CASE AUTH/2435/8/11

GLAXOSMITHKLINE/DIRECTOR v CHIESI

Promotion of an unlicensed indication and breach of undertaking

GlaxoSmithKline complained that, ahead of receiving a marketing authorization, Chiesi had promoted Fostair (beclometasone and formoterol) for use in chronic obstructive pulmonary disease (COPD). Fostair was currently only licensed in the UK for the regular treatment of asthma. The complaint also included an alleged breach of undertaking and that aspect was taken up by the Director as it was the Authority's responsibility to ensure compliance with undertakings.

The detailed response from Chiesi is given below.

GlaxoSmithKline stated that at a Chiesi symposium at the American Thoracic Society (ATS) in May 2011, claims were made regarding the efficacy of Fostair and the extra-fine nature of the product in COPD. As only non-US delegates could attend the Chiesi symposium, there were many European and, particularly, UK attendees. Delegates were notified of the Chiesi symposium by a flyer invitation and through information contained in the abstract book provided in the conference bags. These materials did not indicate that it was a promotional meeting. GlaxoSmithKline alleged a failure to comply with all applicable codes, laws and regulations. This was particularly relevant as Chiesi activities and materials involved more than one country and failed to comply with the European Federation of Pharmaceutical Industries and Associations (EFPIA) Code, the code of the host country and the 2011 ABPI Code.

During the symposium a UK health professional presented the results from a phase III study on the use of Fostair in COPD which demonstrated equivalence with AstraZeneca's product Symbicort (budesonide and formoterol), an established therapy licensed for the treatment of severe COPD. The summary slides concluded that an extra-fine fixed combination of formoterol and beclometasone 'translates to clinical benefits in asthma and COPD'. It was never stated that Fostair was licensed only for the treatment of asthma. There was little doubt that UK attendees unfamiliar with the Fostair marketing authorization would wrongly assume that it was licensed for COPD.

GlaxoSmithKline alleged that such high profile, non-compliant activity at an international symposium attended by a significant number of UK health professionals failed to maintain high standards; such off-licence promotion inevitably brought discredit upon and reduced confidence in the pharmaceutical industry.

GlaxoSmithKline referred to Case AUTH/2379/1/11 in which Chiesi was ruled in breach for distributing the journal Respiratory Disease in Practice, which was deemed to promote Fostair for COPD, from a British conference stand. As the ruling of that case was over a month before the ATS symposium, GlaxoSmithKline was even more concerned that the Chiesi promotional symposium at the ATS conference was certified to include claims about the efficacy of Fostair in COPD. This called into question the gravity ascribed by Chiesi to the previous ruling. GlaxoSmithKline was concerned that the symposium, with its heavy emphasis on the use of Fostair in COPD, condoned the repeated presentation of data about an unlicensed indication in a promotional setting. GlaxoSmithKline alleged that the ongoing promotion of Fostair in COPD was in breach of the undertaking given in Case AUTH/2379/1/11.

The Panel noted that Chiesi referred to a previous case, Case AUTH/2406/5/11, which concerned the same symposium and wherein the Panel had ruled no breach as it considered the matter of complaint was not within the scope of the Code. In accordance with the Constitution and Procedure, there was no published case report.

Turning to the present case, Case AUTH/2435/8/11, the Panel noted that each case had to be decided on its individual set of facts. There were important differences in the evidence before the Panel in the present case and that considered previously. Chiesi had previously submitted, *inter alia*, that Chiesi Ltd had not been involved in any aspect of the arrangements. In the present case, the Panel noted Chiesi's initial submission that any UK health professionals who had attended the symposium had done so at their own wish and not through any Chiesi activity. Chiesi subsequently submitted that Chiesi Ltd's employees had attended the conference, had told UK health professionals at the conference about the symposium and had provided a copy of the flyer to those health professionals. Indeed they had been instructed to do so by Chiesi corporate. The Panel considered that as Chiesi Ltd had invited UK health professionals to the symposium, the symposium was consequently within the scope of the Code. Chiesi Ltd was therefore responsible under the Code for the content of the presentations given at the symposium.

The Panel noted that one presentation covered, *inter alia*, 'BDP/F extrafine inhaler in COPD'. The last five slides dealt with the effects of Fostair on a number of parameters of COPD. The two cited references in this part of the presentation had been published in 2010, ie it was not new data. The fifth slide, the final one of the presentation, was headed 'BDP/F Extrafine: Summary' and stated that Fostair provided a more efficient delivery throughout the entire bronchial tree vs other combination products and that it 'Reaches small airways' and 'Treats small airways'. The final bullet point stated that this 'Translates to clinical benefits in asthma and COPD'.

The Panel noted Chiesi's submission with regard to the legitimate exchange of medical and scientific information during the development of a medicine, which was permitted under the supplementary information to the Code. The Panel queried how presenting data about the use of Fostair in COPD could be considered exchange of information 'during the development of a medicine'. Fostair already had a marketing authorization and was licensed for use in COPD in Turkey. Chiesi had noted that the conference was a truly international event and that Turkey was a major industrialised country; the Panel noted that these factors featured in the supplementary information to the Code, Promotion at International Meetings, not the supplementary information relating to the legitimate exchange of medical and scientific information during the development of a medicine. In the Panel's view, disseminating data to prescribers which expanded a licensed product's market share was different to the legitimate exchange of medical and scientific information during the development of a medicine which implied debate which enhanced the current state of scientific knowledge.

The Panel considered that the presentation promoted the use of Fostair in COPD and was thus not in accordance with the terms of its marketing authorization. A breach was ruled. Chiesi had invited UK health professionals to a symposium at which information on the use of Fostair in an unlicensed indication was presented. The Panel considered that high standards had not been maintained and ruled a breach. The Panel considered that, on balance, given the circumstances of this case, this matter did not warrant a ruling of a breach of Clause 2 of the Code, which was a sign of particular censure and reserved for such. No breach of that clause was ruled.

In relation to the alleged breach of the undertaking given in Case AUTH/2379/1/11, the Panel noted that the previous case concerned the distribution of copies of Respiratory Disease in Practice from a Chiesi stand at a British congress. The journal was sponsored by Chiesi and contained an advertisement for Fostair. The article on the front cover was entitled 'The small airways: an important target in asthma and COPD treatment'. The Panel considered that the distribution of the journal from Chiesi's promotional stand in effect promoted Fostair for an unlicensed indication. In addition, the Panel noted that a Fostair advertisement in the journal referred to the extrafine particles reaching the small airways. In the Panel's view this linked to the article about the treatment of COPD and references to particle size, and it ruled, *inter alia*, a breach of the Code.

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

The undertaking given in Case AUTH/2379/1/11 in March 2011 required that use of the journal in question and any similar material, if not already discontinued or no longer in use, would cease forthwith. The Panel considered that the subsequent symposium which promoted Fostair in COPD meant that this undertaking had not been complied with and it ruled a breach of the Code.

The Panel noted its rulings of breaches of the Code above and considered that Chiesi had failed to meet the requirement to comply with all applicable codes and thus ruled a further breach.

GlaxoSmithKline noted that a further edition of Respiratory Disease in Practice (Spring), sponsored by Chiesi, clearly implied that a COPD marketing authorization was already in place for Fostair. GlaxoSmithKline considered this was further evidence of extensive, on-going, off-licence promotion which was unacceptable.

The Panel noted that companies could sponsor material. It had previously been decided, in relation to material aimed at health professionals, that the content would be subject to the Code if it was promotional in nature or if the company used the material for a promotional purpose. Even if neither of these applied, the company would be liable if it had been able to influence the content of the material in a manner favourable to its own interests. It was possible for a company to sponsor material which mentioned its own products and not be liable under the Code for its content, but only if it had been a strictly arm's length arrangement with no input by the company and no use by the company of the material for promotional purposes. Factors which might mean there had not been a strictly arm's length arrangement would include, *inter alia*, selection of the author by the pharmaceutical company.

The Panel noted that Chiesi had suggested the author for the article that appeared on the front page of the journal at issue. Chiesi thus could not take the benefit of an arm's length agreement, and was responsible under the Code. The article provided details of Fostair clinical trials in COPD, which was not within the terms of the Fostair marketing authorization. An image was also included with the caption 'Beclometasone dipropionate (BDP) crystals. BDP in combination with formoterol is available as Fostair, one of several combination inhalers on the market'.

The Panel considered that the Spring edition of Respiratory Disease in Practice was not in accordance with Fostair's marketing authorization. The undertaking given in Case AUTH/2379/1/11 was that use of the journal in question and any similar material, if not already discontinued or no longer in use, would cease forthwith. The Panel considered that this undertaking had not been complied with and ruled a breach of the Code. High standards had not been maintained and Chiesi had brought discredit upon and reduced confidence in the pharmaceutical industry. Breaches of the Code were ruled including a breach of Clause 2

GlaxoSmithKline was deeply concerned over Chiesi's apparent lack of understanding as to the scope of

the Code and the company's apparent unwillingness to abide by the spirit of it. These concerns were particularly heightened as Chiesi had recently been ruled in breach of the Code in Cases AUTH/2379/1/11 and AUTH/2352/8/10. GlaxoSmithKline alleged that all these activities taken together did not maintain the high standards expected from a pharmaceutical company and brought the industry into disrepute.

The Panel noted that GlaxoSmithKline referred to two previous cases where Chiesi had been ruled in breach of the Code. Case AUTH/2379/1/11 was described above and resulted in a ruling of breaches of the Code. Case AUTH/2352/8/10 concerned a clinical support service which was ruled to be a switch service, in breach of the Code. Breaches of the Code, including of Clause 2, were ruled.

The Panel noted that the allegation of a breach of, *inter alia*, Clause 2 was in relation to a pattern of behaviour as evidenced by Chiesi's conduct in this case, Case AUTH/2435/8/11 and both previous cases. Although all three cases were relatively recent and in the same therapy area, Case AUTH/2352/8/10 related to the provision of a medical and educational service that was linked to a particular product, not the promotion of a product outside of its marketing authorization. Case AUTH/2379/1/11 and the present case, however, both related to the promotion of Fostair outside of its marketing authorization. The Panel considered that repeated breaches of the Code in the same therapy area was a serious matter. Nonetheless, the Panel considered that the discrete rulings of breaches of Clause 2, which was reserved to indicate particular censure, in Case AUTH/2352/8/10 and the present case, Case AUTH/2435/8/11 adequately covered this allegation. The Panel did not consider that the cumulative effect of these cases was such as to warrant additional censure. No further breach of the Code was ruled.

The Panel was very concerned that it had to ask Chiesi three times for information before it got all of the facts needed to make its rulings. Responses were contradictory in relation to the invitation of UK health professionals to the symposium at issue. UK staff had been briefed to encourage UK health professionals to attend which contradicted the company's initial response that UK health professionals attended the symposium at their own wish and not through any Chiesi activity. With regard to the article in Respiratory Disease in Practice it was only when the Panel had asked twice for further information regarding its involvement that the company stated that it had suggested the author. This was unacceptable; self regulation relied upon a full and frank disclosure of the facts at the outset. The Panel considered that Chiesi's conduct in relation to this case warranted consideration by the Appeal Board and it decided to report the company to the Appeal Board under Paragraph 8.2 of the Constitution and Procedure for it to consider whether further sanctions were warranted.

The Appeal Board noted that Chiesi accepted that it had made errors and that it had taken action to improve its processes to avoid similar errors. Nonetheless, the Appeal Board was very concerned at the number of requests the Panel had had to make to obtain all of the relevant information and the fact that the incomplete and thus misleading initial response was signed and therefore agreed by the managing director. There had been three further requests from the Panel.

The Appeal Board considered that it was vital that responses to the Authority were comprehensive and not misleading by omission. The failure to provide complete and accurate information was unacceptable. The Authority and the complaints procedure, relied upon companies providing a comprehensive account of the matter in question and offering all of the relevant information even if it had not specifically been requested. The Appeal Board decided that Chiesi should be publicly reprimanded for its failure to provide comprehensive information at the outset and that, in accordance with Paragraph 11.3 of the Constitution and Procedure, its procedures in relation to the Code should be audited by the Authority. The audit should be conducted in March 2012. On receipt of the audit report the Appeal Board would consider whether further sanctions were necessary.

On receipt of the March 2012 audit report the Appeal Board considered that Chiesi's procedures were not satisfactory. The Appeal Board noted that since the audit new staff were to be appointed. The Appeal Board decided that Chiesi should be re-audited in six months time. Upon receipt of the report for that audit, it would decide whether further sanctions were necessary.

Upon receipt of the October 2012 audit report, the Appeal Board noted that there had been progress since the last audit. The Appeal Board noted that in its comments upon the audit report Chiesi had stated that in addressing the PMCPA's comments about its standard operating procedures (SOPs) it could give the PMCPA a new set of SOPs within four weeks. The Appeal Board thus decided that the PMCPA should examine the revised SOPs and report its findings at the Appeal Board meeting in January 2013. The Appeal Board noted that, providing the revised SOPs were satisfactory, it would be minded to require no further sanctions.

At its meeting in January 2013 the Appeal Board noted from the PMCPA's review of Chiesi's updated SOPs that although there were still some issues to address, sufficient progress had been made and on the basis that this was maintained, no further action was required.

GlaxoSmithKline complained that, ahead of receiving a marketing authorization, Chiesi had promoted Fostair (beclometasone and formoterol) for use in chronic obstructive pulmonary disease (COPD). Fostair was currently licensed in the UK for the regular treatment of asthma where use of a combination product (inhaled corticosteroid and long-acting beta2 agonist) was appropriate. The complaint also included an alleged breach of undertaking and that aspect was taken up by the Director as it was the Authority's responsibility to ensure compliance with undertakings.

1 Alleged promotion of Fostair for chronic obstructive pulmonary disease (COPD) at a Chiesi-sponsored symposium, American Thoracic Society Conference, May 2011

COMPLAINT

GlaxoSmithKline stated that at the Chiesi symposium entitled 'Targeting Small airways: towards an optimized therapeutic management of respiratory disease', explicit claims were made about the efficacy of Fostair and the extra-fine nature of the product in COPD. Fostair was licensed only for the treatment of asthma. As only non-US delegates could attend the Chiesi symposium, there were many European and, particularly, UK attendees. Delegates were notified of the symposium by a flyer invitation and information contained in the abstract book provided in the conference bags. These materials did not indicate that the meeting was promotional. GlaxoSmithKline alleged, therefore, that Chiesi failed to comply with all applicable codes, laws and regulations to which it was subject. This was particularly relevant as Chiesi activities and materials used at the conference involved more than one country and failed to comply with the European Federation of Pharmaceutical Industries and Associations (EFPIA) Code, the code of the host country and the 2011 ABPI Code. GlaxoSmithKline alleged a breach of Clause 1.8.

During the symposium a UK health professional presented the results from a phase III study on the use of Fostair in COPD. The results were regarded as equivalent to AstraZeneca's product Symbicort (budesonide and formoterol), an established therapy licensed for the treatment of patients with severe COPD (FEV1<50% predicted normal) and a history of repeated exacerbations who had significant symptoms despite therapy with long-acting bronchodilators.

The summary slides for the presentation concluded that an extra-fine fixed combination of formoterol and beclometasone 'translates to clinical benefits in asthma and COPD'. It was never stated in the symposium, explicitly or otherwise, that Fostair was licensed only for the treatment of asthma. There was little doubt that UK attendees unfamiliar with the marketing authorization for Fostair would have left the symposium with the erroneous impression that Fostair was licensed for the management of COPD. A breach of Clause 3.2 was alleged.

GlaxoSmithKline stated that given the high profile nature of such non-compliant activity at an international symposium attended by a significant number of UK health professionals, such actions failed to maintain acceptably high standards. As a consequence, GlaxoSmithKline considered that such off-licence promotion inevitably brought discredit upon and reduced confidence in the pharmaceutical industry in breach of Clauses 9.1 and 2.

GlaxoSmithKline referred to Case AUTH/2379/1/11 in which Chiesi was ruled in breach of Clauses 3.2, 7.2 and 7.10 for distributing the journal Respiratory Disease in Practice, which was deemed to promote Fostair for COPD, from its stand at the British Thoracic Society (BTS) Congress. As the ruling of that case was over a month before the ATS symposium, GlaxoSmithKline was even more concerned that the content of a Chiesi promotional symposium at the ATS conference was certified to include claims about the efficacy of Fostair in COPD. GlaxoSmithKline considered that this called into question the gravity ascribed by Chiesi to this ruling and was concerned that the content of the symposium, with its heavy emphasis on the use of Fostair in COPD, condoned the repeated presentation of data about an unlicensed indication in a promotional setting.

As such, GlaxoSmithKline considered that the ongoing promotion of Fostair in COPD was in breach of the undertaking given in Case AUTH/2379/1/11 and in breach of Clause 25 of the Code.

RESPONSE

Chiesi was disappointed that GlaxoSmithKline had raised this matter with the Authority considering that this issue was the subject of Case AUTH/2406/5/11 under which the Panel ruled the matter not within the scope of the Code and hence not a breach by the UK affiliate of Chiesi (hereafter known as Chiesi Ltd).

Chiesi Ltd submitted that the symposium in question was organised and sponsored by its Italian corporate headquarters (hereafter referred to as Chiesi corporate). All arrangements for the symposium were made between Chiesi corporate and the ATS Conference. The speakers, agenda and presentations were organised by Chiesi corporate. Chiesi Ltd was not involved in any aspect of the organisation of the symposium nor did it sponsor the event in any form.

In light of the recent changes to Clause 20, The Use of Consultants, and to prepare for the reporting required from 2012, Chiesi had a system whereby payments to UK health professionals by other Chiesi affiliates, including Chiesi corporate, were reported to Chiesi Ltd. Through this process Chiesi was informed that Chiesi corporate had invited a UK health professional to deliver a lecture at the ATS Conference entitled 'Reaching and treating small airways: the latest evidence with an extrafine fixed combination'. Chiesi was also told about the honorarium that would be paid by Chiesi corporate. Chiesi was not involved in the preparation of the contract with the health professional in question, nor did it pay his honorarium; this was all handled by Chiesi corporate. The UK speaker was one of the two speakers at the event; the other was from the Netherlands.

GlaxoSmithKline mentioned that the symposium was attended by a significant number of UK health professionals. The ATS Conference was a truly international event with over 14,000 delegates from more than 90 countries. The symposium was open to any non-US delegate attending the conference. Chiesi did not arrange for any UK health professionals to attend the conference or the symposium; the UK health professionals attended the symposium at their own wish and not through any Chiesi activity. Flyers for the symposium were placed in the conference delegate bags, along with flyers for all the symposia. The flyers were organised

by Chiesi corporate and again, Chiesi played no role in the organising, printing or distribution of these flyers in the delegate bags.

In response to a request for further information, Chiesi submitted that it did not directly, or via a third party, sponsor or invite any UK health professionals to attend the ATS Conference. In addition Chiesi corporate did not directly, or via a third party, invite any UK health professionals to the conference or the symposium. No third party provider was involved in any way with the conference symposium as the symposium was conducted using the audio-visual services provided by the ATS.

As Chiesi did not have a promotional presence in respiratory [sic] in the US, there was no product booth at the ATS Conference. In accordance with all company-sponsored symposia at the conference, Chiesi had two pull-up banners listing the symposium day, time and agenda. A one page advertisement promoting the symposium was included in the conference programme and flyers for the symposium were also made generally available at the conference, as with the flyers for all other company-sponsored symposia. A copy of the flyer was provided.

Chiesi Ltd submitted that only four of its employees attended the conference. As the Chiesi Ltd team was small, there was no formal briefing document sent to them by Chiesi Ltd, but simply a logistics itinerary provided by a third party company. A copy of an email from that company to one of Chiesi Ltd's employees attending the conference was provided. A general briefing email, sent to the medical directors and commercial directors of all Chiesi affiliates by the global medical marketing team at Chiesi corporate, included a summary of the data to be presented at the ATS Conference including the symposium and a request to invite customers, if possible. Once at the conference, if the Chiesi Ltd staff interacted with a UK health professional, they suggested that (s)he might wish to consider attending the company symposium. There were many other parallel company symposia that the health professional could also have considered attending.

Chiesi submitted that as background to this verbal dialogue, it was important to note that Chiesi had three products licensed for use in respiratory diseases; Atimos Modulite (formoterol) inhaler for asthma and COPD, Clenil Modulite (beclomethasone) inhaler for asthma and Fostair Modulite inhaler for asthma. Fostair was, however, also licensed for COPD in Turkey, a major industrialised country. It was also important to note that the information received by the affiliate staff from the corporate medical marketing team and all subsequent information about the symposium referred to the title of the symposium; 'Targeting Small airways: towards an optimized therapeutic management of airways disease'. The two talks were listed as 'Recognising the role of small airways: a clinical need' and 'Reaching and treating small airways: the latest evidence with an extrafine combination'. No information was provided to the affiliate staff that the second presentation, given by the UK health professional, would include data on Fostair in COPD. Chiesi also noted that of the two presentations, only 4 slides referred to beclomethasone/formoterol and COPD.

Under the Code, Chiesi Ltd and Chiesi corporate understood that the relevant codes relating to this issue were those pertaining to the country of origin of the EU headquarters (Italy) and the country in which the activity took place (US). As the event took place in an international product theatre to which US health professionals were prohibited, this left the code of relevance as being the Italian Farmindustria Code, the ABPI Code was not applicable to this case, as noted in the Panel's ruling in Case AUTH/2406/5/11.

In summary, Chiesi Ltd wholly believed that it did not promote off licence data in COPD. Chiesi Ltd played no role in the organisation of the symposium or the content of the presentations. Chiesi corporate also believed that the activities conducted at the ATS Conference complied with the relevant code of practice, the Italian Farmaindustria Code.

Following a request for further information, Chiesi provided a copy of the briefing email noted above, which was sent to the medical directors and commercial directors of all Chiesi affiliates by the global medical marketing team at Chiesi corporate. The email stated there was a Chiesi symposium at the international product theatre and requested that affiliate staff inform health professionals they knew would be attending the conference about the Chiesi symposium. The flyer for the symposium was attached to the email. There was no mention in the email or the flyer that COPD data would be included in the symposium content.

Chiesi confirmed that Chiesi Ltd staff that attended the conference told UK health professionals that they knew and met at the conference that Chiesi corporate was holding a symposium at the international product theatre and they provided a copy of the flyer to those health professionals that expressed an interest in attending.

Chiesi reiterated that it:

- had no involvement in the development or conduct of the symposium
- had no knowledge of the content of the symposium – all materials it received, the copy of the flyer for the symposium and the briefing materials referred to the symposium subject being 'Targeting Small airways: towards an optimized therapeutic management of respiratory disease'
- did tell UK health professionals that there would be a symposium at the international product theatre. There were a number of company sponsored symposia available to the health professionals to attend if they wished. That a UK health professional attended the Chiesi symposium or any other company sponsored symposium was entirely their own decision and Chiesi Ltd did not consider that it had influenced the health professional in that regard nor did it have a greater influence than any other company

that was also meeting with health professionals and handing out their own symposia flyers.

In relation to this case, Chiesi Ltd sought clarification from the PMCPA on Clause 3 under which 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 that or any other clause.

Chiesi submitted that there seemed to be a wide spectrum of practice that took place across the industry and the recent European Respiratory Society (ERS) meeting in Amsterdam in September was a good example of this. The 'accepted practice' appeared to be that the activities associated with the promotional stands were deemed to be promotional. However, the symposia which were sponsored by the respective pharmaceutical companies were considered to be medical and scientific. As such at the ERS meeting a number of pharmaceutical companies sponsored symposia which focussed entirely on their products which were under development and would not be granted a licence until 2012, according to the presentations. Much of the data presented was only abstract data, presented for the first time at the meeting and hence not published nor had it passed through a scientific peer review process. Chiesi submitted that the presentation of this data by the respective companies was considered the legitimate exchange of scientific and medical information. The flyers for the symposia and all data included in the symposia was out of licence.

Chiesi stated that at the Chiesi corporate symposia at the ATS Conference, the presentation produced by the UK heath professional referred to peer reviewed, published, scientific data in COPD. Furthermore, this was only six slides of the whole medical scientific symposium (a copy of the slides was provided). Chiesi Ltd considered therefore that although it had no involvement in the symposium nor any communication prior to the event that COPD data would be included, the symposium itself was fair, balanced and representative of the peer reviewed and scientific data on the subject of small airways in respiratory disease.

PANEL RULING

The Panel noted that Chiesi referred to a previous case, Case AUTH/2406/5/11, which concerned the same symposium and wherein the Panel had ruled no breach of the Code as it considered the matter of complaint was not within the scope of the Code. The complainant had not appealed the Panel's ruling and so, in accordance with the Constitution and Procedure, there was no published case report.

Turning to the present case, Case AUTH/2435/8/11, the Panel noted that each case had to be decided on its individual set of facts. There were important differences in the evidence before the Panel in the present case and that considered previously. Chiesi had previously submitted, *inter alia*, that Chiesi Ltd had not been involved in any aspect of the arrangements.

In the present case, the Panel noted Chiesi's initial submission that any UK health professionals who had attended the symposium had done so at their own wish and not through any Chiesi activity. Chiesi subsequently submitted that Chiesi Ltd's employees had attended the conference, had told UK health professionals at the conference about the symposium and had provided a copy of the flyer to those health professionals. Indeed they had been instructed to do so in an email by Chiesi corporate. The Panel considered that as Chiesi Ltd had invited UK health professionals to the symposium, the symposium was consequently within the scope of the Code and had to comply with it. Chiesi Ltd was therefore responsible under the Code for the content of the presentations given at the symposium.

The Panel noted that in a slide detailing the outline of the presentation given by the UK heath professional, four topics would be covered, including 'BDP/F extrafine inhaler in COPD'. The last five slides dealt with the effects of Fostair on a number of parameters of COPD. The two cited references in this part of the presentation had been published in 2010, ie it was not new data. The fifth slide, the final one of the presentation, was headed 'BDP/F Extrafine: Summary' and stated that Fostair provided a more efficient delivery throughout the entire bronchial tree vs other combination products and that it '***Reaches*** small airways' and '***Treats*** small airways'. The final bullet point stated that this 'Translates to ***clinical benefits*** in asthma and COPD'.

The Panel noted Chiesi's submission with regard to the legitimate exchange of medical and scientific information during the development of a medicine, which was permitted under the supplementary information to Clause 3. The Panel queried how presenting data about the use of Fostair in COPD could be considered exchange of information 'during the development of a medicine'. Fostair already had a marketing authorization and was licensed for use in COPD in Turkey. Chiesi had noted that the conference was a truly international event and that Turkey was a major industrialised country; the Panel noted that these factors featured in the supplementary information to Clause 3, Promotion at International Meetings, not the supplementary information relating to the legitimate exchange of medical and scientific information during the development of a medicine. In the opinion of the Panel, disseminating data to prescribers which expanded a licensed product's market share was different to the legitimate exchange of medical and scientific information during the development of a medicine which implied debate which enhanced the current state of scientific knowledge.

The Panel considered that the presentation at issue promoted the use of Fostair in COPD and was thus not in accordance with the terms of its marketing authorization. A breach of Clause 3.2 was ruled. Chiesi had invited UK health professionals to a symposium at which information was presented on the use of Fostair in an unlicensed indication. The Panel considered that high standards had not been maintained and ruled a breach of Clause 9.1. The Panel considered that, on balance, given the circumstances of this case, this matter did not warrant a ruling of a breach of Clause 2

of the Code, which was a sign of particular censure and reserved for such. No breach of that clause was ruled.

In relation to the alleged breach of the undertaking given in Case AUTH/2379/1/11, the Panel noted that the previous case concerned the distribution of copies of Respiratory Disease in Practice, Volume 21 Number 1 from a Chiesi stand at a British Thoracic Society (BTS) congress. The journal was sponsored by Chiesi and contained an advertisement for Fostair. The article on the front cover was entitled 'The small airways: an important target in asthma and COPD treatment'. The Panel considered that the distribution of the journal from Chiesi's promotional stand in effect promoted Fostair for an unlicensed indication. In addition, the Panel noted that a Fostair advertisement in the journal referred to the extrafine particles reaching the small airways. In the Panel's view this linked to the article about the treatment of COPD and references to particle size, and it ruled, *inter alia*, a breach of Clause 3.2.

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 undertaking given in Case AUTH/2379/1/11 and dated 25 March 2011 required that use of the journal in question and any similar material, if not already discontinued or no longer in use, would cease forthwith. The Panel considered that the subsequent symposium which promoted Fostair in COPD meant that this undertaking had not been complied with and it ruled a breach of Clause 25.

In relation to the GlaxoSmithKline's allegation of a breach of Clause 1.8, the Panel noted that this clause required that pharmaceutical companies must ensure that they complied with all applicable codes, laws and regulations to which they were subject. The Panel noted its rulings of breaches of the Code above. The Panel considered that by failing to comply with the UK Code, Chiesi had failed to meet this requirement. A breach of Clause 1.8 was ruled.

2 Spring 2011 Respiratory Disease in Practice

COMPLAINT

GlaxoSmithKline was increasingly concerned that Chiesi was promoting Fostair, deliberately or otherwise, for COPD ahead of it receiving a marketing authorization for this indication. Such activities gave the impression of a UK and, indeed, multinational, co-ordinated, concerted pre-licence, multi-channel campaign. GlaxoSmithKline had noted yet a further edition of the publication sponsored by Chiesi cited in Case AUTH/2379/1/11 (a copy of which was provided). This publication clearly implied that a marketing authorization was already in place for Fostair in COPD. GlaxoSmithKline considered this was further evidence of ongoing breaches of the Code in relation to extensive off-licence promotion and considered that such ongoing activity was totally unacceptable.

When writing to Chiesi the Authority asked it to respond in relation to Clauses 2 and 9.1 with regard to the alleged breach of undertaking.

RESPONSE

Chiesi submitted that it had had no communication with GlaxoSmithKline about Chiesi's support of the Spring 2011 edition of Respiratory Disease in Practice and it was unclear as to exactly how its support of this journal constituted a breach of undertaking. Respiratory Disease in Practice was an independent journal title. In response to an approach from the publisher, Chiesi had agreed to provide an unrestricted educational grant to fund a fixed number of issues over a set period of time. Its support was clearly declared on the front page of the journal. On page 3 of the journal, the publisher stated: 'The sponsor has no editorial input into, or control over, the content of this publication. Sponsorship is for four issues to be published in 2011. The data, opinions and statements appearing in the articles herein are those of the contributor(s) concerned; they are not necessarily endorsed by the sponsor, publisher, Editor or Editorial Board'.

In line with this agreement Chiesi had had no input into any edition of the journal, including the Spring 2011 edition. Following the ruling in Case AUTH/2379/1/11, the company had also had no involvement with the distribution of the journal and had not purchased reprints or used the journal in promotion. The distribution of the journal to health professionals was conducted by the publishers with no input from Chiesi. Chiesi had not reviewed or commented on the content of the journal. The only Chiesi advertisement in the Spring 2011 edition of the journal was a corporate advertisement.

Since it had no input into the content of the journal and had not used it for promotional purposes Chiesi considered that it had adhered to its undertaking in relation to Case AUTH/2379/1/11 and denied any breach of the Code.

Chiesi noted that the Spring 2011 edition featured a review of combination inhaler trials in COPD which examined published studies of all the available combination inhalers including Fostair ('BDP/F'). GlaxoSmithKline stated that the publication 'clearly implied that a marketing authorization was already in place for Fostair in COPD' but in fact the article stated clearly 'BDP/F does not yet have a licence for COPD …'.

In response to a request for further information, Chiesi submitted that it did not have on file a signed written contract with the publishers regarding Respiratory Disease in Practice but it provided a copy of the contract that Chiesi did receive. The terms and conditions on which the sponsorship was made were also provided. Chiesi Ltd considered that the acceptance of the terms and conditions constituted a legally binding contract.

Chiesi submitted that the title, scope and content of the article at issue in the Spring 2011 edition of the journal was commissioned by an editorial director, written by a health professional (the author) and prepared for publication by a sub-editor who was responsible for

commissioning content at the request of the editorial board, liaising with authors and the editor over copy and proofs and also sub-editing and producing the journal. The article was reviewed and accepted for publication by the journal's editor. Chiesi received a copy of the article, in accordance with the contract and reviewed it for scientific accuracy only. There was no other involvement by Chiesi in the article.

A copy of a letter from the publishers and the editor was provided which outlined the processes of the journal to ensure Code compliance. The publishers had also included documents relevant to the case including emails detailing the editor's comments and a communication regarding the article with Chiesi Ltd.

With respect to the undertakings by Chiesi Ltd following Case AUTH/2379/1/11, a breach was ruled relating to the distribution of the journal from a promotional stand at the BTS. Following this ruling, Chiesi had not distributed any copies of that edition (volume 21) or the current Spring edition (volume 22) directly to health professionals and had not used the journal in any promotional activities. The second ruling of the case was in relation to the use of the Fostair advertisement on the back page of the journal. In volume 22, this was replaced with a corporate advertisement with no reference to any Chiesi products. Chiesi considered therefore that it had taken reasonable steps to address the issues raised in Case AUTH/2379/1/11.

In response to a further request for further information, Chiesi submitted that the limit of its involvement with the Spring edition was to suggest the author for the cover article entitled 'A review of combination inhaler trials in COPD'. The article referred, *inter alia*, to Fostair clinical trial results in COPD. A second letter from the publishers was submitted that stated that the title, scope and content of the article was agreed between the editor and the author following his agreement to contribute to the journal. Chiesi did not provide any information for inclusion in the article or have any involvement in its publication. The letter also stated that none of the publication's sponsors had any influence, or contribution to, the circulation of the journal and no details of the circulation list were provided to them. The target audience of the journal was health professionals that were relevant to the title.

Chiesi submitted that it received 200 copies of the journal as part of the standard terms of the sponsorship. This was the first time that Chiesi had seen the final and complete publication. Its internal process was then to review the publication. If any of the articles in the publication referred to any Chiesi products, the content was checked to ensure it complied with the product licences. If the publication complied with its product licences, it was then reviewed through its approval process for promotional material to formally approve the content and to approve the intended use. If the articles were not within the terms of its product licences then the publication was not reviewed through the approval process and was simply retained by the medical department in case it might be useful to respond to specific medical information enquiries, should this be appropriate. The 200 copies of the volume 22 publication were reviewed as above but as the article on COPD was not considered suitable for promotional use they remained in the medical department at Chiesi.

PANEL RULING

The Panel noted that it was acceptable for companies to sponsor material. It had previously been decided in relation to material aimed at health professionals that the content would be subject to the Code if it was promotional in nature or if the company used the material for a promotional purpose. Even if neither of these applied, the company would be liable if it had been able to influence the content of the material in a manner favourable to its own interests. It was possible for a company to sponsor material which mentioned its own products and not be liable under the Code for its content, but only if it had been a strictly arm's length arrangement with no input by the company and no use by the company of the material for promotional purposes. Factors which might mean there had not been a strictly arm's length arrangement would include, *inter alia*, selection of the author by the pharmaceutical company.

The Panel noted that Chiesi had suggested the author for the article that appeared on the front page of the journal at issue. The Panel considered that Chiesi thus could not take the benefit of an arm's length agreement in this case, and was responsible for the article's content under the Code. The article provided details of Fostair clinical trials in COPD, which was not within the terms of the marketing authorization for the medicine. An image was also included with the caption 'Beclometasone dipropionate (BDP) crystals. BDP in combination with formoterol is available as Fostair, one of several combination inhalers on the market'.

The Panel considered that the Spring edition of Respiratory Disease in Practice was not in accordance with Fostair's marketing authorization. The undertaking given in Case AUTH/2379/1/11 was that use of the journal in question and any similar material, if not already discontinued or no longer in use, would cease forthwith. The Panel considered that this undertaking had not been complied with and ruled a breach of Clause 25. High standards had not been maintained and the Panel ruled a breach of Clause 9.1. By not complying with the undertaking given in Case AUTH/2379/1/11, Chiesi had brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled.

3 Alleged breach of Clauses 2 and 9.1

COMPLAINT

GlaxoSmithKline stated that it was deeply concerned over Chiesi's apparent lack of understanding as to the scope of the Code and the company's apparent unwillingness to abide by the spirit of the Code. These concerns were particularly heightened as it had recently been ruled in breach of Clauses 2, 3.2, 7.2, 7.10, 9.1 and 18.4 of the Code in Cases AUTH/2379/1/11 and AUTH/2352/8/10. GlaxoSmithKline welcomed the PMCPA's involvement at this stage following the failure of inter-company dialogue, and sought the Authority's views on what immediate action might be possible to stop on-going recurring breaches of the Code whilst this complaint was being processed. GlaxoSmithKline

alleged that all these activities taken together did not maintain the high standards expected from a pharmaceutical company (breach of Clause 9.1) and indeed brought the industry into disrepute (breach of Clause 2).

RESPONSE

Chiesi did not address specifically GlaxoSmithKline's allegations of a breach of Clauses 9.1 and 2.

PANEL RULING

The Panel noted that GlaxoSmithKline referred to two previous cases where Chiesi had been ruled in breach of the Code. Case AUTH/2379/1/11 was described at point 1 above and resulted in a ruling of a breach of Clauses 3.2, 7.2, and 7.10. Case AUTH/2352/8/10 concerned a clinical support service which was ruled to be a switch service, in breach of Clause 18.4. A breach of Clauses 9.1 and 2 was also ruled.

The Panel noted that GlaxoSmithKline's allegation of a breach of Clauses 9.1 and 2 was in relation to a pattern of behaviour as evidenced by Chiesi's conduct in this case, Case AUTH/2435/8/11 and both previous cases. Although all three cases were relatively recent and in relation to activity in the same therapy area, Case AUTH/2352/8/10 related to the provision of a medical and educational service that was linked to a particular product, not the promotion of a product outside of its marketing authorization. Case AUTH/2379/1/11 and the present case, however, both related to the promotion of Fostair outside of its marketing authorization. The Panel considered that repeated breaches of the Code in the same therapy area was a serious matter. Nonetheless, the Panel considered that the discrete rulings of breaches of Clause 2, which was reserved to indicate particular censure, in Case AUTH/2352/8/10 and the present case, Case AUTH/2435/8/11 adequately covered this allegation. The Panel did not consider that the cumulative effect of these cases was such as to warrant additional censure. No further breach of Clauses 9.1 or 2 was ruled.

The Panel was very concerned that following the company's initial response, it had to go back to Chiesi three times in order to obtain all the relevant information required to make its rulings. Responses dated 17 October and 28 September in relation to the invitation of UK health professionals to the symposium at issue revealed that UK staff had been briefed to encourage UK health professionals to attend. This contradicted the company's initial response dated 13 September that UK health professionals attended the symposium at their own wish and not through any Chiesi activity. With regard to the article in Respiratory Disease in Practice it was only when the Panel had asked twice for further information regarding its involvement that the company stated that it had suggested the author. This was unacceptable; self regulation relied upon a full and frank disclosure of the facts at the outset. The Panel considered that Chiesi's conduct in relation to this case warranted consideration by the Code of Practice Appeal Board and it decided to report the company to the Appeal Board under Paragraph 8.2 of the Constitution and Procedure for it to consider whether further sanctions were warranted.

COMMENTS FROM CHIESI ON THE REPORT

Chiesi was extremely concerned that, in the Panel's view it was unwilling to abide by the spirit of the Code. Chiesi took compliance with the Code extremely seriously. Chiesi had, however, been managing some circumstances that were relevant to this case. In addition it had acted recently, prior to the ruling, to address some of the issues raised in the complaint.

The inconsistencies seen in the responses in the recent case were extremely unfortunate. They were, however, not driven by an unwillingness to disclose information to the Panel but as a result of using different consultancy resources whilst recruiting new staff. Chiesi considered that it had demonstrated its willingness to give a full and frank disclosure by providing documents that were not requested, such as the presentation slides from the ATS symposium.

Chiesi submitted that GlaxoSmithKline's complaint implied that there was a concerted plan to promote Fostair in COPD; this was not the case. The symposium at the ATS was conducted entirely by the Chiesi corporate team. Chiesi Ltd (the UK affiliate) had informally invited health professionals to the symposium in good faith that the symposium did not promote Fostair outside of its licence. No information from the corporate team gave any insight into the content of the symposium. Chiesi admitted that this was an error on its part – it should have sought to clarify the content of the symposium.

The Panel had ruled a breach of undertaking in relation to Case AUTH/2379/1/11 due to the activity conducted at the ATS. There was, however, no link in the activities between the current case (Case AUTH/2435/8/11) and Case AUTH/2379/1/11. They were conducted in complete isolation from one another and Chiesi now realised that this was its failing. In respect of the ruling in Case AUTH/2379/1/11 Chiesi only considered the activities of the UK affiliate and not those of the broader Chiesi group.

Chiesi submitted that with respect to the Spring edition of Respiratory Disease in Practice, the relationship with the publishers was managed within the marketing department and not the medical department and although this was not a cause of the issues the company realised that it was not appropriate. All such activities and relationships of sponsorship now sat within the medical department and the company no longer sponsored Respiratory Disease in Practice.

Chiesi stated that prior to the ruling it had already made significant steps to resolve the issues raised by the case. Chiesi had recruited new individuals and organised refresher training on the Code. Chiesi had also acted to ensure that the Chiesi corporate team did not conduct any activities that promoted Fostair in COPD. When Chiesi received the complaint in relation to this case, it immediately shared it with the corporate team to ensure that there was no mention of scientific data on COPD at the corporate symposium at the ERS delivered on 27 September.

Chiesi reiterated that it took compliance with the Code extremely seriously. A number of factors had

contributed to the recent complaints but significant steps and corrective action had been taken to ensure that the related issues were addressed and would continue to be so.

At the consideration of the report the representatives from Chiesi acknowledged that failings had occurred resulting in conflicting submissions to the Panel. The first response to the Panel dated 13 September was written by an external consultant. The company representatives who attended for the consideration of the report were unsure what investigation the consultant undertook in compiling the response to the complaint. The subsequent responses were written by the new medical director after investigation in response to requests by the Panel.

The Chiesi representatives submitted that actions had already been put in place to address the issues raised in this case. Regular meetings with Chiesi corporate had been set up and there was good communication on the requirements of the Code to ensure that Chiesi corporate were compliant and did not put Chiesi UK at risk. Complaints would be shared with medical and marketing to provide input in to the response. Outcomes of cases were now shared with medical and marketing and other appropriate staff to ensure understanding and compliance. There had been a review of all standard operating procedures and processes. All key staff were due to undergo refresher training on the Code. Meetings with GlaxoSmithKline had been established to discuss respective concerns.

APPEAL BOARD CONSIDERATION

The Appeal Board noted that Chiesi had accepted that it had made errors and that it had taken action to improve its processes to avoid similar errors. A new medical director had been appointed.

Nonetheless, the Appeal Board was very concerned at the number of requests the Panel had had to make to obtain all of the relevant information and the fact that the incomplete and thus misleading initial response was signed and therefore agreed by the managing director. There had been three further requests from the Panel.

The Appeal Board considered that it was vital that responses to the Authority were comprehensive and not misleading by omission. The failure to provide complete and accurate information was unacceptable. The Authority and the complaints procedure, relied upon companies providing a comprehensive account of the matter in question and offering all of the relevant information even if it had not specifically been requested. In that regard the Appeal Board considered that Chiesi's provision of the slides from the ATS symposium was only to be expected. The Appeal Board decided that Chiesi should be publicly reprimanded for its failure to provide comprehensive information at the outset. It also decided in accordance with Paragraph 11.3 of the Constitution and Procedure, to require an audit of Chiesi's procedures in relation to the Code to be carried out by the Authority. The audit should be conducted in March 2012. On receipt of the audit report the Appeal Board would consider whether further sanctions were necessary.

FURTHER CONSIDERATION BY THE APPEAL BOARD

The Appeal Board considered that the March 2012 report showed that Chiesi's procedures were not satisfactory. The Appeal Board noted that since the audit new staff were to be appointed. The Appeal Board decided that Chiesi should be re-audited in six months time. Upon receipt of the report for that audit, it would decide whether further sanctions were necessary.

Upon receipt of the October 2012 audit report, the Appeal Board noted that there had been progress since the last audit. The Appeal Board noted that in its comments upon the audit report Chiesi had stated that in addressing the PMCPA's comments about its standard operating procedures (SOPs) it could give the PMCPA a new set of SOPs within four weeks. The Appeal Board thus decided that the PMCPA should examine the revised SOPs and report its findings at the Appeal Board meeting in January 2013. The Appeal Board noted that, providing the revised SOPs were satisfactory, it would be minded to require no further sanctions.

At its meeting in January 2013 the Appeal Board noted from the PMCPA's subsequent review of Chiesi's updated SOPs that although there were still some issues to address, sufficient progress had been made and on the basis that this was maintained, no further action was required.

Complaint received	**30 August 2011**
Undertaking received	**9 November 2011**
Appeal Board consideration	**7 December 2011** **19 April 2012** **15 November 2012** **10 January 2013**
Interim case report first published	**12 June 2012**
Case completed	**10 January 2013**