CASE AUTH/2618/7/13

ASTRAZENECA v CHIESI

Promotion of Fostair

AstraZeneca complained about a Fostair (formoterol/beclometasone pressurised inhalation solution) leavepiece issued by Chiesi. AstraZeneca marketed Symbicort (budesonide/formoterol turbohaler). Both medicines were indicated in the regular treatment of asthma where use of a combination (inhaled corticosteroid (ICS) and long-acting ß$_2$ adrenoceptor agonist (LABA)) was appropriate.

The detailed response from Chiesi is given below.

AstraZeneca alleged that 'for an extra fine day', immediately below 'New licence for Maintenance And Reliever Therapy' on page 1 of the leavepiece, was an unqualified and unsubstantiated claim for Fostair which suggested that patients returned to an improved pre-symptom state with Fostair; the illusion was compounded by the illustration.

The Panel noted that 'for an extra fine day' appeared within the headline 'New licence for Maintenance And Reliever Therapy for an extra fine day'. The Panel noted that 'extra fine' in the claim at issue had been written as two words. It appeared as one word 'extrafine' in the SPC when describing the formulation.

The Panel accepted that the use of 'for an extra fine day' was a play on words but considered that the heading to page 1 was not sufficiently clear about what 'extra fine' referred to, there was an implication that it referred to a clinical benefit and not just to the product's formulation as submitted by Chiesi and it was ambiguous in this regard. 'Extra' by implication rendered the claim 'for an extra fine day' comparative; use of the product for the new licence provided an extra clinical benefit over and above an appropriate comparator. This implication was misleading. Chiesi provided no data to support such an advantage. The Panel noted AstraZeneca's submission that there was no robust clinical evidence to show that Fostair's extrafine formulation translated into a clinical benefit compared with other licensed treatments.

The Panel did not consider that, within the context of the front page of the leavepiece, the heading and the image of a woman in a field with her arms outstretched implied that patients would return to a pre-symptom state with Fostair as alleged.

The Panel considered that the claim 'New licence for Maintenance And Reliever Therapy for an extra fine day' was ambiguous, misleading and could not be substantiated. Breaches of the Code were ruled. The Panel did not consider that in these circumstances Chiesi had failed to maintain high standards and no breach of the Code was ruled.

Following notification of the Panel ruling AstraZeneca wrote to the Authority, noting, *inter alia*, that it was surprised by the first paragraph of the Panel ruling which implied that during inter-company dialogue EXTRA FINE was put into upper case for emphasis as the leavepiece provided by Chiesi used lower case letters only within the claim at issue. This was at odds with the leavepiece upon which AstraZeneca had based its complaint, a copy of which it now provided.

Chiesi returned the signed undertaking on 4 September. On 11 September, before the Authority had contacted the company about this matter, Chiesi advised the Authority that a product manager had unilaterally altered the leavepiece after it had been electronically certified such that 'extra fine' read 'EXTRA FINE'. Chiesi was asked to explain the circumstances.

Following receipt of the additional information from both parties the original Panel reconvened to consider the matter in relation to Paragraph 8 of the Constitution and Procedure. Chiesi was so informed and asked to provide detailed comments which are summarized below.

The Panel considered the matter in relation to Paragraph 8.2 of the Constitution and Procedure which provided that the Panel might report a company to the Appeal Board. Such a report might be made notwithstanding the fact that a company had provided an undertaking requested by the Panel.

The Panel noted that it had considered the complaint in relation to the copy of the leavepiece provided by Chiesi in its response to the complaint, which bore the correct reference number and featured the claim 'extra fine' in lower case. The Panel noted that this version of the leavepiece had never been distributed. According to Chiesi, a product manager had unilaterally altered the leavepiece such that the claim in question was in upper case ('EXTRA FINE') and thus aligned with other Fostair materials. The signatories certified a printed version of a PDF file which had previously been electronically approved in Zinc. It was wrongly assumed that no changes had been made to the previously approved artwork. It appeared that it was this version that was provided to the Panel rather than the item in its final form as amended by the product manager. Chiesi stated that the employees in question had clearly acted outwith the company's standard operating procedure (SOP). It was not known why he/she had not followed the relevant SOP.

The Panel did not accept Chiesi's conclusion that this was evidence of a lone employee failing to

accord with approved SOPs. Firstly, the Panel noted that other Chiesi employees had been copied in on the relevant employee's emails to the agency. Secondly in the Panel's view, it should have been abundantly clear to each signatory that the version provided for certification was not in its final form as required by the Code and the relevant SOP. In the Panel's view, this raised concerns about the competence of each of the Code signatories given each had certified that they had examined the final form of the material.

The Panel considered that the failure of both the product manager and the signatories to adhere to the SOP was a matter of concern and raised questions about the importance of compliance within the company.

The Panel expressed concern about the certification arrangements.

The Panel was extremely concerned that Chiesi's response to the complaint quoted throughout the claim at issue in upper case whereas the leaflet supplied used lower case for 'extra fine'. The Panel was concerned that Chiesi had not noted the discrepancy on a number of occasions through from approval, inter-company dialogue and its response to the complaint. That the company only became aware of the matter when it was notified of the Panel's rulings was unacceptable. It further transpired that the company's original undertaking in this case incorrectly stated that the material was last used on 17 March 2013 and that was not so. A revised undertaking with a later date of final use had been provided. The Panel noted that an undertaking was an important document and the Authority must be able to rely on its accuracy.

The Panel was extremely disappointed by the conduct of Chiesi as outlined above. Self-regulation relied, *inter alia*, upon the provision of complete and accurate information to the Panel. Its previous conduct in this regard was not irrelevant. The Panel considered that the circumstances warranted reporting the company to the Appeal Board under Paragraph 8.2 for it to consider in relation to Paragraphs 11.3 and 11.4 of the Constitution and Procedure.

On considering the report the Appeal Board noted that as a result of staff failing to follow the relevant company SOP, the final printed version of the leavepiece at issue featured 'EXTRA FINE' in upper case whereas the Zinc copy approved by Chiesi's signatories featured 'extra fine' in lower case. Chiesi had provided the Zinc 'lower case' copy of the leavepiece in its response to the complaint without checking that that copy matched the final printed file 'upper case' copy; this despite the fact that in inter-company dialogue and throughout the complaints procedure, both parties had consistently referred to 'EXTRA FINE' in upper case. In the Appeal Board's view, the discrepancy between the two versions of the leavepiece should have been obvious to Chiesi from the outset. Chiesi had not certified the final form of the leavepiece. The PDF certified was not the final form as some of the pages were not the correct size and, in addition, the version certified used 'extra fine' in lower case and not 'EXTRA FINE' in upper case as on the final version. Neither the product manager nor the signatories had followed the company's SOP.

The Appeal Board also noted with concern that Chiesi's original undertaking and assurance in respect of the breaches ruled in this case was incorrect with regard to the final date on which the leavepiece was used.

The Appeal Board noted Chiesi's submission that the failure to follow the correct approval process, and to recognise the difference between the approved leavepiece and the one that was distributed, and the mistakes in the undertaking arose from human error and lack of attention to detail. In that regard the Appeal Board noted Chiesi had previously been censured for providing the PMCPA with inaccurate information (Case AUTH/2435/8/11). In that case the Appeal Board decided that Chiesi should be publicly reprimanded and it should undergo an audit of its procedures in relation to the Code to be carried out by the Authority. This was carried out in March 2012 and a second audit was required (carried out in October 2012). The report for the second audit included a recommendation that 'Chiesi needed to ensure…that all information provided to the PMCPA was accurate'. The Appeal Board considered that Chiesi's repeated failure to provide accurate information to the PMCPA was completely unacceptable.

Self regulation relied upon the provision of complete and accurate information by pharmaceutical companies. The Appeal Board was extremely concerned about Chiesi's conduct, and having considered all the sanctions available under Paragraph 11.3 of the Constitution and Procedure it decided that the company should be publicly reprimanded for providing inaccurate information to the Authority.

The Appeal Board also decided to require an audit of Chiesi's procedures in relation to the Code. Given the details of the company's ongoing and planned compliance activities, the Appeal Board decided that the audit should be conducted in five months' time (March 2014). On receipt of the audit report the Appeal Board would consider whether further sanctions were necessary.

Upon receipt of the March 2014 audit report, the Appeal Board considered that Chiesi's embarrassment at the errors which had led to the requirement for it to be audited were well founded.

The Appeal Board was extremely concerned that Chiesi had been audited twice in 2012 and that the current audit report highlighted a number of serious issues with Chiesi's compliance procedures and materials; it appeared that the company still had much work to do. The Appeal Board provided a number of detailed comments including its serious concerns that Chiesi had stated that a standard operating procedure had been updated when it had not. The Appeal Board was appalled that, in this regard, it appeared that Chiesi had yet again provided false information to the PMCPA; this

was completely unacceptable. The Appeal Board considered that its further concerns about the provision of false information should be added to the detail of that public reprimand. The Appeal Board was also concerned about the outcome of Chiesi's job bag audit (conducted by an external compliance consultant). A second job bag audit was due in April 2014 and the Appeal Board requested that the results, which needed to show a significant improvement, be provided at the next PMCPA audit.

The Appeal Board noted that the company had already been given a significant amount of time to ensure its procedures, policies and culture supported a robust compliance framework. The Appeal Board decided that Chiesi should be re-audited in October 2014 when the company must be able to demonstrate significant improvement. Upon receipt of the report for the re-audit, the Appeal Board would decide whether further sanctions were necessary.

Upon receipt of the October 2014 audit report, the Appeal Board noted that Chiesi had made progress since the audit in March 2014. The Appeal Board noted that this was not the first case in which Chiesi had been censured for failing to provide accurate information; such failings were completely unacceptable and must not happen again. The Appeal Board noted that Chiesi provided details of its plans to implement the audit report recommendations. On the basis that this work was completed, progress was continued and the company wide focus on compliance was maintained, the Appeal Board decided that, on balance, no further action was required.

AstraZeneca UK Limited complained about the promotion of Fostair (formoterol/beclometasone pressurised inhalation solution). The material at issue was a leavepiece (ref CHFOS20130051). The front page read 'New licence for Maintenance and And Reliever Therapy for an extra fine day' above an image of a woman in a field with her arms outstretched. Beneath the illustration the claim 'Fostair is the first and only pMDI combination inhaler in the UK licensed for Maintenance and Reliever Therapy in asthma' was followed by the brand name in logo format and the strapline 'Extra-fine formulation. Adult asthma control'.

AstraZeneca marketed Symbicort (budesonide/formoterol turbohaler). Both Fostair and Symbicort were indicated in the regular treatment of asthma where use of a combination (inhaled corticosteroid (ICS) and long-acting $ß_2$ adrenoceptor agonist (LABA)) was appropriate. Inter-company dialogue had not resolved this matter.

COMPLAINT

AstraZeneca was concerned about the claim '… for an extra fine day' which appeared on the front cover of the leavepiece and was also used in other promotional material for Fostair. AstraZeneca noted that the wording '… for an extra fine day' appeared immediately below 'New licence for Maintenance And Reliever Therapy' which, in its view, therefore clearly represented a claim for Fostair that was unqualified and not substantiated. The claim suggested that the patient returned to an improved pre-symptom state with use of Fostair. This illusion was further compounded by the illustration.

AstraZeneca accepted that Fostair had an extra fine formulation and that reference to 'extra fine' within that context was acceptable. Furthermore, AstraZeneca accepted that Fostair was used on a [twice] daily basis. However, AstraZeneca alleged that linking aspects of the formulation to 'day' as in 'extra fine day' was a product claim which implied an efficacy suggestion that was at least ambiguous and not substantiated. In addition it was not clear about what this efficacy benefit was compared to. Further, linking of the statements 'New licence for Maintenance And Reliever Therapy' with 'extra fine day' by use of the word 'for' amounted to a promise as in 'New licence for Maintenance And Reliever Therapy **for** an extra fine day' (emphasis added).

AstraZeneca stated that there was no robust clinical evidence to show that Fostair's extra-fine formulation translated into a clinical benefit when compared with other licensed treatments. AstraZeneca had identified several studies that had evaluated the extra-fine formulation against other treatments and had yet to identify any that showed a clinical superiority in favour of the extra-fine formulation over clinically appropriate comparators. AstraZeneca noted that a number of review articles hypothesised on the potential benefits of extra-fine formulation but did not offer any substantive clinical evidence in support.

AstraZeneca alleged that the claim was misleading in breach of Clause 7.2 and incapable of substantiation in breach of Clause 7.4. AstraZeneca also alleged that the claim was in breach of Clause 9.1 as it failed to maintain high standards.

RESPONSE

Chiesi submitted that it took compliance with the Code very seriously and set out why the claim in question was not in breach of the Code as alleged by AstraZeneca.

A comparison of AstraZeneca's initial complaint sent to Chiesi and that submitted to the PMCPA demonstrated that the exact nature of the complaint was not entirely clear. Chiesi was unsure whether the use of the line 'an extra fine day', which had been used in isolation throughout the Fostair campaign for over twelve months since March 2012, or the use of the claim 'for an extra fine day', which had only been used in a campaign specifically relating to the launch of the new Fostair licence for maintenance and reliever therapy (MART) since February 2013, was what was at issue.

Chiesi noted that in April 2013 AstraZeneca raised the issue of 'an extra fine day' in the Fostair MART leavepiece (ref CHFOS20130051). The wording 'for an extra fine day' appeared at the end of the headline, 'New licence for Maintenance And Reliever Therapy', on the leavepiece at issue. Chiesi submitted that 'an extra fine day' was the focus of its response letter to AstraZeneca and discussions

during the subsequent telephone conference in June and it was used in isolation and without the word 'for' throughout the main Fostair campaign.

During inter-company dialogue Chiesi decided to continue using the line 'for an extra fine day' in the context outlined and which appeared in the Fostair MART leavepiece as it did not consider it to be in breach of the Code. Both parties were unable to reach a satisfactory resolution on this point and it was agreed that AstraZeneca would raise the issue with the PMCPA. Chiesi was now responding to a complaint about the use of the claim 'for an extra fine day' as contextualised in the Fostair MART leavepiece.

Chiesi submitted that 'for an extra fine day' was a reference to Fostair's extrafine formulation which was substantiated by Fostair's summary of product characteristics (SPC), Section 4.2 of which stated:

> 'Beclometasone dipropionate in Fostair is characterised by an extrafine particle size distribution which results in a more potent effect than formulations of beclometasone dipropionate with a non-extrafine particle size distribution (100 micrograms of beclometasone dipropionate extrafine in Fostair are equivalent to 250 micrograms of beclometasone dipropionate in a non-extrafine formulation). Therefore the total daily dose of beclometasone dipropionate administered in Fostair should be lower than the total daily dose of beclometasone dipropionate administered in a non-extrafine beclometasone dipropionate formulation. This should be taken into consideration when a patient is transferred from a beclometasone dipropionate non-extrafine formulation to Fostair; the dose of beclometasone dipropionate should be lower and will need to be adjusted to the individual needs of the patients.'

Chiesi submitted that the wording 'Extra-fine formulation' used on the same page reinforced the link between the use of the headline 'for an extra fine day' and the formulation of the product. Similarly the use of capitals for 'extra fine' highlighted that message further. Due to the different potencies of the available beclometasone containing pressurised metered dose inhalers (pMDIs), Chiesi considered the extrafine formulation of Fostair to be an important safety message which had to be communicated to potential prescribers. Chiesi noted that in 2006 the Medicines and Healthcare products Regulatory Agency (MHRA) issued advice highlighting the potential safety issue concerning beclometasone pMDIs regarding extrafine formulations having a 2 to 2.5 fold greater potency than non-extrafine formulations. It was the potential safety issue that led to the Fostair campaign being based on 'an extra fine day'.

Chiesi submitted that the imagery served to further communicate and emphasise the extrafine formulation which was unique to Fostair in combination therapy. The illustration was constructed from small pink dots designed to represent extrafine particles. Chiesi had reviewed the imagery and confirmed it was appropriate and within the scope of suitability detailed in the supplementary information to Clauses 9.1 and 9.2. Chiesi disagreed with AstraZeneca's view that the imagery was misleading and considered that the imagery depicted a situation that was perfectly in line with the expectations of a patient with moderate asthma and strongly objected to it being considered an 'illusion'.

Chiesi submitted that the wording 'for an extra fine day' also reflected the posology of Fostair from the SPC which stated that it had to be taken on a daily basis. A patient who was prescribed Fostair would be taking an extrafine formulation daily and therefore each day would have an extrafine element to it because of Fostair's formulation.

Chiesi further submitted that the linking of the new MART licence to 'an extra fine day' on the leavepiece in the headline ''New licence for Maintenance And Reliever Therapy' for an extra fine day' was used to communicate that there was now another posology option available for treating patients with Fostair, with reinforcement of the above safety message relating to its extrafine formulation. Chiesi claimed that if a patient was treated with a maintenance and reliever therapy regimen they could potentially be using their inhaler at other times during the day as well as on a twice daily basis. That posology further supported the use of 'extra fine day'. Chiesi consequently refuted that the use of 'for an extra fine day' was a breach of Clause 7.4 as it was substantiated by the SPC.

Chiesi submitted that the Fostair MART campaign compared two different posology methods both from a clinical and patient perspective when treating asthma. There was no comparison of the efficacy of Fostair with any alternative inhaled corticosteroid/long acting beta agonist combination inhaler. The only efficacy comparisons made within the leavepiece were between Fostair MART and Fostair maintenance therapy. With there being no efficacy claims between Fostair and any other ICS/LABA combination inhalers available Chiesi disagreed that the piece inferred clinical superiority over any other product as alleged.

Chiesi noted that the only comparison made was a cost comparison between Fostair and Symbicort on page 5 and as part of the summary on page 6. A cost comparison between the only two ICS/LABA combination inhalers with a MART licence was relevant information to disseminate but it had agreed to cease doing so at AstraZeneca's request following inter-company dialogue. With cost being the only comparison made in the leavepiece Chiesi disagreed that the reader would interpret the piece as claiming clinical superiority of Fostair over the available alternative.

The leavepiece focussed on severe exacerbations, hospitalisations and systemic corticosteroid courses based on data from the MART-2 study. There was nothing in the leavepiece that suggested patients would be symptom free, in fact asthma symptoms were not referred to in any of the claims and were only mentioned with regard to how Fostair MART should be prescribed ie additional inhalations should be taken in response to symptoms. As there was

no focus on any reduction in asthma symptoms Chiesi disagreed that the claim 'for an extra fine day' suggested a patient returning to a pre-symptom state as alleged by AstraZeneca. Furthermore, the illustration represented the freedom and flexibility that a MART approach could offer a patient when managing their own asthma treatment and was not intended to be representative of a symptom free patient. Chiesi therefore did not consider that the illustration or the claim 'for an extra fine day' was in breach of Clauses 7.2 or 7.4.

Chiesi submitted that the claim 'New licence for Maintenance And Reliever Therapy for an extra fine day' was accurate, balanced, fair, objective and unambiguous and based on an up to date evaluation of all of the evidence and therefore denied any breach of Clause 7.2. The information was capable of substantiation as shown above and therefore Chiesi denied any breach of Clause 7.4 and thus denied a breach of Clause 9.1.

In summary, Chiesi submitted that it was unfortunate that inter-company dialogue had failed to reach a full resolution on the matters raised by AstraZeneca however this was in part due to a lack of clarity and the somewhat changing nature of the complaint. Chiesi submitted that as it had demonstrated that it was able to substantiate all wording and meet all of the necessary requirements of Clause 7.2, it denied a breach of Clauses 7.2, 7.4 and 9.1 as alleged by AstraZeneca.

PANEL RULING

The Panel noted that both AstraZeneca and Chiesi referred to 'extra fine' within the claim at issue in upper case both during inter-company dialogue and in their respective complaint and response to the PMCPA. However, the only promotional material was provided by Chiesi and this (the leavepiece in question) used lower case for 'extra fine' in the claim at issue. The Panel was unsure of the relevance of Chiesi's response with regard to the use of upper case for EXTRA FINE highlighting the link between 'for an extra fine day' and the formulation of the product.

The Panel noted the claim at issue 'for an extra fine day' appeared within the headline 'New licence for Maintenance And Reliever Therapy for an extra fine day'. 'Fostair is the first and only pMDI combination inhaler in the UK licensed for Maintenance And Reliever Therapy in asthma' appeared beneath the visual of a women with her arms stretched out in a field. 'Extra-fine formulation. Adult asthma control' appeared at the bottom in between the product logo and an image of an inhaler. The Panel noted Chiesi's submission that the use of the phrase 'for an extra fine day' was a reference to Fostair's extrafine formulation which was substantiated by the SPC. The Panel noted that Section 4.2 of the Fostair SPC, Posology and method of administration stated that 'Beclometasone dipropionate in Fostair is characterised by an extrafine particle size distribution which results in a more potent effect than formulations of beclometasone dipropionate with a non-extrafine particle size distribution …'.

The Panel noted Chiesi's submission that the use of the wording 'Extra-fine formulation' on the same page reinforced the link between the use of the headline 'for an extra fine day' and the product's formulation. The Panel noted that in this instance 'extra-fine' had been hyphenated when describing the formulation whilst 'extra fine' in the claim at issue had been written as two words. It appeared as one word 'extrafine' in Section 4.2 of the SPC.

The Panel accepted that the use of 'for an extra fine day' was a play on words but considered that the heading to page 1 was not sufficiently clear about what 'extra fine' was referring to, there was an implication that it referred to a clinical benefit and not just to the product's formulation as submitted by Chiesi and it was ambiguous in this regard. Use of the word 'extra' by implication rendered the claim 'for an extra fine day' comparative; use of the product for the new licence provided an extra clinical benefit over and above an appropriate comparator. This implication was misleading. Chiesi provided no data to support such an advantage. The Panel noted AstraZeneca's submission that there was no robust clinical evidence to show that Fostair's extrafine formulation translated into a clinical benefit compared with other licensed treatments. The Panel considered that the implied claim could not be substantiated. The Panel did not consider that, within the context of the front page of the leavepiece the heading and the image implied that patients would return to a pre-symptom state with the use of Fostair as alleged. The Panel noted that the leavepiece included various comparisons. Page 3 compared various clinical outcomes of Fostair MART vs Fostair plus salbutamol. Page 5 included a cost comparison between Fostair and Symbicort which Chiesi had agreed to discontinue using during inter-company dialogue. The Panel noted nonetheless that the front page of the leavepiece must be capable of standing alone as regards the requirements of the Code.

The Panel considered that the claim 'New licence for Maintenance And Reliever Therapy for an extra fine day' was ambiguous, misleading and could not be substantiated. Breaches of Clauses 7.2 and 7.4 were ruled. The Panel did not consider that in these circumstances Chiesi had failed to maintain high standards and no breach of Clause 9.1 was ruled.

FURTHER INFORMATION FROM THE COMPLAINANT FOLLOWING NOTIFICATION OF THE PANEL'S RULING

Following notification of the Panel ruling AstraZeneca wrote to the Authority, noting, *inter alia*, that it was surprised by the first paragraph of the Panel ruling which implied that during inter-company dialogue EXTRA FINE was put into upper case for emphasis as the leavepiece provided by Chiesi used lower case letters only within the claim at issue. This was at odds with the leavepiece that AstraZeneca had based this complaint upon, a copy of which it now provided. AstraZeneca explained that the reason that it did not submit the item in question with its original letter was because it only had a poor quality copy.

FURTHER INFORMATION FROM CHIESI FOLLOWING NOTIFICATION OF THE PANEL RULING

Chiesi returned the signed undertaking on 4 September. On 11 September, before the Authority had contacted Chiesi about this matter, Chiesi initiated and held a teleconference with the Authority where it briefly advised that a product manager had unilaterally altered the leavepiece after it had been electronically certified such that 'extra fine' read 'EXTRA FINE'. Chiesi was asked to explain the circumstances briefly by email.

FURTHER PMCPA CONSIDERATION

Following receipt of the additional information from both parties the Authority decided that the original Panel should reconvene to consider this matter in relation to Paragraph 8 of the Constitution and Procedure. Chiesi was so informed and asked to provide detailed comments.

COMMENTS FROM CHIESI

Chiesi explained that following receipt of the PMCPA's letter advising it of the Panel's ruling it initiated an internal investigation to identify the cause of the discrepancy between the standard operating procedure (SOP) approved version and final printed version of the leavepiece. Chiesi stated that whilst not altering the intent of the message, the difference in type setting represented a breach of its SOP. An investigation found that the change to the final approved item was initiated by a product manager after certification and thus in breach of the relevant SOP. The change was made by a verbal order directly to the creative agency responsible for the production. The verbal order was confirmed in a series of emails which Chiesi submitted demonstrated that the change was made by the manager alone with no other member of Chiesi staff made aware of the specific change and as the resultant item matched other approved materials, there was no suspicion of this activity. The manager responsible was trained on the current SOP in March 2013 and its predecessor in March 2012. It appeared that the update was made in a moment of expediency prior to a key launch meeting, to align the leavepiece with other materials in which the term 'Extra Fine', appeared in upper case. The manager had left Chiesi.

In accordance with the current and previous SOP under which this leavepiece was approved, final signatories must provide wet ink signatures to confirm the final printed version was identical to the 'approved' electronic version. In this situation it appeared that the signatories were provided only with an office printed final version (with 'extra fine' in lower case) rather than a printer's proof, as such the version to be distributed was never checked. This represented a safety check which, in this isolated case, was bypassed by the individual involved. The approval of versions other than printer's proofs represented a breach of both SOPs and an audit by an external compliance company had thus been initiated.

The leavepiece was withdrawn from circulation on 30 March 2013; it was previously communicated to the PMCPA that this was 17 March 2013. During the company's investigation it transpired that not all field based staff had confirmed withdrawal by 17 March and thus 30 March represented the absolute final potential date of use. An updated acceptance of undertaking form was provided to supersede that previously sent.

Chiesi recognised that this additional information contained evidence of a lone employee failing to accord with approved SOPs and, as such, had facilitated the use of an uncertified item. It also apologised for the inaccurate date previously supplied.

Chiesi reassured the PMCPA that it had robust SOPs that were followed and regularly reviewed and trained upon in order to maintain high standards. In spite of this, it had undertaken a full audit of approved material carried out by an external company to assure Chiesi of compliance.

In response to a request for further information, Chiesi provided a copy of the email exchange between the relevant employee, the printing agency and the creative agency regarding approval of the leavepiece in question. Chiesi stated that clearly at numerous points throughout this interaction, the employee in question should have halted the print run and initiated a re-approval.

In response to a request for sight of the training provided to the manager about certification and the SOPs, Chiesi stated that both SOPs stated the originator had to ensure certain elements were complied with including ensuring that the final item was identical to the final artwork or proof approved electronically. Chiesi's manager was the originator of the leavepiece and had been documented as completing 'Read and Understand' SOP training in both cases. Coincidentally, Chiesi's manager was involved in the development of both SOPs, indicating more than a working knowledge of their contents.

Chiesi explained that as per its SOP, the material presented to the final signatories for certification was the item in its final form. The copy job bag submitted to the PMCPA with Chiesi's original response contained a copy of the certificate and a copy of the artwork that was electronically approved in January 2013. The electronic approval via Zinc was the authorisation for the material to go to print. The material was not considered certified at this point. There was no reason to believe any changes were implemented to the artwork approved on 29 January. Clean copies taken from these approved PDFs were provided to the certifiers for their final wet ink approval. Unfortunately, this assumption was incorrect.

Chiesi explained that a printer's proof came in two formats; either digital or hard copy. Essentially, the development of printing methods from litho press to digital press had led Chiesi to accept standard PDFs (digital proofs) as the *final form*. Once again, Chiesi hoped the answers provided reassured the Panel

that there was no malicious intent and, although representing a serious breach of a critical SOP, the situation was contained and not representative of the company's normal behaviours.

FURTHER CONSIDERATION OF THE CODE OF PRACTICE PANEL

The Panel noted that it was considering this matter in relation to Paragraph 8.2 of the Constitution and Procedure which provided that the Panel might report to the Appeal Board any company whose conduct in relation to the Code, or in relation to a particular case before it, or because it repeatedly breached the Code such that it raised concerns about the company's procedures, warranted consideration by the Appeal Board. Such a report to the Appeal Board may be made notwithstanding the fact that a company had provided an undertaking requested by the Panel.

The Panel noted that it had considered the complaint in relation to the copy of the leavepiece provided by Chiesi in its response to the complaint, which bore the correct reference number and featured the claim 'extra fine' in lower case. The Panel noted that this version of the leavepiece had never been distributed. According to Chiesi, a product manager had unilaterally altered the leavepiece such that the claim in question was in upper case ('EXTRA FINE') and thus aligned with other materials in anticipation of a key launch meeting. The signatories certified a printed version of a PDF file which had previously been electronically approved in Zinc. It was wrongly assumed that no changes had been made to the previously approved artwork. It appeared that it was this version that was provided to the Panel rather than the item in its final form as amended by the product manager.

The Panel considered that the relevant SOP made it abundantly clear that a print of a PDF document should not be used for final certification. The manager in question had clearly acted outwith the SOP. The Panel noted that the individual had received training on the relevant SOP and its successor UK-SOP-005. The training comprised a self-declaration that he/she had read the relevant SOP. It was not known why the manager had not followed the relevant SOP on such a vital matter.

The Panel did not accept Chiesi's conclusion that this was evidence of a lone employee failing to accord with approved SOPs. Firstly, the Panel noted that other Chiesi employees had been copied in on the manager's emails to the agency. Secondly in the Panel's view, it should have been abundantly clear to each signatory that the version provided for certification was not in its final form as required by the Code and the relevant SOP. In the Panel's view, this raised concerns about the competence of each of the Code signatories given each had certified that they had examined the final form of the material and that was not so.

The Panel considered that the failure of both the manager and the signatories to adhere to the SOP was a matter of concern and raised questions about the importance of compliance within the company.

The Panel noted that the relevant SOP had subsequently been updated (UK-SOP-005) and noted the differences between the two in relation to certification.

The Panel was concerned about the current certification arrangements as set out in Section M, Certification SOP 005 and Chiesi's explanation thereof and queried whether the final form of the materials was currently being certified by Chiesi. Final form did not just apply to the text/colour etc it also applied to the physical form of the material.

The Panel was extremely concerned that Chiesi's response to the complaint quoted throughout the claim at issue in upper case whereas the leaflet supplied used lower case for 'extra fine'. It was vital for effective self-regulation that the Panel and Code of Practice Appeal Board were able to rely on the accuracy of a company's response. The Panel was concerned that Chiesi had not noted the discrepancy on a number of occasions through form of approval, inter-company dialogue and its response to the complaint. That the company only became aware of the matter when it was notified of the Panel ruling was unacceptable. To compound these concerns it also transpired as a result of further questioning by the Panel regarding the claim and how long the material in question was in circulation that the company's original undertaking in this case incorrectly stated that the material was last used on 17 March 2013 and that was not so. A revised undertaking with a later date of final use had been provided. The Panel noted that an undertaking was an important document and the Authority must be able to rely on the accuracy of the information therein.

The Panel considered that the previous conduct of Chiesi was not irrelevant and noted that Chiesi had been the subject of previous audits.

The Panel was extremely disappointed by the conduct of Chiesi as outlined above. Self-regulation relied, *inter alia*, upon the provision of complete and accurate information to the Panel. It considered that the circumstances warranted reporting the company to the Appeal Board under Paragraph 8.2 for it to consider in relation to Paragraphs 11.3 and 11.4 of the Constitution and Procedure.

COMMENTS FROM CHIESI ON THE REPORT

At the consideration of the report Chiesi submitted that although errors had been made, it took the Code extremely seriously and was committed to making improvements; it had taken and had planned many actions to effect change. The company provided a detailed account of its 2013 compliance activities and a copy of its 2014 compliance programme. Chiesi submitted that it was committed to work with the PMCPA to improve its processes.

APPEAL BOARD CONSIDERATION

The Appeal Board noted that as a result of staff failing to follow the relevant company SOP, the final printed version of the leavepiece at issue featured 'EXTRA FINE' in upper case whereas the Zinc copy

approved by Chiesi's signatories featured 'extra fine' in lower case. Chiesi had provided the Zinc 'lower case' copy of the leavepiece in its response to the complaint without checking that that copy matched the final printed file 'upper case' copy; this despite the fact that in inter-company dialogue and throughout the complaints procedure, both parties had consistently referred to 'EXTRA FINE' in upper case. In the Appeal Board's view, the discrepancy between the two versions of the leavepiece should have been obvious to Chiesi from the outset. Chiesi had not certified the final form of the leavepiece. The PDF certified was not the final form as some of the pages were not the correct size and, in addition, the version certified used 'extra fine' in lower case and not 'EXTRA FINE' in upper case as on the final version. Neither the manager nor the signatories had followed the company's SOP.

The Appeal Board also noted with concern that Chiesi's original undertaking and assurance in respect of the breaches ruled in this case was incorrect with regard to the final date on which the leavepiece was used.

The Appeal Board noted Chiesi's submission that the failure to follow the correct approval process, and to recognise the difference between the approved leavepiece and the one that was distributed, and the mistakes in the undertaking arose from human error and lack of attention to detail. In that regard the Appeal Board noted Chiesi had previously been censured for providing the PMCPA with inaccurate information (Case AUTH/2435/8/11). In that case the Appeal Board decided that Chiesi should be publicly reprimanded and that, in accordance with Paragraph 11.3 of the Constitution and Procedure, it should undergo an audit of its procedures in relation to the Code to be carried out by the Authority. This was carried out in March 2012 and a second audit was required (carried out in October 2012). The report for the second audit had stated as a recommendation that 'Chiesi needed to ensure…that all information provided to the PMCPA was accurate'. The Appeal Board considered that Chiesi's repeated failure to provide accurate information to the PMCPA was completely unacceptable.

Self regulation relied upon the provision of complete and accurate information by pharmaceutical companies. The Appeal Board was extremely concerned about Chiesi's conduct, and having considered all the sanctions available under Paragraph 11.3 of the Constitution and Procedure it decided that the company should be publicly reprimanded for providing inaccurate information to the Authority.

The Appeal Board also decided to require an audit of Chiesi's procedures in relation to the Code. Given the details of the company's ongoing and planned compliance activities, the Appeal Board decided that the audit should be conducted in five months' time (March 2014). On receipt of the audit report the Appeal Board would consider whether further sanctions were necessary.

APPEAL BOARD FURTHER CONSIDERATION

Upon receipt of the March 2014 audit report, the Appeal Board considered that Chiesi's embarrassment at the errors which had led to the requirement for it to be audited were well founded.

The Appeal Board was extremely concerned that Chiesi had been audited twice in 2012 and that the current audit report highlighted a number of serious issues with Chiesi's compliance procedures and materials; it appeared that the company still had much work to do. The Appeal Board provided a number of detailed comments including its serious concerns that Chiesi had stated that a standard operating procedure had been updated when it had not. The Appeal Board was appalled that, in this regard, it appeared that Chiesi had yet again provided false information to the PMCPA; this was completely unacceptable. The Appeal Board considered that its further concerns about the provision of false information should be added to the detail of that public reprimand. The Appeal Board was also concerned about the outcome of Chiesi's job bag audit (conducted by an external compliance consultant). A second job bag audit was due in April 2014 and the Appeal Board requested that the results, which needed to show a significant improvement, be provided at the next PMCPA audit.

The Appeal Board noted that the company had already been given a significant amount of time to ensure its procedures, policies and culture supported a robust compliance framework. The Appeal Board decided that Chiesi should be re-audited in October 2014 when the company must be able to demonstrate significant improvement. Upon receipt of the report for the re-audit, the Appeal Board would decide whether further sanctions were necessary.

Upon receipt of the October 2014 audit report, the Appeal Board noted that Chiesi had made progress since the audit in March 2014. The Appeal Board noted that this was not the first case in which Chiesi had been censured for failing to provide accurate information to the Panel; the Appeal Board reiterated that such failings were completely unacceptable and must not happen again. The Appeal Board noted that Chiesi provided details of its plans to implement the recommendations in the audit report. On the basis that this work was completed, progress was continued and a company wide focus on compliance was maintained, the Appeal Board decided that, on balance, no further action was required.

Complaint received	**22 July 2013**
Undertaking received	**4 September 2013**
Appeal Board Consideration	**15 October 2013, 9 April 2014, 10 December 2014**
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