call. This provision of the spreadsheets had not constituted a promotional action as the information was not discussed in a call it was merely provided as had been requested. The representative had completed her call in the usual way and, during the call mentioned comparative efficacy, tolerability and cost. A resulting direct question from the practice manager after the promotional call resulted in the representative extracting and posting the chart in question with other accompanying material.

Daiichi-Sankyo conceded that the representative's actions were not in line with established process for information requests as these would normally be handled through the medical information service. However, the representative's inexperience (less than 6 months' industry experience) and her initiative prompted her to spontaneously provide information to the practice manager without considering the consequences. This issue had been addressed with the representative by planning re-training around information requests and further reiteration of guidance for use of the spreadsheet. The provision of information was not in breach of Clause 7.2.

With regard to Clause 9.2, Daiichi-Sankyo did not consider that the activity had failed to recognise the special nature of medicines as the question raised (and answered) applied specifically to comparative costs. The professional standing of the practice manager was clearly recognised by the representative who provided requested information. The provision of the spreadsheet was unlikely to have caused offence because it was requested and no complaint or suggestion of offence to the practice manager had arisen as a result.

It must be borne in mind that the spreadsheets reached the complainant second hand as they were not primarily intended for him and he received no explanation from the company, but nonetheless there was nothing contained within that might have offended. As he was not present at the promotional call Daiichi-Sankyo failed to understand how the complainant could imply that the representative had promoted solely on the matter of cost which was not the case.

Finally Daiichi-Sankyo stated that the usual internal process would be for the representative to refer a specific question to the Medical Services Department to answer. The representative was new to pharmaceutical work and as she had the data to hand she decided to provide it as a result of this request and as a good service to her customer. While not strictly within its usual procedures Daiichi-Sankyo did not believe that this was a breach of the Code, nor that the actions might have caused offence. There might have been a lack of understanding of the process and use of the spreadsheet by the representative, and although the process was reasonably laid out in documentation, this was not followed. Daiichi-Sankyo had already rectified this issue.

In conclusion Daiichi-Sankyo denied a breach of either Clause 7.2 or 9.2. In response to a request for comments in relation to Clause 15.2 of the Code the company did not believe that the representative had breached Clause 15.2 of the Code. The representative responded to a specific request from the practice manager and promptly provided the information required. The information was factual and correct and did not form part of either a promotional visit or a promotional exercise. The request for information came outside a promotional call.

Daiichi-Sankyo again noted that the complainant received the document from the practice manager and not from the representative who was not aware that the data might be passed to a third party. Furthermore the practice manager who requested the information did not and had not complained about the conduct of, or the data provided by, the representative.

The representative had apologised to the practice manager immediately after being told of the complaint even though the practice manager was unaware that a complaint had been made. Daiichi-Sankyo submitted that this illustrated another example of proper and courteous professional behaviour by the representative.

Daiichi-Sankyo recognised that the representative's action might not have been in line with the normal internal process for information requests, however high ethical standards and the requirements of the Code were not compromised.

The representative ensured that the material provided in response to this 'one off' customer request was accurate and relevant. This information met the needs of the customer and did not contravene Clause 15.2.

PANEL RULING

The Panel noted Daiichi-Sankyo's submission that the charts had been provided to the practice manager after a normal promotional call. Daiichi-Sankyo stated that the practice manager had specifically asked for a cost comparison and further information as he was interested in setting up a practice formulary; thus the information was provided in response to an individual enquiry.

The Panel noted that Clause 1.2 of the Code stated, *inter alia*, that replies made in response to individual enquiries from health professionals or appropriate administrative staff were exempt from the definition of promotion but only if they related solely to the subject matter of the letter or enquiry, were accurate and did not mislead and were not promotional in nature. The relevant supplementary information referred to the exemption applying only to unsolicited enquiries. The Panel did not know if the representative had promoted Olmetec to the practice manager and if such a discussion had referred to cost. If that had been so then the practice manager's request was not unsolicited. In any event the Panel considered that the spreadsheets went beyond what was necessary to answer the practice manager's enquiry. The inclusion of the drug tariff

reimbursement price, dispensing discount, wholesaler discount and profit per script was more information than was needed for a non-dispensing practice. Thus the spreadsheets could not take the benefit of the exemption from promotion given in Clause 1.2 of the Code.

The Panel considered that the representative had in effect produced her own promotional material which had not been certified nor did it include prescribing information. Focusing on profit in a non-dispensing practice would not influence prescribing as alleged. Nonetheless it was misleading to show to a non dispensing practice how much profit could be made.

A breach of Clause 7.2 was thus ruled. The Panel considered that the representative by producing and supplying the spreadsheets to the practice manager had not complied with the Code and thus a breach of Clause 15.2 of the Code was ruled.

The Panel considered that its ruling of Clause 15.2 covered the situation and thus ruled that there was no breach of Clause 9.2 of the Code.

Complaint received **19 July 2006**

Case completed **2 October 2006**

CASE AUTH/1872/7/06 *NO BREACH OF THE CODE*

HOSPITAL CHIEF PHARMACIST/DIRECTOR v SHIRE

Alleged breach of undertaking

A hospital chief pharmacist noted that a paper on taste used by Shire had previously been ruled in breach of the Code (Case AUTH/1825/4/06). Shire was still using the paper to promote Calcichew-D_3 Forte; it was being shown to GP practices to encourage prescribing of Calcichew. It had also been circulated to hospital drug and therapeutic committees to support inclusion in the formulary. The complainant sat on a [named] drug and therapeutics committee and had received a copy of this paper in July.

As the matter related to a potential breach of undertaking, it was taken up by the Director as it was the responsibility of the Authority itself to ensure compliance with undertakings. This accorded with advice previously given by the Code of Practice Appeal Board.

The Panel noted that Case AUTH/1825/4/06 had concerned the presentation of data from Rees and Howe which was a study to compare the acceptability of Calcichew-D_3 Forte with Adcal-D_3. The Panel had been concerned that not enough detail had been given in an advertisement such that readers would not know what it was about Calcichew-D_3 Forte that patients preferred. In that regard the Panel considered that the advertisement was misleading and a breach of the Code had been ruled.

The matter now at issue, Case AUTH/1872/6/06, concerned the use of Rees and Howe by Shire. The Panel considered that by using the actual paper Shire had provided all of the information to recipients such that they would be able to tell why patients preferred Calcichew-D_3 Forte. The representatives' briefing material stated that Rees and Howe was essential in differentiating Calcichew-D_3 Forte from its competitors. It showed that 80% of patients preferred Calcichew-D_3 Forte to Adcal-D_3 when comparing grittiness, chalkiness, ease of chewing, swallowing and stickiness.

The Panel considered that use of Rees and Howe was not a misleading comparison. The Panel did not consider that the use of Rees and Howe represented a breach of the undertaking given in Case AUTH/1825/4/06. No breach of the Code was ruled.

A hospital chief pharmacist noted that on 26 May 2006 it had been ruled that Shire Pharmaceuticals Ltd's paper on taste breached Clauses 7.2 and 7.3 of the Code and was unfair and misleading. The complainant alleged that Shire was still using the paper.

As the matter related to a potential breach of undertaking, it was taken up by the Director as it was the responsibility of the Authority itself to ensure compliance with undertakings. This accorded with advice previously given by the Code of Practice Appeal Board.

COMPLAINT

The complainant noted that Shire was still using the paper to promote Calcichew-D_3 Forte. This paper was being shown to GP practices to encourage prescribing of Calcichew. It had also been circulated to hospital drug and therapeutic committees to support inclusion in the formulary. The complainant sat on a [named] drug and therapeutics committee and had received a copy of this paper in July 2006.

The complainant made this complaint about this unethical behaviour on behalf of all the GPs in a [named] PCT and also on behalf of the [named] drug and therapeutics committee.

When writing to Shire, the Authority asked it to respond in relation to Clauses 2, 9.1 and 22 of the Code in addition to Clauses 7.2 and 7.3 mentioned by the complainant.

RESPONSE

Shire assumed that the complainant was referring to Case AUTH/1825/4/06 which was not about the physical use of reprints of the paper to promote Calcichew-D_3 Forte. It was about claims made in an advertising leaflet, which were referenced to Rees and

Howe (2001), which Shire assumed to be the 'paper on taste'. The paper reported a randomised, controlled crossover trial in which two proprietary preparations of calcium and vitamin D were compared. The publication reported a 'comparison of acceptability' (not 'taste') of the two medicines. The variables studied included patients' perception of tablet taste (assessed on a visual analogue scale, ranging from 'very sweet' to 'very bitter', not 'good' to 'bad') but also perceptions of several other organoleptic properties (again assessed on a visual analogue scale but interpretable as relatively 'good' or 'bad') and overall preference. The Panel noted in Case AUTH/1825/4/06 that it was not unreasonable to make the comparison. The actual ruling stated:

> 'Overall the Panel considered that the claim at issue 'Chew Calcichew-D_3 Forte for Ten Seconds for a pleasant surprise. In a comparative study, Calcichew-D_3 Forte was preferred over Adcal-D_3 by 80% of patients' was a misleading comparison. Thus the Panel ruled breaches of Clauses 7.2 and 7.3 of the Code.'

In summary Shire did not believe that the Panel had ruled out the use of, reference to or distribution of, reprints of Rees and Howe in Case AUTH/1825/4/06. The complainant's belief was incorrect. Shire therefore submitted that there was no case to answer.

Shire submitted that Rees and Howe reported a randomised controlled trial (grade A evidence) and was published in a peer review journal. The paper was refereed. The Code permitted the unsolicited distribution of this type of publication (Clause 11.1). Shire had not breached the Code by distributing the paper. In this era of evidence based medicine it was surely preferable for the source document to be distributed than for potentially misleading advertisements, based on data derived from it, to be published and distributed instead. Furthermore distribution of published results of randomised, controlled trials was entirely consistent with the requirement set out in the Medicines and Healthcare products Regulatory Agency's booklet on the rules governing advertising which stated that promotional activity must encourage the rational use of medicines: Rees and Howe provided useful insights into factors which might be relevant to patient compliance with long-term treatment and therefore helped prescribers and drug and therapeutics committees to make rational choices about medicines.

Shire noted that the complainant stated that the complaint was made 'about this unethical behaviour on behalf of all the GPs in a [named] PCT and also on behalf of the [named] drug and therapeutic committee'.

Shire submitted that its response above clearly demonstrated that it had not behaved in an unethical manner. Shire hoped that the outcome of this case would be communicated to all the GPs in the [named] PCT and also to all of the members of the [named] drug and therapeutics committee who had expressed concern about this matter via the complainant.

Shire submitted that for the reasons set out above it did not believe that it had breached the undertaking given in relation to Case AUTH/1825/4/06 and thus had not breached Clause 22.

Shire did not believe that it had failed to maintain high standards and thus had not breached Clause 9.1.

Shire did not believe that its activities in distributing reprints of a peer reviewed publication (as allowed under Clause 11.1 of the Code) had undermined confidence in the pharmaceutical industry or brought discredit upon it and thus Shire had not breached Clause 2.

Shire rejected the assertion that it had breached the Code as alleged and contended that its activities had not been unethical.

Shire provided a copy of extracts from its Cycle Briefing Document dated January 2006, for its representatives. In this document, six peer reviewed publications (including Rees and Howe) were recommended for use by the representatives in their calls on health professionals. These publications would also be used, as opportunity arose, to support formulary applications. Shire could not comment on the individual case, not knowing the identity of the pharmacist and PCT in question.

PANEL RULING

The Panel noted that Case AUTH/1825/4/06 had concerned the presentation of data from Rees and Howe which was a study to compare the acceptability of Calcichew-D_3 Forte compared with Adcal-D_3. The Panel had been concerned that not enough detail had been given in an advertisement such that readers would not know what it was about Calcichew-D_3 Forte that patients preferred. In that regard the Panel considered that the advertisement was misleading and a breach of the Code had been ruled.

The matter now at issue, Case AUTH/1872/6/06, concerned the use of Rees and Howe by Shire. The Panel considered that by using the actual paper Shire had provided all of the information to recipients such that they would be able to tell why patients preferred Calcichew-D_3 Forte. The representatives' briefing material stated that Rees and Howe was essential in differentiating Calcichew-D_3 Forte from the competitors. It showed that 80% of patients preferred Calcichew-D_3 Forte to Adcal-D_3 when comparing grittiness, chalkiness, ease of chewing, swallowing and stickiness.

The Panel considered that use of Rees and Howe was not a misleading comparison. No breach of Clauses 7.2 and 7.3 was ruled.

The Panel did not consider that the use of Rees and Howe represented a breach of the undertaking given in Case AUTH/1825/4/06. No breach of Clauses 2, 9.1 and 22 was ruled.

Complaint received **28 July 2006**

Case completed **5 September 2006**

CASE AUTH/1873/8/06

SCRUTINY/DIRECTOR v GLAXOSMITHKLINE

TORCH journal advertisement

During the course of scrutiny a journal advertisement was taken up with GlaxoSmithKline because it appeared not to comply with the requirements of the Code concerning the provision of prescribing information. The advertisement featured the TORCH (Towards a revolution in COPD health) study and had appeared in Hospital Doctor.

The Authority noted that the TORCH study was a study sponsored by GlaxoSmithKline comparing, *inter alia*, GlaxoSmithKline's product Seretide upon survival in patients with COPD. The Authority considered that the advertisement was promotional and that it was a full advertisement in which no prescribing information had been provided.

GlaxoSmithKline considered that the advertisement was not promotional for a product and did not come within the scope of the Code. The Authority did not accept this, noting that the TORCH study specifically examined the efficacy of three GlaxoSmithKline products and in particular all cause mortality in patients treated with Seretide. In the Authority's view by 'advertising' the TORCH study through paid-for space, GlaxoSmithKline had indirectly referred to, and thus advertised, Serevent (salmetrol), Flixotide (fluticasone) and Seretide (salmeterol/fluticasone combination). It was a long established principle that paid-for space in a journal constituted an advertisement.

GlaxoSmithKline maintained its position and, having considered the company's comments, the Director decided that a *prima facie* case had been established and took the matter up as a formal complaint.

The Panel noted GlaxoSmithKline's submission that the purpose of the advertisement was, *inter alia*, to promote the company's role in supporting significant research studies. In the Panel's view the purpose of the advertisement was much more specific than that. It was, as submitted, to ensure that health professionals were aware that the results from the TORCH study would be available soon. GlaxoSmithKline had stated that the advertisements were to increase awareness of the study which was of major medical significance. The TORCH study was sponsored by GlaxoSmithKline and used three of its medicines. The GlaxoSmithKline press release referred to the preliminary results as being positive for Seretide. Further that GlaxoSmithKline believed the results were clinically important and would have a positive impact on the future management of COPD.

The Panel considered it immaterial that the advertisement did not refer to any clinical results. Merely raising awareness of a specific study would draw attention to it. Readers would be prompted to find out more and in that regard the Panel noted that Vestbo *et al* which described the protocol and design had been published.

The advertisement appeared in medical journals and occupied space paid for by GlaxoSmithKline. It was a long established principle that any 'paid-for' space in a journal constituted an advertisement. In the Panel's view the advertisement was not a corporate advertisement; it referred to the TORCH study in COPD, a study which specifically examined the efficacy of three GlaxoSmithKline products and in particular all cause mortality in patients treated with Seretide. On balance the Panel considered that by 'advertising' the TORCH study, GlaxoSmithKline had indirectly referred to, and thus advertised, Serevent, Flixotide and Seretide. If this were not the case then companies could pay for space and 'advertise' their latest clinical trials, and thus their products, without being bound by the restrictions in the Code. A breach of the Code was ruled.

During the course of scrutiny in accordance with Paragraph 18 of the Authority's Constitution and Procedure, a journal advertisement was taken up with GlaxoSmithKline UK Ltd because it appeared not to comply with Clause 4.1 of the Code concerning the provision of prescribing information. The advertisement (ref SFC/AVL/06/24428/1) featured the TORCH (Towards a revolution in COPD health) study and had appeared in Hospital Doctor on 20 April.

COMPLAINT

During scrutiny the Authority had noted that the advertisement related to the TORCH study which was a study sponsored by GlaxoSmithKline comparing, *inter alia*, GlaxoSmithKline's product Seretide upon survival in patients with COPD. The Authority considered that the advertisement was promotional and that it was a full advertisement in which no prescribing information had been provided, contrary to Clause 4.1 of the Code.

GlaxoSmithKline dissented from this view as it considered that the advertisement was not promotional for a product and did not come within the scope of the Code as defined in Clause 1.1 and was covered by the exclusions in Clause 1.2. The Authority did not accept this, noting that the TORCH study specifically examined the efficacy of three GlaxoSmithKline products and in particular all cause mortality in patients treated with Seretide. In the Authority's view by 'advertising' the TORCH study through paid-for space, GlaxoSmithKline had indirectly referred to, and thus advertised, Serevent (salmetrol), Flixotide (fluticasone) and Seretide (salmeterol/fluticasone combination). It was a long established principle that paid-for space in a journal constituted an advertisement.

GlaxoSmithKline maintained its position and, having considered the company's comments, the Director decided that a *prima facie* case had been established and took the matter up as a formal complaint. This accorded with Paragraph 18.5 of the Constitution and Procedure.

RESPONSE

GlaxoSmithKline stated that COPD was a chronic disease with a significant mortality that placed a large health burden on patients, carers and the NHS. It was characterised by exacerbations and an inevitable decline in respiratory function leading to disability and death. Most studies had examined symptom relief as their primary end point and as yet, no pharmaceutical intervention had been shown to be disease modifying with a benefit on survival.

The TORCH study was the largest prospective study undertaken in COPD. It was a double blind, randomised controlled trial with four arms including three GlaxoSmithKline medicines – Serevent, Flixotide, Seretide and placebo (allowing other normal therapies in the background).

The primary outcome was to determine whether there was a significant reduction in all cause mortality in COPD patients treated with Seretide compared with placebo. The full results of this study were awaited. No study had hitherto shown whether pharmacotherapy could improve survival in this disease. A number of secondary outcomes, including changes in health status and exacerbation frequency were also examined in the study, making its outcome extremely relevant to the practice of medicine in an area that was part of the government's quality outcome framework.

The TORCH study was of major medical significance whether its outcomes demonstrated a survival benefit to patients suffering from COPD or not. A result either way would provide valuable information about the usefulness of therapies used in COPD and might be able to establish the relative value of treating exacerbations. The importance of the study was underlined by the publication of a full paper describing the study protocol and design (Vestbo *et al* 2004). In constructing the advertisement, GlaxoSmithKline was mindful of the requirements of the Code in indirectly referring to its medicines and as such did not refer prescribers to that publication, recognising that there was not a licensed indication for COPD for all of the medicines in the study.

Equally, because of the importance of this study, and its share price sensitivity, a Stock Exchange announcement was made in March 2006 confirming its completion and giving only preliminary results. Analysis of the data continued however and no publication of results (either as abstracts or in full) had yet appeared.

The purpose of the advertisement was to promote the role of GlaxoSmithKline in supporting significant research studies and to ensure that health practitioners were aware that the results of this important study with enormous public health implications would be available shortly. COPD was one of the government's key areas for intervention in primary care and thus of major importance and interest to healthcare providers. Whether the results were positive or negative, the results of such a landmark study would answer an important question about the appropriateness of these interventions in COPD patients and might have major implications for healthcare resource use. Given the potential impact of these results and their importance and interest to health professionals, prior notice was quite reasonable for a study of this importance and magnitude.

Whilst GlaxoSmithKline accepted the Authority's point that paid-for space constituted an advertisement, this did not promote a particular product. GlaxoSmithKline strongly believed that both disease awareness advertisements and advertisements such as this one, publicising forthcoming study results, did not promote any medicine directly or indirectly. They were placed to inform health professionals of important factual information and were one method of increasing awareness.

The advertisement was carefully designed not to be promotional and GlaxoSmithKline emphasised the following:

- care was taken not to mention any specific product or intervention being investigated in the study
- the results of the study were not yet in the public domain, preventing anyone reading the advertisement making any inference about the outcomes of the study and thus any implied claims for any product
- given that the analysis was ongoing it was impossible at this time to comment in a balanced way on the results of the study or interpret which of the four arms produced what data; as such it would be totally inappropriate to mention one or more products and thus include prescribing information
- the study design included therapeutic indications and patients who were not within the licensed population for the three medicines under study; to include prescribing information for one or all of the three products would thus be inappropriate and would constitute promotion of one or all of these medicines outside their licensed indications
- with this knowledge GlaxoSmithKline designed the advertisement to provide information only and be strictly non promotional.

In summary, the advertisement gave health professionals advance notice of an important scientific study, which was likely to report within the next few months; it was not an advertisement for any product. No mention either directly, or indirectly was made of any product.

Given the evidence above and the careful manner in which GlaxoSmithKline had undertaken this advertisement, it anticipated that the Authority would recognise the intent and the care taken and agree with GlaxoSmithKline's interpretation of the Code.

As such GlaxoSmithKline firmly believed that this advertisement did not fall within the scope of the Code as defined by Clause 1.1 and was covered by the exclusions in Clause 1.2. GlaxoSmithKline therefore strongly believed that it could not be in breach of Clause 4.1.

PANEL RULING

The advertisement was unlike any previously considered and there were thus no case precedents to guide the Panel.

The Panel noted the submission that the purpose of the advertisement was, *inter alia*, to promote the role of GlaxoSmithKline in supporting significant research studies. In the Panel's view the purpose of the advertisement was much more specific than that. It was, as submitted, to ensure that health professionals were aware that the results from the TORCH study would be available soon. GlaxoSmithKline had stated that the advertisements were to increase awareness of the study which was of major medical significance. The TORCH study was sponsored by GlaxoSmithKline and used three of its medicines. The GlaxoSmithKline press release referred to the preliminary results as being positive for Seretide. Further that GlaxoSmithKline believed the results were clinically important and would have a positive impact on the future management of COPD.

The Panel considered it immaterial that the advertisement did not refer to any clinical results. Merely raising awareness of a specific study would draw attention to it. Readers would be prompted to find out more and in that regard the Panel noted that Vestbo *et al* which described the protocol and design had been published.

The advertisement appeared in medical journals and occupied space paid for by GlaxoSmithKline. It was a long established principle that any paid-for space in a journal constituted an advertisement. In the Panel's view the advertisement was not a corporate advertisement; it referred to the TORCH study in COPD, a study which specifically examined the efficacy of three GlaxoSmithKline products and in particular all cause mortality in patients treated with Seretide. On balance the Panel considered that by advertising the TORCH study, GlaxoSmithKline had indirectly referred to, and thus advertised, Serevent, Flixotide and Seretide. If this were not the case then companies could pay for space and advertise their latest clinical trials, and thus their products, without being bound by the restrictions in the Code.

The advertisement did not include any prescribing information. A breach of Clause 4.1 was ruled.

Proceedings commenced 2 August 2006

Case completed 4 September 2006

CASE AUTH/1877/8/06 *NO BREACH OF THE CODE*

VOLUNTARY ADMISSION BY SHIRE

No breach of undertaking

Shire voluntarily advised the Authority that an advertisement for Calcichew-D_3 Forte, which was a version of one found in breach of the Code in Case AUTH/1825/4/06, had been published despite clear instructions from Shire that such copy be destroyed.

As the matter related to a potential breach of undertaking it was sufficiently serious for it to be taken up and dealt with as a formal complaint under the Code in accordance with the Constitution and Procedure.

The Panel noted that in Case AUTH/1825/4/06 it considered the claim 'Chew Calcichew-D_3 Forte for Ten Seconds for a pleasant surprise. In a comparative study, Calcichew-D_3 Forte was preferred over Adacal-D_3 by 80% of patients', to be a misleading comparison in breach of the Code.

When the Authority was informed that the advertisement now at issue 'was a version of the one found in breach of the Code in Case AUTH/1825/4/06', it was assumed, as a copy of the advertisement itself was not provided, that Shire was voluntarily admitting a breach of undertaking. The Panel noted, however, on receiving a copy of the advertisement, that the comparative claim at issue in Case AUTH/1825/4/06 was not included. Although the advertisement was part of the same campaign it did not compare patient preference for Calcichew-D_3 Forte with that for Adcal-D_3. In that regard the Panel did not consider that publication of the advertisement represented a breach of the undertaking given in Case AUTH/1825/4/06. No breach of the Code was ruled.

Shire Pharmaceuticals Ltd voluntarily advised the Authority that an advertisement (ref 003/0422a) for Calcichew-D_3 Forte, which was a version of one found in breach of the Code in Case AUTH/1825/4/06, had appeared in the August edition of MIMS despite clear instructions from Shire that such copy be destroyed. MIMS had taken full responsibility for the incorrect copy running.

COMPLAINT

As the matter related to a potential breach of undertaking it was sufficiently serious for it to be taken up and dealt with as a formal complaint under the Code (Paragraph 5.4 of the Constitution and Procedure refers). Shire was asked to respond in relation to Clauses 2, 9.1 and 22 of the Code.

RESPONSE

Shire stated that following Case AUTH/1825/4/06, it decided to withdraw material containing claims relating to 'The Ten Second Trial' in order to review its position. The advertisement in the August edition of MIMS was one of this series of promotional items. The letter from the company's medical director which had instigated the current case had been intended to draw the Authority's attention to the erroneous publication of the advertisement in MIMS, which had apologised for its mistake.

This advertisement in MIMS did not refer to Rees and Howe (2001), a comparative trial of Calcichew-D_3 Forte and Adcal-D_3 that was at issue, in conjunction with the phrase 'Chew Calcichew-D_3 Forte for ten seconds for a pleasant surprise', in the ruling in Case AUTH/1825/4/06. Shire therefore believed that this advertisement was not in breach of undertaking, Clause 22, nor in breach of Clauses 2 or 9.1.

PANEL RULING

The Panel noted that in Case AUTH/1825/4/06 it considered the claim 'Chew Calcichew-D_3 Forte for Ten Seconds for a pleasant surprise. In a comparative study, Calcichew-D_3 Forte was preferred over Adacal-D_3 by 80% of patients', to be a misleading comparison in breach of the Code.

When the Authority was informed that the advertisement now at issue 'was a version of the one found in breach of the Code in Case AUTH/1825/4/06', it was assumed, as a copy of the advertisement itself was not provided, that Shire was voluntarily admitting a breach of undertaking. Thus the matter was taken up as a formal complaint. The Panel noted, however, on receiving a copy of the advertisement, that the comparative claim at issue in Case AUTH/1825/4/06 was not included. Although the advertisement was part of the same campaign it did not compare patient preference for Calcichew-D_3 Forte with that for Adcal-D_3. In that regard the Panel did not consider that publication of the advertisement represented a breach of the undertaking given in Case AUTH/1825/4/06. No breach of Clause 22 of the Code was ruled. It followed that there was also no breach of Clauses 9.1 and 2 of the Code.

Complaint received **3 August 2006**

Case completed **30 August 2006**

CASE AUTH/1879/7/06 *NO BREACH OF THE CODE*

PARAGRAPH 17/DIRECTOR v JANSSEN-CILAG

Cost of a promotional aid

During the consideration of Case AUTH/1868/7/06 the Panel queried whether a stethoscope offered as a promotional aid to GPs met the requirements of the supplementary information to the Code that such items must cost the donor company no more than £6 excluding VAT and have a similar perceived value to the recipient.

The Panel noted that, in addition to the requirements regarding actual and perceived value, promotional aids had to be relevant to the recipient's work. There was no doubt that a stethoscope was relevant to a GP's work. The stethoscopes at issue had cost Janssen-Cilag £2.20 each. The Panel noted the company's submission regarding the perceived value of a stethoscope. It appeared that whilst some stethoscopes could cost a lot more than £6 each, there were many which did not. The Panel accepted that from its photograph the stethoscope on offer did not appear to be an expensive one. No breach of the Code was ruled.

COMPLAINT

During the consideration of Case AUTH/1868/7/06 the Panel noted that readers were invited to claim a free stethoscope and queried whether the offer met the requirements of the supplementary information to Clause 18.2 that promotional aids must cost the donor company no more than £6 excluding VAT and have a similar perceived value to the recipient. The Panel decided to take the matter up with Janssen-Cilag as a complaint under Paragraph 17 of the Constitution and Procedure for the Authority.

When writing to Janssen-Cilag the Authority asked the company to respond in relation to Clause 18.1 of the Code.

RESPONSE

Janssen-Cilag noted that Clause 18.2 allowed promotional aids to be distributed to health professionals provided that they were inexpensive and relevant to the practice of their profession. A stethoscope was definitely relevant to the practice of medicine. The company was also aware of the price restrictions on promotional aids and also importantly that the perceived value to the recipient should also not exceed £6 (excluding VAT) such that the offer could not be misconstrued in respect of Clause 18.1.

Stethoscopes varied in their cost and also worth (both real and perceived) to health professionals. A good stethoscope such as a Littmanns could cost in excess of £60 and this definitely would not be consistent with the Code. At the other extreme there was a myriad of stethoscopes available of much lower quality and price. The cost to Janssen-Cilag of the stethoscope offered within the Tramacet edetail aid was £2.16 and thus fulfilled the cost requirements stated in the Code.

With regard to perceived value, it was important that the stethoscope did not appear to be of good or exceptional quality, and indeed the picture of it in the edetail aid would indicate to most health professionals that the stethoscope offered was inexpensive.

The target audience for the Tramacet edetail aid was GPs, and as the item was provided electronically, the company contended that individuals who would have received and read it would be familiar with other electronic media, such as on the internet. There were several readily available sources of inexpensive

stethoscopes on the internet with prices starting from 50p on ebay, and at several other sites at fixed prices of £3.99 and £4.60, which would indicate to a health professional that such stethoscopes were commodity items and not of a special value.

Janssen-Cilag therefore contended that the stethoscope fulfilled the requirements laid out within Clause 18.1 and 18.2 (including supplementary information) and so the company denied a breach of the Code in that respect.

PANEL RULING

The Panel noted that the supplementary information to Clause 18.2 of the Code stated that promotional aids could cost a donor company no more than £6 each, excluding VAT. The perceived value to the recipient had to be similar. Promotional aids also had to be relevant to the recipient's work.

There was no doubt that a stethoscope was relevant to a GP's work. The stethoscopes at issue had cost Janssen-Cilag £2.20 each excluding VAT but including the charge for the artwork. The Panel noted the company's submission regarding the perceived value of a stethoscope. It appeared that whilst some stethoscopes could cost a lot more than £6 each there were many which did not. The Panel accepted that from its photograph the stethoscope on offer did not appear to be an expensive one. No breach of Clause 18.1 was ruled.

Proceedings commenced 11 August 2006

Case completed 5 September 2006

CASE AUTH/1880/8/06 *NO BREACH OF THE CODE*

CONSULTANT PHYSICIAN v MERCK SHARP & DOHME

Market research survey

A consultant physician complained about a market research survey and letter sent on behalf of Merck Sharp & Dohme. The questionnaire enabled the recipient to nominate those physicians from whom he/she sought medical guidance/ knowledge in specified therapy areas. It was stated in the letter that the information would be used to help structure future medical educational programmes according to need.

In the complainant's view such unsolicited mail was not appropriate. He was worried that the company was paying him to send it information regarding other doctors who could then be contacted in a similar unsolicited way.

The Panel noted from the letter that the nominated colleagues and the addressee would be invited to 'speak at or take part in relevant professional meetings, scientific partnerships and research initiatives' and that the information received would be used to 'deliver tailored information to you and them'. Physicians might also be approached for their knowledge of a specific disease area and its environment. The questionnaire asked for details of local and regional asthma and allergic rhinitis specialists and referred to the general approach to managing the associated risk with adopting new treatment options.

The Panel did not consider that it was unacceptable for Merck Sharp & Dohme to have commissioned market research to validate its understanding of networks in asthma and allergic rhinitis. The arrangements for such research must not contravene the Code.

The Panel noted that whilst the covering letter made Merck Sharp and Dohme's involvement clear no such explanation appeared on the questionnaire itself. The Panel queried whether the honorarium of £25 online gift vouchers was excessive given the very simplistic nature of the questionnaire. The Panel thus had some concerns about the material. Nonetheless the material was not such as to constitute disguised promotion and thus the Panel ruled no breach of the Code.

A consultant physician complained about a market research survey and covering letter sent by an agency on behalf of Merck Sharp & Dohme Limited. The covering letter explained that the questionnaire was to enable the recipient to nominate those physicians from whom he/she sought medical guidance/ knowledge in specified therapy areas. The information would be used to help structure future medical educational programmes according to need.

COMPLAINT

In the complainant's view such unsolicited mail was not appropriate. He was worried that the company was paying him to send it information regarding other doctors who could then be contacted in a similar unsolicited way.

When writing to Merck Sharp & Dohme, the Authority asked it to respond in relation to Clause 10.2 of the Code.

RESPONSE

Merck Sharp & Dohme explained that the market research survey was conducted with full intent to comply with the Code as well as with the British Healthcare Business Intelligence Association (BHBIA) Legal and Ethical Framework for Healthcare Market Research.

The survey was to validate Merck Sharp & Dohme's understanding of the secondary care networks in asthma and allergic rhinitis, by asking specialists to:

- nominate UK leading specialists in asthma
- nominate local/regional specialists in allergic rhinitis

- nominate local/regional specialists in asthma
- nominate doctors whose practice and opinion is respected
- provide a personal perception of one's general approach to managing the associated risk with adopting new treatment options into practice.

The survey was not commissioned to establish a database. The company already had a customer database, which contained names, addresses, and therapeutic specialty for health professionals, and complied with all applicable privacy laws. The personal data provided would be cross referenced against and integrated into its internal database and used to invite health professionals to attend conferences and to participate in other programmes, to deliver educational materials as well as other products and services, including promotional activities that might be of interest. This complied with the requirements of Clause 10.2 of the Code.

In terms of the market research approach undertaken and how the information provided would be used to ensure compliance with the Code and the BHBIA framework the following standards were applied:

➢ The research was conducted through a reputable market research agency. The agency was a member of BHBIA, the European Pharmaceutical Marketing Research Association (EphMRA) and the Pharmaceutical Business Intelligence and Research Group (PBIRG) and, as such, was bound by the 'The Legal and Ethical Framework for Healthcare Market Research', as referred to in Clause 10.2 of the Code. The agency concerned understood that this research complied with the Code.

➢ The survey was designed to comply with the core principles of the BHBIA Framework.

- Participants were honestly and comprehensively informed about the research in which they were taking part. The covering letter explicitly stated the purpose of the research and how the information was intended to be used, ensuring full transparency. No attempt was made to disguise the nature of the study.
- The survey clearly stated the research was being commissioned by Merck Sharp and Dohme as required by the Code; there was no implication that the survey was independent from the company.
- The survey explicitly outlined how the personal data provided would be used, and aimed to address this up-front, to ensure the respondent was not misled in anyway.
- In compliance with the BHBIA framework informed consent was also required in order for the information provided by participants to be processed and was not and would not be accessible to Merck Sharp & Dohme if not completed correctly. Merck Sharp & Dohme had tried to provide participants with sufficient relevant information to enable them to make an informed judgement about whether to take part.
- The honorarium for specialists was £25 of online gift vouchers which Merck Sharp & Dohme submitted was in accordance with the current EphMRA guidance, referred to in the 'The Legal and Ethical Framework for Healthcare Market Research'.
- In comparison to standard agency fees for such a study, the amount given to recipients was also set towards the lower end of the usual honaria offered by pharmaceutical market research agencies.
- The agency, rather than Merck Sharp & Dohme, was solely responsible for the distribution of this incentive to respondents.

In summary, the survey was to validate Merck Sharp & Dohme's understanding of the secondary care networks in asthma and allergic rhinitis. The survey did not refer to any products and was not disguised promotion. At all times the company aimed to provide an honest and comprehensive description of the survey's purpose and how the personal data collected would be used. Informed consent was integral to the participation and processing of information received from the survey; ultimately this ensured that Merck Sharp and Dohme complied with the requirements of Clause 10.2 of the Code.

PANEL RULING

The Panel noted that the market research questionnaire had been sent by a market research company on behalf of Merck Sharp & Dohme. It was an established principle under the Code that activities carried out by a third party on behalf of a pharmaceutical company were the responsibility of that pharmaceutical company. Merck Sharp & Dohme was thus responsible for the questionnaire.

The Panel noted that the specimen covering letter described the questionnaire as an opportunity to nominate physicians from whom the addressee would seek medical guidance/knowledge in specified therapy areas. The input would be used to help structure future medical education programmes. The section headed 'Protecting personal information about you' stated that the objective was to invite the nominated colleagues and the addressee to 'speak at or take part in relevant professional meetings, scientific partnerships and research initiatives as well as deliver tailored information to you and them'. Physicians might also be approached for their knowledge of a specific disease area and its environment. Four questions in the accompanying questionnaire asked for details of local and regional asthma and allergic rhinitis specialists. The fifth question referred to the general approach to managing the associated risk with adopting new treatment options.

The Panel noted Merck Sharp & Dohme's submission that the material was market research. Clause 10.2 of the Code required that such activity must not be disguised promotion. The Panel did not consider that it was unacceptable for Merck Sharp & Dohme to have commissioned market research to validate its understanding of networks in asthma and allergic

rhinitis. The arrangements for such research must not contravene the Code.

The Panel noted that both Merck Sharp & Dohme and the supplementary information to Clause 10.2 of the Code drew attention to guidelines – The Legal and Ethical Framework for Healthcare Market Research – produced by BHBIA in consultation with The Association of the British Pharmaceutical Industry (ABPI). The framework document explained that database building was incompatible with market research; names and addresses of respondents should not be passed on to any third party and respondent details should not be placed onto a client database, used in the development of customer intelligence for the purposes of direct promotion and/or used for the purposes of direct marketing following research.

The Panel noted Merck Sharp & Dohme's submission that the survey was not commissioned to establish a database. The company already had a customer database and the data would be cross referenced against and integrated into its internal database. Doctors named in the questionnaire would be contacted as, *inter alia*, possible speakers for Merck Sharp & Dohme; they would also be sent 'tailored information'. In that regard the Panel considered that the results of the questionnaire were likely to be used in the development of customer intelligence for the purposes of direct promotion. The Panel thus queried whether such activity was compatible with the requirements set out in the BHBIA framework document.

The Panel noted that whilst the covering letter made Merck Sharp and Dohme's involvement clear no such explanation appeared on the questionnaire itself. The Panel queried whether the honorarium of £25 online gift vouchers was excessive given the very simplistic nature of the questionnaire. The Panel thus had some concerns about the material. Nonetheless the material was not such as to constitute disguised promotion and thus the Panel ruled no breach of Clause 10.2 of the Code.

Complaint received **8 August 2006**

Case completed **21 September 2006**

CASE AUTH/1882/8/06

GENERAL PRACTITIONER v SANOFI-AVENTIS

Acomplia page tag

A general practitioner complained about an Acomplia (rimonabant) page tag issued by Sanofi-Aventis and attached to a full page MIMS advertisement for Acomplia. The tag, which featured the product name, did not have the approved name on it. It was clearly for promotional purposes since it pointed the way to the advertisement.

The Panel disagreed with Sanofi-Aventis' submission that the page tag was a promotional aid. It was not provided as a stationery item and it drew attention to the advertisement. Given its purpose and the fact that it included the brand name the Panel's view was that the page tag constituted an advertisement and thus required prescribing information and the non-proprietary name of the medicine. It was a detachable, separate item and thus could not rely on the prescribing information in the actual advertisement. It had to stand alone with regard to all of the requirements of the Code. Breaches of the Code were ruled.

A general practitioner complained about the promotion of Acomplia (rimonabant) by Sanofi-Aventis. The material at issue was a page tag which featured the product name and appeared in MIMS August 2006 attached to a full page advertisement for Acomplia.

COMPLAINT

The complainant explained that the page tag was attached to page 227 in MIMS which was a full page advertisement for Acomplia. Page 226 contained the MIMS entry for Acomplia. The problem was that the tag did not have the approved name on it. It was clearly for promotional purposes since it pointed the way to the advertisement. The complainant alleged a breach of the Code.

When writing to Sanofi-Aventis the Authority asked it to respond in relation to Clauses 4.1 and 4.3 of the Code.

RESPONSE

Sanofi-Aventis explained that the page tag was attached to the September 2006 edition of MIMS as a page-marker for the published entry for Acomplia, directing the reader to this information; it was a simple detachable page-marker, containing only the brand name of the product, Acomplia. This was a minor stationery item containing the name of the product only, with no other information such as indication or claim being present. The tag was detachable and reusable and not designed to be an integral part of the advertisement to which it was attached. As a reusable minor stationery item, this was clearly a promotional aid, meeting the requirements of Clause 18.3 of the Code which stated specifically that 'the brand name or the non-proprietary name' was to be used on such an item. To have included the non-proprietary name, as suggested by the complainant, would have been a breach of this clause. Had an indication also been included, that would then have constituted an advertisement and be subject to the requirements of Clause 4 of the Code.

In summary, Sanofi-Aventis submitted that this item complied with the Code and that high standards had been maintained.

PANEL RULING

The Panel noted that the page tag, which appeared to be similar to a Post-it index tab, was stuck to a full page advertisement for Acomplia. The MIMS entry for Acomplia was on the opposite page. The page tag featured no information other than the brand name. It was detachable and could easily be removed and placed elsewhere. Sanofi-Aventis referred to it as being reusable.

The Panel did not agree with Sanofi-Aventis' submission that the page tag was a promotional aid. It was not provided as a stationery item and it drew attention to the advertisement. Given its purpose and the fact that it included the brand name the Panel's view was that the page tag constituted an advertisement and thus required prescribing information and the non-proprietary name of the medicine. It was a detachable, separate item and thus could not rely on the prescribing information in the actual advertisement. It had to stand alone with regard to all of the requirements of the Code. Breaches of Clauses 4.1 and 4.3 were thus ruled.

Complaint received **10 August 2006**

Case completed **26 September 2006**

CODE OF PRACTICE REVIEW – NOVEMBER 2006

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

1807/3/06 and 1810/3/06	**The Sunday Times/Director and a General Practitioner v Pfizer**	**Sponsored nurses**	**Breaches Clauses 2, 9.1 and 18.1 (2003 edition)**	**No appeal**	**Page 3**
1814/3/06	**Former Employee v Merck Sharp & Dohme**	**Nurse audit programme**	**Breaches Clauses 2, 9.1, and 18.1 (2003 edition)** **Audit required by Appeal Board** **Merck Sharp & Dohme required by Appeal Board to issue a corrective statement** **Public reprimand by Appeal Board** **ABPI Board suspended Merck Sharp & Dohme from ABPI membership for a minimum of three months** **Further audit required by Appeal Board in November 2006**	**No appeal** **Report from Panel to Appeal Board** **Report from Appeal Board to ABPI Board**	**Page 13**
1822/4/06 and 1823/4/06	**Novartis v ApoPharma and Swedish Orphan**	**Promotion of Ferriprox**	**ApoPharma Breaches Clauses 4.1, 7.2 and 7.4** **Swedish Orphan Breaches Clauses 7.2, 7.4, 20.1 and 20.2**	**No appeal**	**Page 20**
1831/4/06	General Practitioner v Janssen-Cilag	Durogesic DTrans email	No breach	No appeal	Page 24
1833/5/06	**AstraZeneca v GlaxoSmithKline**	**CONCEPT study leavepiece**	**Breaches Clauses 7.2 and 7.3**	**No appeal**	**Page 25**
1841/5/06	**Takeda v Daiichi-Sankyo**	**Promotion of Olmetec**	**Two breaches Clause 7.2 Two breaches Clause 7.3**	**Appeal by respondent**	**Page 33**
1842/6/06	Senior Community Mental Health Nurse/MHRA v Janssen-Cilag	Promotion of Risperdal and Risperdal Consta	No breach	No appeal	Page 43
1843/6/06	**Anonymous v Serono**	**Representative call rates**	**Breach Clause 15.4**	**No appeal**	**Page 46**
1844/6/06	**Primary Care Trust Head of Prescribing v Sanofi-Aventis**	**Rimonabant email**	**Breaches Clauses 3.1 and 9.9**	**No appeal**	**Page 48**
1845/6/06	**Primary Care Trust Assistant Director of Public Health v AstraZeneca**	**Arimidex journal advertisement**	**Breach Clause 7.2**	**No appeal**	**Page 50**

1846/6/06	Former Employee v Merck Sharp & Dohme	Memorandum and briefing document	No breach	No appeal	Page 51
1847/6/06	**Primary Care Trust Head of Prescribing v Altana Pharma**	**Conduct of representative**	**Breaches Clauses 7.2, 7.4, 9.1, 11.3 and 15.2**	**Appeal by respondent**	**Page 54**
1848/6/06	**Media/Director v Janssen-Cilag**	**Payments offered to journalists**	**Breaches Clauses 2, 9.1 and 19.1**	**Appeal by respondent**	**Page 61**
1849/6/06	Media/Director v AstraZeneca	Disclosure of patient group involvement	No breach	No appeal	Page 65
1850/6/06	Media/Director v Novartis	Disclosure of patient group involvement	No breach	No appeal	Page 68
1851/6/06	**Roche v Novartis**	**Promotion of Myfortic**	**Breach Clause 3.2**	**No appeal**	**Page 70**
1852/6/06	General Practitioner v Pfizer	Alleged disguised promotion of Lipitor	No breach	No appeal	Page 73
1853/6/06	**Anonymous Hospital Consultant v AstraZeneca**	**Symbicort journal advertisement**	**Breaches Clauses 7.2 and 7.4**	**No appeal**	**Page 75**
1854/6/06	Principal Hospital Pharmacist/ Director v Servier	Alleged breach of undertaking	No breach	No appeal	Page 77
1856/6/06	Media/Director v AstraZeneca	Criticism of a meeting	No breach	No appeal	Page 78
1858/6/06	Pharmacist v Pfizer	Newspaper article about the use of statins	No breach	No appeal	Page 80
1860/7/06	Anonymous General Practitioner v Profile Pharma	Promotion of Promixin	No breach	No appeal	Page 83
1861/7/06	Anonymous v Ferring	Sponsorship of a sporting venue	No breach	No appeal	Page 85
1863/7/06	Media/Director v Sanofi-Aventis	Patient organisation meeting	No breach	No appeal	Page 86
1864/7/06	Member of the Public v Lilly	Erectile dysfunction television advertisement	No breach	No appeal	Page 91
1865/7/06	Anonymous v Bristol-Myers Squibb	Arrangements for a meeting	No breach	No appeal	Page 93
1866/7/06	**Voluntary Admission by Daiichi-Sankyo**	**Breach of undertaking**	**Breaches Clauses 2, 9.1 and 22**	**No appeal**	**Page 95**
1867/7/06	Anonymous Employees v Roche	Activities at a meeting and call rates	No breach	No appeal	Page 98
1868/7/06	**Doctor v Janssen-Cilag**	**Tramacet electronic advertisement**	**Breaches Clauses 7.2 and 7.3**	**No appeal**	**Page 100**
1869/7/06	**Primary Care Trust Chief Pharmacist v Daiichi-Sankyo**	**Olmetec spreadsheets**	**Breaches Clauses 7.2 and 15.2**	**No appeal**	**Page 101**
1872/7/06	Hospital Chief Pharmacist/ Director v Shire	Alleged breach of undertaking	No breach	No appeal	Page 104
1873/8/06	**Scrutiny/Director v GlaxoSmithKline**	**TORCH journal advertisement**	**Breach Clause 4.1**	**No appeal**	**Page 106**
1877/8/06	Voluntary Admission by Shire	No breach of undertaking	No breach	No appeal	Page 108
1879/7/06	Paragraph 17/Director v Janssen-Cilag	Cost of a promotional aid	No breach	No appeal	Page 109
1880/8/06	Consultant Physician v Merck Sharp & Dohme	Market research survey	No breach	No appeal	Page 110
1882/8/06	**General Practitioner v Sanofi-Aventis**	**Acomplia page tag**	**Breaches Clauses 4.1 and 4.3**	**No appeal**	**Page 112**

PRESCRIPTION MEDICINES
CODE OF PRACTICE AUTHORITY

The Prescription Medicines Code of Practice Authority was established by The Association of the British Pharmaceutical Industry (ABPI) in 1993 to operate the Code of Practice for the Pharmaceutical Industry at arm's length from the ABPI itself.

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

The Code covers the advertising of medicines to health professionals and administrative staff and also covers information about prescription only medicines made available to the public.

It covers:

- journal and direct mail advertising
- the activities of representatives, including detail aids and other printed material used by representatives
- the supply of samples
- the provision of inducements to prescribe, supply, administer, recommend, buy or sell medicines by the gift, offer or promise of any benefit or bonus, whether in money or in kind
- the provision of hospitality
- the sponsorship of promotional meetings
- the sponsorship of scientific and other meetings, including payment of travelling and accommodation expenses
- the provision of information to the public either directly or indirectly, including by means of the Internet
- all other sales promotion in whatever form, such as participation in exhibitions, the use of audio-cassettes, films, records, tapes, video recordings, electronic media, interactive data systems, the Internet and the like.

Complaints submitted under the Code are considered by the Code of Practice Panel which consists of the three members of the Code of Practice Authority acting with the assistance of independent expert advisers where appropriate. Both complainants and respondents may appeal to the Code of Practice Appeal Board against rulings made by the Panel. The Code of Practice Appeal Board is chaired by an independent legally qualified Chairman, Mr William Harbage QC, and includes independent members from outside the industry.

In each case where a breach of the Code is ruled, the company concerned must give an undertaking that the practice in question has ceased forthwith and that all possible steps have been taken to avoid a similar breach in the future. An undertaking must be accompanied by details of the action taken to implement the ruling. Additional sanctions are imposed in serious cases.

Complaints about the promotion of medicines, or the provision of information to the public, should be sent to the Director of the Prescription Medicines Code of Practice Authority, 12 Whitehall, London SW1A 2DY
(telephone 020 7930 9677
facsimile 020 7930 4554)
By email to: complaints@pmcpa.org.uk.