**CASE AUTH/2335/7/10 MERZ/DIRECTOR v ALLERGAN**

**Breach of undertaking Clause 2 breach**

Merz alleged that at the FACE (facial aesthetic conference and exhibition) congress, a meeting of aesthetic practitioners held in early July 2010, Allergan had breached the undertaking given in

Case AUTH/2183/11/08 by implying that Botox/Vistabel (botulinum toxin) was more potent than Merz’s products Xeomin/Bocouture (also botulinum toxin). Bocouture was launched at that meeting and the summary of product characteristics (SPC) was available on Merz’s stand from the beginning of the congress.

As the complaint involved an alleged breach of undertaking, it was taken up by the Director as it was the responsibility of the Authority to ensure compliance with undertakings.

Merz explained that the congress organisers had asked Merz, Allergan and Ipsen [all of which marketed forms of botulinum toxin] to deliver a non-promotional presentation entitled ‘Scientific Workshop on Pharmacology, Diffusion and Potency of Available Botulinum Toxins’.

Merz noted that Allergan’s presentation, by one of its employees, included a series of efficacy comparisons which favoured the Allergan product, Vistabel (sometimes described as Botox), when compared with the two competitor products and a number of slides showed only the efficacy for Vistabel. The first slide featured a statement that Vistabel prescribing information was available and the last slide was of the prescribing information. All of this together with a misleading presentation of potency data made the presentation promotional; it therefore fell within the scope of the Code.

Data from Hunt et al (2009) was presented on two slides. In the first slide the data was presented next to data from Dressler et al (2008) which demonstrated that Botox and Xeomin had approximately the same potency using the Merz assay for botulinum toxin. The speaker obliquely criticised this assay as being a gelatine-based assay whereas the Botox assay used a more ‘clinically relevant diluent’ (saline). The speaker then went on to show the data by Hunt et al in a table headed ‘Corrected potency units’ which implied that these data, in fact, were the correct potency for Xeomin. The speaker described the potency of Xeomin as being ‘up to 30% lower’ when measured with the Allergan ‘standard’. Further data on the potency of Xeomin was boxed in red on the next slide and was again shown as considerably less than 100 units. The data for Botox, as measured by this assay, was not shown. The speaker stated that this demonstrated that different assays gave different results and that it: ‘Calls into question any claims that the Xeomin unit, or Bocouture unit, is exactly the same as the Botox unit – that they are interchangeable, that they are 1:1 because if they were you would expect to see 100 unit Xeomin coming up on the Botox reference standard’.

When Case AUTH/2183/11/08 was considered the data from Hunt et al had only been presented in poster form however it had now been published as a scientific paper. Merz stated that this was clearly a reference to the extrapolation of this in vitro data to the clinical situation and a promotional message. This went against the ruling in Case AUTH/2183/11/08 in which the Panel ruled that the direct relevance or significance of this data to the clinical situation had not been demonstrated and that this was inconsistent with the SPCs which had similar dosing regimens for the products. In addition, Section 4.2 of the Bocouture SPC (Bocouture was the same product as Xeomin but marketed under a different name for the treatment of glabellar lines) stated that: ‘Comparative clinical study results suggest that Bocouture and the comparator product containing conventional Botulinum toxin type A complex (900 kD) are of equal potency’.

At the end of the presentation the chairman of the session asked for the Botox data as a comparator for the Xeomin potency data presented but the presenter did not directly answer this question which further reinforced the argument that this was not a scientific debate as full data was not provided even when requested, or that there was no comparator in the study which raised questions about the study itself and thus made any conclusions even more misleading.

Merz explained that, following the outcome of Case AUTH/2183/11/08, it became aware that the Hunt et al data was still used by Allergan. Following extensive inter-company dialogue, Allergan agreed only to use this data in response to specific requests for information.

Given the inter-company agreement and the undertaking given in the previous case, Merz alleged that the continued use of Hunt et al was likely to bring discredit upon or reduce confidence in the industry in breach of Clause 2.

The detailed response from Allergan is given below.

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

The Panel noted that the congress organisers had invited speakers from interested companies to present for 20 minutes each at the scientific workshop on pharmacology, diffusion and potency of botulinum toxins. A letter from FACE to Merz referred to presenting on the differences in pharmacology of available toxins. The FACE guidelines for presentation stated the presentation should not be used as an opportunity to market any single product or device.

The Panel considered that it was difficult to view Allergan’s presentation as anything other than promotional given its title and its delivery by an employee. It would promote the use of, inter alia, Allergan’s medicines. The Panel thus considered that the presentation needed to comply with the Code.

The Panel noted that slide 12 compared the potency of Xeomin and Botox according to results obtained using the Merz ‘gelatin-like’ LD50 assay. The mean potency of Xeomin was given as 103 and that of Botox as 101.7. Although not entirely clear from the slide, this data was from Dressler et al (poster). The Dressler abstract concluded that the potencies of Xeomin and Botox were equivalent. To the right of the table of data from Dressler et al was another table reporting the results for Xeomin from the Allergan saline-based LD50 assay (Hunt et al). The authors reported the corrected potency of three lots of Xeomin to be 75U/vial, 69U/vial and 78U/vial. No corresponding data was given for Botox. The Panel considered that the audience would inevitably compare the figures from the two tables of data and conclude that Xeomin was less potent than Botox. The following slide (slide 13) also featured a table of data which showed that the potency of Xeomin was less than 100 units (potency reported ranged from 61 to 78 units). Again, no corresponding data for Botox was reported. Although not stated on the slides, both assays (Hunt et al and Dressler et al) were performed in mice.

Slides 25 and 26 demonstrated a clinical advantage for Vistabel vs Xeomin (Moers-Carpi) which delegates might assume was due to the favourable potency data given on slides 12 and 13.

Slide 30 was headed ‘Are they [botulinum toxins] all the same’ followed by ‘They are not interchangeable. Difference in: …….. - clinical performance’.

The Panel noted that in Case AUTH/2183/11/08 Allergan had been ruled in breach of the Code; the Panel referred to its ruling in that case.

Case AUTH/2183/11/08

In the Panel’s view the data presented in a product monograph and an objection handler which derived from Hunt et al implied that there was a difference in potencies between Xeomin and Botox in favour of Botox. This was inconsistent with the summaries of product characteristics (SPCs) which showed similar dosing regimens for the two products. The Panel accepted that there was some animal data that possibly showed a difference. However, the supplementary information to the Code was clear that animal data should not be extrapolated to the clinical situation unless there was data to show that it was of direct relevance and significance. This had not been demonstrated. The Panel considered that the comparison could not be substantiated and did not reflect all of the evidence. Breaches of the Code were ruled.

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The Panel noted that since it had considered Case AUTH/2183/11/08 Merz had launched Bocouture – which was the same as Xeomin but was only indicated for the temporary improvement in the appearance of moderate to severe glabellar frown lines in adults below 65 years when the severity of those lines had an important psychological impact for the patient. The Bocouture SPC stated in Section 4.2 that ‘Comparative clinical study results suggest that Bocouture and the comparator product containing conventional Botulinum toxin type A complex (900 kD) [i.e. Botox] are of equal potency’. The Panel noted that Allergan had only recently obtained a copy of the Merz data-on-file document to support the grant of the Bocouture licence and, the Panel assumed, the statement in Section 4.2 of the Bocouture SPC. In contrast to that statement, Allergan had submitted clinical data which demonstrated a statistically significant clinical advantage for Vistabel vs Bocouture (Moers-Carpi).

The Panel considered that the comparative data shown in the presentation was sufficiently different to the material considered in Case AUTH/2183/11/08 for it not to be caught by the undertaking given in that case. The previous material had not referred to Dressler et al or the Moers-Carpi data as shown later in the presentation. The Panel did not consider that the presentation was in breach of the undertaking given in Case AUTH/2183/11/08 and in that regard high standards had been maintained. No breaches of the Code were ruled.

The Panel considered that as there had been no breach of the undertaking there could be no breach of Clause 2. No breach of that clause was ruled.

Upon appeal by Merz the Appeal Board noted that the title of Allergan’s presentation was ‘Pharmacology, diffusion and potency of Botulinum Toxins’. Slide 1 listed the various botulinum toxins available from the three manufacturers. Slide 3 of the presentation showed a number of vials of different sizes and was headed ‘Are they all the same?’. Beneath the picture of the vials was the second question ‘Are they non-interchangeable – Structure? Unit potency? Stability? Diffusion characteristics? Clinical performance?’. The last slide had the same heading and picture of vials below which was now the statement ‘They are non-interchangeable. Differences in: Structure, Unit potency, Stability, Diffusion characteristics, Clinical performance’.

The Appeal Board noted that Merz had drawn attention to slides 12 and 13 of the presentation. These were headed ‘Differences in LD50 assays’ and ‘Xeomin potency’. Slide 10 made it clear that the products were different ‘… and non-interchangeable potency units are specific’. Slide 11 was headed ‘Reasons for potency differences’ with the sub headings ‘Intrinsic differences in product characteristics’ and ‘Differences in LD50 assays’.

The Appeal Board noted that the presentation had included data from the small (n=12) Moers-Carpi study which was a split-face comparison of Vistabel and Xeomin in the forehead region of healthy volunteers. The results presented were those which showed a statistically significant advantage for Vistabel [Botox] vs Xeomin when brow position was assessed by digital photography. The results of the patients’ own evaluation of therapy, however, were not included; these showed no difference between the products.

The Appeal Board noted that the Bocouture [Xeomin] SPC stated in Section 4.2 that ‘Comparative clinical study results suggest that Bocouture and the comparator product containing conventional Botulinum toxin type A complex (900KD) [ie Botox] are of equal potency’. The Appeal Board noted that the relevant data was an unpublished non-inferiority study which Allergan had received from Merz after the meeting in question.

The Appeal Board did not accept Allergan’s submission that the inclusion of the Dressler et al and Moers-Carpi studies meant that the presentation was substantially different to the product monograph and objection handler at issue in Case AUTH/2183/11/08.

Overall, the Appeal Board considered that the presentation had implied that Xeomin was less potent than Botox using, inter alia, the same data, ie Hunt et al, as that at issue in Case

AUTH/2183/11/08. The Appeal Board considered that the presentation breached the undertaking and in that regard high standards had not been maintained. Breaches of the Code were ruled. The appeal on both points was successful. The Appeal Board noted that an undertaking was an important document. The Appeal Board considered that Allergan’s conduct was such as to bring discredit upon and reduce confidence in the pharmaceutical industry. The Appeal Board ruled a breach of Clause 2. The appeal on this point was successful.

Merz alleged that at the FACE (facial aesthetic conference and exhibition) congress, a meeting of aesthetic practitioners held at the Royal College of Physicians 2-4 July 2010, Allergan had breached the undertaking given in Case AUTH/2183/11/08 by implying that Botox/Vistabel (botulinum toxin) was more potent than Merz’s products Xeomin/Bocouture (also botulinum toxin). Merz explained that it launched Bocouture at this meeting having been granted a marketing authorization on Tuesday, 29 June 2010. The promotional stand made it clear that a marketing authorization had been granted and the summary of product characteristics (SPC) was available on the stand from the beginning of the congress.

As the complaint involved an alleged breach of undertaking, it was taken up by the Director as it was the responsibility of the Authority to ensure compliance with undertakings.

COMPLAINT

Merz referred to a presentation delivered by an Allergan employee at the congress on 2 July and provided photographs of the slides taken at the event. Merz, Allergan and Ipsen [all of which marketed forms of botulinum toxin] were asked to present at the congress. It had been made clear to the Merz speaker that the presentation should not be promotional and that the presentation was a ‘Scientific Workshop on Pharmacology, Diffusion and Potency of Available Botulinum Toxins’.

Merz believed that the same brief was sent to all companies. Allergan’s opening slide stated that it was an invited talk and thus non-promotional. Had it remained true to the original brief of ‘Pharmacology, Diffusion and Potency’, as indicated by the title and requested by the event organisers, it would have been non-promotional. However, a series of efficacy comparisons favoured the Allergan product, Vistabel (sometimes described as Botox), when compared with the two competitor products (slides 25-32), a number of slides showed only the efficacy for Vistabel (slides 21-24), the first slide featured a statement that prescribing information for Vistabel was available and the last slide was of the prescribing information. All of this together with a misleading presentation of potency data made the presentation promotional; it therefore fell within the scope of the Code.

Data from Hunt et al (2009) was presented on two slides. In the first slide the data was presented next to data from Dressler et al (2008) which demonstrated that Botox and Xeomin had approximately the same potency using the Merz assay for botulinum toxin. Allergan’s speaker obliquely criticised this assay as being a gelatine-based assay whereas the Botox assay used a more ‘clinically relevant diluent’ (saline) and went on to show the data by Hunt et al in a table headed ‘Corrected potency units’ which implied that these data, in fact, were the correct potency for Xeomin. The speaker described the potency of Xeomin as being ‘up to 30% lower’ when measured with the Allergan ‘standard’. Further data on the potency of Xeomin was boxed in red on the next slide and was again shown as considerably less than 100 units. The data for Botox, as measured by this assay, was not shown. The speaker stated that this demonstrated that different assays gave different results and that it:

‘Calls into question any claims that the Xeomin unit, or Bocouture unit, is exactly the same as the Botox unit – that they are interchangeable, that they are 1:1 because if they were you would expect to see 100 unit Xeomin coming up on the Botox reference standard’. [An audio recording of the presentation was provided].

When Case AUTH/2183/11/08 was considered the data from Hunt et al had only been presented in poster form however it had now been published as a scientific paper.

Merz stated that this was clearly a reference to the extrapolation of this in vitro data to the clinical situation and a promotional message. This went against Case AUTH/2183/11/08 in which the Panel ruled that the direct relevance or significance of this data to the clinical situation had not been demonstrated and that this was inconsistent with the SPCs which had similar dosing regimens for the products. In addition, Section 4.2 of the Bocouture SPC (Bocouture was the same product as Xeomin but marketed under a different name for the treatment of glabellar lines) stated that: ‘Comparative clinical study results suggest that Bocouture and the comparator product containing conventional Botulinum toxin type A complex (900 kD) are of equal potency’.

Merz submitted that the presentation was not exempt from the Code because:

Clause 1.2 required that responses to individual enquiries could only relate solely to the subject matter in the enquiry, were accurate and did not mislead. The subject matter requested was exceeded in this presentation as efficacy data was presented in addition to potency data. The efficacy data presented clearly positioned Allergan’s product as superior. The presentation was misleading as it presented data that contradicted Section 4.2 of the Bocouture SPC. In addition the speaker’s words directly contradicted Section 4.2 of the Bocouture SPC.

The presentation of the potency data from Hunt et al was also misleading as both Xeomin (Bocouture) and Botox (Vistabel) had similar dosing regimens. This was commented upon for Xeomin and Botox in Case AUTH/2183/11/08 and cited as a reason why the data was misleading.

This was no less true now than it was then. It was not ‘scientific debate’ as it was misleading and contained promotional messages.

At the end of the presentation the chairman asked for the Botox data as a comparator for the Xeomin potency data presented but the presenter avoided directly answering this question which further reinforced the argument that this was not a scientific debate as full data was not provided even when requested, or that there was no comparator in the study which raised questions about the study itself and thus made any conclusions even more misleading.

Merz explained that, following the outcome of Case AUTH/2183/11/08, it became aware that the data was still being used in that a medical liaison executive, accompanied by a sales representative, had presented this data proactively at a meeting in May 2009 at a teaching hospital. Merz contacted Allergan about this and, following extensive inter-company dialogue, the two companies agreed that Allergan would not use this data at all except in response to specific requests for information. Directors of Merz and Allergan signed a letter to cement this agreement.

This activity represented a breach of undertaking and thus Clause 25. Merz alleged that Allergan had failed to maintain high standards in breach of Clause 9.1. Furthermore, Allergan’s action in that it entered into an undertaking to the PMCPA which it later did not honour, was given a ‘second chance’ by Merz which it flouted by breaching the undertaking again, was likely to bring discredit upon or reduce confidence in the industry in breach of Clause 2.

RESPONSE

Allergan disagreed that it had breached its undertaking given in Case AUTH/2183/11/08 or that the presentation was promotional. Given that Merz, Allergan and Ipsen were all invited to provide speakers for the scientific workshop at issue, and given the nature of the topic provided by the conference organisers, Allergan rigorously scrutinised the presenter’s presentation to ensure full compliance with the Code, specifically in relation to content, its non-promotional nature and previous PMCPA rulings. The company ensured that it was a stand alone presentation, that it was non-promotional i.e. scientifically accurate and balanced and addressed the topic requested ‘Pharmacology, Diffusion and Potency of Botulinum Toxins’.

Allergan noted that the congress was organised by Wigmore, suppliers of Dysport/Azzalure and Xeomin/Bocouture to the UK market.

Allergan agreed with Merz that this was a non-promotional scientific workshop. The presentations were delivered within the congress rather than a company sponsored workshop. In order to provide balance, representatives from all three UK manufacturers of botulinum toxins were invited to present on ‘Pharmacology, Diffusion and Potency of Botulinum Toxins’. This title was set by the FACE organisers. Allergan engaged in extensive dialogue with the organisers of FACE to establish the non-promotional nature of the workshop.

The presentation in question was discussed in depth with the FACE conference organiser to ensure that its content met the requirements for a non-promotional scientific debate. In particular, the conference organiser confirmed that it was appropriate to include clinical and comparative data in order that the clinical relevance of the pre-clinical data could be presented in clinical context. This was confirmed in correspondence in which the conference organiser, inter alia, reassured Allergan that the content was as requested.

Allergan strongly disagreed that the presentation was promotional or indeed that it breached either its undertaking or the inter-company dialogue agreement with Merz.

Allergan noted that Merz made much of the launch of Bocouture at FACE. Allergan provided some context around statements made by Merz on this matter although ultimately did not believe the availability of the Bocouture marketing authorization was germane to this complaint.

The presenter was not aware of the imminent launch of Bocouture or indeed the content of the Bocouture SPC, when the presentation was prepared. In order to ensure full compliance with the Code and Allergan’s processes, the presentation was examined in advance of the workshop which was held on 2 July, the first day of the congress. Allergan was not aware of any press release or publicity activities to announce the grant of the Bocouture marketing authorization before or on 2 July 2010. Furthermore, the Bocouture SPC was not available on the electronic Medicines Compendium (eMC) on 2 July.

Allergan noted that following its presentation, Merz’s presenter stated that he would only refer to Xeomin, as Bocouture was not yet approved for cosmetic use in the UK. Clearly, Merz’s own speaker did not know that the company had just gained the marketing authorization for Bocouture.

As stated in the declaration on the first slide, Allergan’s presenter had been invited to participate in a scientific debate and the presentation was examined to ensure it was non-promotional. The fact that the presentation referred to clinical data on Vistabel (or Botox where relevant in the context of the data being discussed) did not per se make it promotional, although it did provide clinical context.

Allergan abided by the brief given and provided a scientifically accurate, balanced, non-promotional presentation for the reasons discussed below.

Balance was provided within the presentation through the data from Dressler et al, Lowe et al (2010) and Kerscher et al (2009) (all of which provided a contrary view to Allergan’s position), and also due to the fact that the three companies each presented their view on the same topic. Allergan did not have an audio recording or photographs of the presentation made by Merz or Ipsen as the conference organisers prohibited the use of audio or video recording at the conference. A clear notice to this effect was given at the start of the session. The photographs of the slides submitted by Merz were of a poor quality and so Allergan assumed they were taken with a hidden camera/phone.

However, Allergan provided abstracts of the two other presentations and requested that Merz provided its presentation for context and the FACE conference organisers should be asked to supply the Ipsen presentation. It was only when all three presentations were viewed together that Allergan’s presentation could be fairly assessed for balance.

On viewing the full presentation and listening to the audio provided by Merz, Allergan believed it would be clear that this was a fair and balanced presentation of the available scientific data on the topic requested by the conference organisers.

Slide 3 set the scene by looking at the differences between the products and the fact, as stated in the SPCs for all the botulinum toxins, that unit doses of the various products were not interchangeable.

Slides 4-9 discussed the pharmacology of the botulinum toxins.

Slides 10-13 covered the topic of potency – as requested by the conference organisers. Again this information was contextualised by the slide entitled ‘BoNT products are different AND non-interchangeable potency units are specific’ (slide 10). In the US new non-proprietary (generic) names had been established to reinforce the lack of interchangeability of the unit doses. This slide was considered to be relevant to the audience in the context of a scientific debate on the potency of botulinum toxins as US speakers frequently presented at EU congresses.

There were two slides which detailed data from Hunt et al (slides 12 and 13). As acknowledged by Merz, the data were balanced by the inclusion of data on slide 12 from Dressler et al, which demonstrated similar numbers of potency units for Botox and Xeomin when tested using the Merz reference LD50 assay. Allergan believed there were genuine criticisms of the data from Dressler et al and that a scientific forum was an appropriate place to raise these concerns. The data from Hunt et al showed that in the Allergan LD50 assay, with Botox as the reference standard, Xeomin units were not equivalent to Botox units. The presenter used this data to support the fact that unit doses of the botulinum toxins were not interchangeable.

Aside from two slides on stability (slides 14 and 15) and a summary slide (slide 30), the remaining slides looked at the topic of diffusion, as requested by the conference organisers, and which clearly related to both the safety and efficacy profiles of all three botulinum toxins. The presenter’s presentation reviewed the available data on clinical models of diffusion using anhidrosis halos and supporting clinical data to illustrate what was found from the clinical models. This was done in a balanced way including studies sponsored by Merz and Allergan.

Allergan acknowledged that the presentation referred to the location of prescribing information and contained prescribing information at the end. The addition of prescribing information was a ‘belt and braces’ approach to demonstrate the level of scrutiny applied to this presentation. Whilst the inclusion of the prescribing information might have been incorrect and given the wrong impression, Allergan stood completely by the fact that this was a balanced, scientifically accurate, non-promotional presentation.

Regarding Merz’s specific comments/allegations about the data itself, Allergan stated that it believed that the data from Hunt et al were relevant in the context of a non-promotional presentation, as they supported the fact that the botulinum toxin units were not interchangeable due to differences in LD50 assay techniques between different manufacturers. Furthermore the data were supported by recently available clinical data from Moers-Carpi (2010) (slides 25 and 26) which demonstrated that in a clinical split-face comparison of Vistabel (12 units) and Xeomin (12 units), the two products were not equivalent. Therefore, these data were relevant to the clinical situation and use in a non-promotional setting did not go against the ruling in Case AUTH/2183/11/08.

As stated above, the presenter did not know about the imminent launch of Bocouture, or the content of the Bocouture SPC, when the presentation was prepared. The presentation was prepared in good faith; the Xeomin SPC was used as a reference. Given that the Bocouture marketing authorization was only announced on the day of the FACE conference and that even the Merz speaker was unaware of this, Allergan did not believe it was misleading for it to present only the Moers-Carpi data without referring to the new SPC statement ‘Comparative clinical study results suggest that Bocouture and the comparator product containing conventional botulinum toxin type A complex (900 kD) are of equal potency’ (emphasis added by Allergan). This statement was based on an unpublished non-inferiority study. As established in Case AUTH/2270/10/09, all that could be claimed from a non-inferiority study was that one product was no worse than another by the pre-specified margin in the study. Allergan had just received the Merz data-on-file document to support the grant of the licence and would ensure that any future scientific presentations reflected this unpublished non-inferiority data.

Allergan was unaware of any other comparative data publically available and therefore believed the presentation was a fair and accurate representation of the available data.

In summary Allergan submitted that:

The presentation was examined by a Code signatory and confirmed to be balanced, scientifically accurate and therefore non-promotional; it was not certified as it was not considered promotional.

The presentation clearly addressed the subject requested by the conference organisers, who confirmed that it was entirely appropriate to present clinical and comparative data to provide context. The reference to efficacy data did not make this a promotional presentation if presented in a balanced way and in the context of the diffusion of the products. Balance was also provided by the presentations of the two other company speakers, as was the nature of a debate.

The presentation was prepared in good faith, prior to the public availability of the Bocouture SPC. That said the presentation did not contradict the SPC which only suggested the products were of equal potency based on a non-inferiority study. Case AUTH/2270/10/09 established that equivalence or equal potency could not be claimed from a non-inferiority study. The presentation of the Hunt et al data was not misleading. It was fully contextualised with comparative data (Dressler et al) and the pre-clinical findings had recently been confirmed in a clinical study (Moers-Carpi). This was a non-promotional presentation within a scientific debate.

Allergan submitted that if every presentation made at a scientific congress was now to be assessed as potentially promotional it would limit future legitimate scientific exchange.

Allergan disagreed that the presentation had breached its inter-company agreement with Merz. Allergan continued to abide by the letter and spirit of its part of the agreement despite the recent case about claims based on non-inferiority studies (Case AUTH/2270/10/09) which were contrary to Merz’s part of the agreement.

Finally, scientific debates by their nature involved different parties, typically with opposing views, stating their case in order that the audience could assess the balance of evidence and draw their own conclusions. Although these scientific debates presented pharmaceutical companies with significant challenges they remained of particular interest to clinicians attending such conferences. Allergan considered that it was legitimate, in the context of a scientific debate, balanced not only with opposing data but also contextualised with recently available clinical data from Moers-Carpi, to present the two slides containing the Hunt et al data.

Allergan refuted any allegation of a breach of undertaking and thus Clause 25 of the Code. Similarly it denied a breach of Clause 9.1 or 2. Allergan also denied the alleged breaches of Clauses 7.2 and 7.3.

PANEL RULING

The Panel noted that an undertaking was an important document. It included an assurance that all possible steps would be taken to avoid similar breaches of the Code in future. It was very important for the reputation of the industry that companies complied with undertakings. The Panel considered that given the Authority’s responsibility in ensuring compliance with undertakings, inter-company dialogue as set out in Paragraph 5.2 of the Constitution and Procedure was not required in this regard before a complaint could be accepted.

The Panel noted that the organisers of the FACE congress had invited speakers from interested companies to present for 20 minutes each at the scientific workshop on pharmacology, diffusion and potency of botulinum toxins. A letter from FACE to Merz referred to presenting on the differences in pharmacology of available toxins. The FACE guidelines for presentation stated the presentation should not be used as an opportunity to market any single product or device.

The Panel considered that it was difficult to view the presentation as anything other than promotional given its title and its delivery by an Allergan employee. It would promote the use of, inter alia, Allergan’s medicines. The Panel thus considered that the presentation, given by an Allergan employee and including information about Allergan’s product Botox/Vistabel, needed to comply with the Code. The Panel disagreed with Allergan’s submission that the presentation at issue should be viewed in the context of the other two presentations. In the Panel’s view, each presentation had to stand alone under the Code; none could rely on any of the others for balance.

The Panel noted that slide 12 compared the potency of Xeomin and Botox according to results obtained using the Merz ‘gelatin-like’ LD50 assay. The mean potency of Xeomin was given as 103 and that of Botox as 101.7. Although not entirely clear from the slide, this data was from Dressler et al (poster). The Dressler abstract concluded that the potencies of Xeomin and Botox were equivalent. To the right of the table of data from Dressler et al was another table reporting the results for Xeomin from the Allergan saline-based LD50 assay (Hunt et al). The authors reported the corrected potency of three lots of Xeomin to be 75U/vial, 69U/vial and 78U/vial. No corresponding data was given for Botox. The Panel considered that the audience would inevitably compare the figures from the two tables of data and conclude that Xeomin was less potent than Botox. The following slide (slide 13) also featured a table of data which showed that the potency of Xeomin was less than 100 units (potency reported ranged from 61 to 78 units). Again, no corresponding data for Botox was reported. Although not stated on the slides, both assays (Hunt et al and Dressler et al) were performed in mice.

Slides 25 and 26 demonstrated a clinical advantage for Vistabel vs Xeomin (Moers-Carpi) which delegates might assume was due to the favourable potency data given on slides 12 and 13.

Slide 30 was headed ‘Are they [botulinum toxins] all the same’ followed by ‘They are not interchangeable. Difference in: …….. - clinical performance’.

The Panel noted that in Case AUTH/2183/11/08 Allergan had been ruled in breach of the Code; the Panel referred to its ruling in that case.

Case AUTH/2183/11/08

In the Panel’s view the data presented in a product monograph and an objection handler which derived from Hunt et al implied that there was a difference in potencies between Xeomin and Botox in favour of Botox. This was inconsistent with the summaries of product characteristics (SPCs) which showed similar dosing regimens for the two products. The Panel accepted that there was some animal data that possibly showed a difference. However, the supplementary information to the Code was clear that animal data should not be extrapolated to the clinical situation unless there was data to show that it was of direct relevance and significance. This had not been demonstrated. The Panel considered that the comparison could not be substantiated and did not reflect all of the evidence. Breaches of, inter alia, Clauses 7.2, 7.3 and 7.10 of the Code were ruled.

Case AUTH/2335/7/10

The Panel noted that since it had considered Case AUTH/2183/11/08 Merz had launched Bocouture – which was the same as Xeomin but was only indicated for the temporary improvement in the appearance of moderate to severe glabellar frown lines in adults below 65 years when the severity of those lines had an important psychological impact for the patient. The Bocouture SPC stated in Section 4.2 that ‘Comparative clinical study results suggest that Bocouture and the comparator product containing conventional Botulinum toxin type A complex (900 kD) [i.e. Botox] are of equal potency’. The Panel noted that Allergan had only recently obtained a copy of the Merz data-on-file document to support the grant of the Bocouture licence and, the Panel assumed, the statement in Section 4.2 of the Bocouture SPC. In contrast to that statement, Allergan had submitted clinical data which demonstrated a statistically significant clinical advantage for Vistabel vs Bocouture (Moers-Carpi).

The Panel considered that the comparative data shown in the presenter’s presentation was sufficiently different to the material considered in Case AUTH/2183/11/08 for it not to be caught by the undertaking given in that case. The previous material had not referred to Dressler et al or the Moers-Carpi data as shown later in the presentation. The Panel did not consider that the presentation was in breach of the undertaking given in Case AUTH/2183/11/08 and so it ruled no breach of Clause 25. In that regard high standards had been maintained. No breach of Clause 9.1 was ruled.

The Panel considered that as there had been no breach of the undertaking there could be no breach of Clause 2. No breach of that clause was ruled.

During the consideration of this case the Panel noted Allergan’s submission that the presentation given by the presenter referred to all the data of which Allergan was aware. Clinical data was presented which appeared to support the in vivo potency data. Contrary clinical data was referred to in the Bocouture SPC but the SPC gave the date of first authorization as 29 June 2010 ie three working days before the presentation was given. (The Panel had not been given a copy of that data). The Panel noted Allergan’s submission that it had only recently obtained a copy of the data referred to in the Bocouture SPC and that future presentations would reflect that data. Nonetheless, the Panel considered that the presentation had not referred to the totality of the clinical efficacy data and in that regard it queried whether by only referring to Moers-Carpi, the presenter’s presentation was misleading and unbalanced. It appeared that the comparative clinical efficacy of Vistabel and Bocouture had not been resolved clearly in favour of one product or the other. Where a clinical or scientific issue existed which had not been clearly resolved in favour of one generally accepted viewpoint, the Code required particular care to be taken to ensure that the issue was treated in a balanced manner in promotional material. The Panel requested that Allergan be advised of its concerns in this regard.

APPEAL BY MERZ

Merz alleged that Allergan had breached the undertaking given in Case AUTH/2183/11/08 by seeking to convince medical practitioners that Xeomin was less potent than Botox using the same data. This claim was inconsistent with the respective product SPCs and head-to-head clinical comparisons. The use of this data to create this argument was found to be unsubstantiated and not to encourage the rational use of a medicine in Case AUTH/2183/11/08. The inclusion of additional data that did not support this claim did not prevent the presenter from concluding that Xeomin was less potent than Botox. Further animal data was cited to reinforce this point and the presenter summarised with the unambiguous claim that the presence of these data ‘Calls into questions any claims that the Xeomin unit, or Bocouture unit, is exactly the same as the Botox unit – that they are interchangeable, that they are 1:1 because if they were you could expect to see 100 unit Xeomin coming up on the Botox reference standard’. The Panel acknowledged that the data, as presented, would lead the audience to conclude that Xeomin was significantly [sic] less potent than Botox. The Panel was also clear, as was Merz, that the presentation was promotional in tone and context and so fell under the Code. In Case AUTH/2183/11/08 the Panel drew the same conclusion from the same data when it concluded: ‘…that on the balance of probabilities the Allergan representative had claimed there was a difference in potency for the products. This was inconsistent with the SPCs which had similar dosing regimens for the products’. In that case, the Panel further stated that ‘The comparison could not be substantiated and did not reflect all the evidence’. Merz alleged that the Panel’s ruling in Case AUTH/2183/11/08 clearly applied to Allergan’s presentation delivered at the FACE congress. It was as true now as it was then and the very large data set which showed clinical non-inferiority of Xeomin to Botox remained unchallenged.

Merz alleged that the comparative potencies of the Allergan (Botox/Vistabel) and Merz (Xeomin/Bocouture) toxins was further reinforced in the Bocouture SPC (which was available on the Merz stand that clearly launched Bocouture at the FACE conference) where the regulators concluded that all the data suggested that the two products were equipotent. For such a statement to appear in an SPC meant that this was not a matter of scientific debate but had been clearly positioned by the regulator. Merz noted that the medicine in Botox was identical to that in Vistabel and Xeomin was identical to that in Bocouture.

Merz noted Allergan’s reference to Moers-Carpi. This data was presented 12 slides after the potency tables in question. Merz noted that this study was in a small patient population (n=12) in an indication that was outside the licensed indications for Bocouture and Vistabel.

Merz alleged that Allergan omitted to convey the comparison was outside of the product licenses for both products and consequently not relevant. Allergan went on to present data that highlighted a technical difference in the results for the two products rather than the clinically relevant outcome in this therapeutic area, of patient subjective evaluation, for which there was no difference. Allergan could not therefore use this off label data to show that Hunt et al was of clinical reference or significance.

Allergan, however, was aware of the very large data set which compared Xeomin and Botox and clearly and unambiguously showed that Xeomin was not inferior to Botox in the clinical setting (Benecke et al 2005, Roggenkämper et al 2006, Merz data on file). Allergan also knew that, based upon these data the regulator very deliberately adopted the same dosage schedule for Xeomin as adopted for Botox, and subsequently Bocouture as for Vistabel. Allergan should also have known, as the information was available before the presentation, that the regulators clearly viewed Vistabel and Bocouture as equipotent, a fact that was unambiguously articulated in the Bocouture SPC.

Merz alleged that this represented a breach of undertaking as:

Allergan sought to convince the audience in a clearly promotional presentation that Xeomin was less potent than Botox by presenting animal data which conflicted with all relevant clinical evaluations

The animal data from which the speaker’s conclusion was drawn were exactly the same data subject to the undertaking in Case

AUTH/2183/11/08

The Panel accepted that this presentation of the same data in Case AUTH/2183/11/08 would lead the audience to the same conclusion, namely that Xeomin was less potent than Botox The presentation of the data would go against the Panel’s view in Case AUTH/2183/11/08 and it remained inconsistent with the identical dosing That the much later presentation of partial results of a small study outside the license of either product, whilst not referring to a very large relevant clinical data set, did not detract from the clear intention to present misleading argument and not promote the rational use of a medicine.

Merz questioned the value of undertakings if they allowed a company to present data ruled in breach of the Code in a slightly different way but draw the same conclusion. Merz alleged that Allergan intended the presentation to circumvent the undertaking given following Case AUTH/2183/11/08 whilst ensuring that the same message was communicated. This eroded the purpose of undertakings. The presentation of the data and the conclusions drawn were clearly in breach of the undertaking given in Case AUTH/2183/11/08 and therefore in breach of Clauses 2, 9.1 and 25.

COMMENTS FROM ALLERGAN

Allergan disagreed that it had breached the undertaking given in Case AUTH/2335/7/10. Allergan was well aware of that case ruling and the undertaking it had given and had rigorously scrutinized the presentation at issue to ensure that it had fully taken into account its undertaking; it was confident that the presentation did not constitute a breach of undertaking.

Allergan submitted that the presentation was reviewed for compliance with the Code as a stand alone presentation. Specifically it was reviewed to ensure that it was scientifically accurate and balanced and addressed the topic requested; ‘Pharmacology, Diffusion and Potency of Botulinum Toxins’. At the time of preparation and approval it took into account all the publically available information. The presentation was given by a senior employee.

Allergan submitted that the appeal rested on Merz’s assertion that Allergan breached the undertaking in respect of Case AUTH/2183/11/08. The case report ensured the full context was provided but the key concluding section of the Panel ruling was (\*asterisked clarification added by Allergan):

‘The Panel considered that given the comparative potency information in the product monograph and objection handler [\*derived from Hunt et al (2006) – now available as a full publication] it was not unrealistic that representatives might have used this information when promoting Botox to health professionals. There was no instruction about how to use the information comparing the potency of Xeomin and Botox. The Panel considered on the balance of probabilities the Allergan representative had claimed there was a difference in potency for the products. This was inconsistent with the summaries of product characteristics (SPCs) which showed similar dosing regimens for the two products. The Panel accepted that there was some animal data that possibly showed a difference. However, the supplementary information to Clause 7.2 was clear that animal data should not be extrapolated to the clinical situation unless there was data to show that it was of direct relevance and significance. This had not been demonstrated. The Panel considered that the product monograph and objection handler were misleading with regard to the information about potency. The comparison could not be substantiated and did not reflect all of the evidence. The material would not encourage the rational use of a medicine. Thus the Panel ruled breaches of Clauses 7.2, 7.3 and 7.10.’

Allergan submitted that it would be clear from the evidence placed below that it had taken into account the requirement for balance, reflection of all the available data (at the time of the presentation) and the care required when presenting and extrapolating animal data. Allergan submitted that it had not breached its undertaking or attempted to circumvent the undertaking as alleged by Merz, and it had complied with both the letter and spirit of the Code.

Allergan reiterated some of the information provided previously to give appropriate context to address the points raised by Merz:

Allergan submitted that the FACE congress took place on the 2-4 July 2010, in London, UK. This conference was organised by Wigmore, suppliers of Dysport/Azzalure and Xeomin/Bocouture to the UK market.

Allergan understood this was a non-promotional scientific workshop. The presentations were delivered within the congress rather than a company sponsored workshop. In order to provide balance, representatives from all three manufacturers of botulinum toxins in the UK were invited by the FACE organisers to present on the pharmacology, diffusion and potency of botulinum toxins. Allergan engaged in extensive dialogue with the organisers of FACE to establish the non-promotional nature of the workshop.

The presentation in question was discussed in depth with the FACE conference organiser to ensure that the content met the organiser’s requirements for a non-promotional scientific debate. In particular, the organiser confirmed that it was entirely appropriate to include clinical and comparative data in order that the clinical relevance of the pre-clinical data could be presented in clinical context. This was confirmed in correspondence in which Allergan was reassured that the content was as requested. As stated in the declaration on the first slide, the presenter was an invited speaker, participating in a scientific debate. Allergan had abided by the brief given and provided a scientifically accurate, balanced, non-promotional presentation for the reasons discussed below.

Allergan noted that in its ruling the Panel considered it difficult to view the presentation as anything other than promotional given its title and delivery by an Allergan employee. Allergan had previously outlined why the presentation was non-promotional. However, even when considered as a promotional presentation it did not breach the undertaking. It provided a balanced overview of all the available data on the requested topics as outlined below and as recommended in the ruling with respect to Case AUTH/2183/11/08.

Allergan noted that on viewing the presentation, and listening to the audio provided by Merz to the PMCPA (copy supplied to Allergan via the PMCPA), it submitted that it would be clear that this was a fair and balanced presentation of the available scientific data on the topic requested by the conference organisers. Slide 3 set the scene and looked at the differences between the products and the fact, as stated in the SPCs for all the botulinum toxins, that unit doses of the various toxins were not interchangeable. Slides 4 – 9 discussed the pharmacology of the botulinum toxins. Slides 10 13 covered the topic of potency – as requested by the conference organisers. Again this information was contextualised by the slide entitled ‘BoNT products are different AND non-interchangeable potency units are specific’ (slide 10). In the US new non-proprietary (generic) names had been established to reinforce the lack of interchangeability of the unit doses. Slide 11 was relevant to the audience in the context of a scientific debate on potency of the botulinum toxins as US speakers frequently presented in EU congresses.

Allergan noted that slides 12 and 13 referred to Hunt et al. As acknowledged by Merz, the data were balanced by the inclusion on slide 12 of Dressler et al which demonstrated a similar number of potency units for Botox and Xeomin when tested using the Merz reference LD50 assay. Allergan submitted there were genuine criticisms of the Dressler data and that a scientific forum was an appropriate place to raise these concerns. The data by Hunt et al showed that in the Allergan LD50 assay, with Botox set as the reference standard, Xeomin units were not equivalent to Botox units. The presenter used this data to support the fact that unit doses of the botulinum toxins were not interchangeable.

Allergan noted that the relevant section of the audio recording provided by Merz (minutes 9 through to 12) was heard with the context of the accompanying slides (slides10-13) the isolated quotation, ‘Calls into question any claims that the Xeomin unit, or Bocouture unit, is exactly the same as the Botox unit – that they are interchangeable. That they are 1:1 because if they were you would expect to see 100 units Xeomin coming up on the reference standard’, could be seen as a balanced summary of the preceding data and a clear message that the products were not interchangeable. It was not, as Merz suggested, a conclusion by Allergan that Xeomin had was less potent than Botox, only that the two were not interchangeable.

Allergan submitted that aside from slides 14 and 15 on stability and a summary slide, the remaining slides referred to diffusion, as requested by the conference organisers, which clearly related to the safety and efficacy profiles of all three botulinum toxins. The presentation reviewed the available data on clinical models of diffusion using anhidrosis halos and supporting clinical data to illustrate what was found from the clinical models. This was done in a balanced way including studies sponsored by Merz and Allergan.

Aside from the balance provided around the issue of lack of interchangeability with the inclusion of Dressler et al the presentation did not contradict the Xeomin SPC and continued to reflect the Xeomin non-inferiority data cited by Merz (Benecke et al; Roggenkämper et al). It was well established (Case AUTH/2270/10/09) that equivalence or equal potency could not be claimed from a non-inferiority study.

Allergan submitted that Merz made much of the launch of Bocouture at FACE; Allergan provided some context around statements made by Merz on this matter although ultimately Allergan did not believe the availability of the Bocouture marketing authorization was germane to this complaint. The presenter was not aware of the imminent launch of Bocouture or indeed the content of the Bocouture SPC, when the presentation was prepared. In order to ensure full compliance with the Code and Allergan’s processes, the presentation was examined in advance of the workshop which was held on the 2 July, the first day of the congress. Allergan were not aware of any press release or publicity activities to announce the grant of the Bocouture marketing authorization prior to or indeed on the 2 July 2010. Furthermore, the Bocouture SPC was not available on the electronic medicines compendium (eMC) on the 2 July. Allergan noted that a presenter, who presented after the presenter on behalf of Merz at the scientific workshop under discussion, stated at the outset that he would only refer to Xeomin, as Bocouture was not yet approved for cosmetic use in the UK. Clearly, Merz’s own speaker was not aware that Merz UK had just gained the marketing authorization.

Allergan submitted that the presenter’s presentation was prepared in good faith with reference to the existing Xeomin SPC. Given that the Bocouture marketing authorization was only announced on the day of the FACE conference and that even the Merz speaker was unaware of this, Allergan did not believe it was misleading to present only the Moers-Carpi data without reference to the Bocouture SPC statement below.

‘4.2 Posology and method of administration Unit doses recommended for Bocouture are not interchangeable with those for other preparations of Botulinum toxin. [in bold in the SPC]

Comparative clinical study results suggest that Bocouture and the comparator product containing conventional botulinum toxin type A complex (900 kD) are of equal potency’. (emphasis added).

Allergan submitted that the statement above was based on an unpublished non-inferiority study. As had been well established in Case AUTH/2270/10/09, all that could be claimed from a non-inferiority study was that one product was no worse than another by the pre-specified margin in the study.

Allergan had requested the Merz data on file to support the grant of the licence on 22 July and received it on 27 July. This data was not available in the public domain. Allergan could only request it once promotional material citing it became available. In future, as previously stated, Allergan would ensure that any future scientific presentations reflected this unpublished non-inferiority data.

Allergan noted that recently available clinical data from Moers-Carpi (slides 25 and 26) was presented which demonstrated that in a clinical split-face comparison of Vistabel (12 units) and Xeomin (12 units), the two products were not equivalent. Therefore, these data were relevant to the clinical situation and their use in a non-promotional setting (as Allergan understood the context of the presentation to be) did not go against the ruling of Case AUTH/2183/11/08.

In conclusion, Allergan submitted that the presentation, with contextualised reference to Hunt et al did not constitute a breach of undertaking because:

The data presented was substantially different to the materials considered in Case AUTH/2183/11/08.

The presentation was balanced and scientifically accurate and evaluated all the reasonably available evidence at the time of preparation and presentation.

The presentation of Hunt et al was fully contextualised with comparative data (Dressler et al) and the pre-clinical findings had recently been confirmed in a clinical study (Moers-Carpi). The presentation was prepared in good faith, before the Bocouture SPC was publicly available. That said the presentation did not contradict the SPC which stated that unit doses recommended for Bocouture were not interchangeable with those for other botulinum toxins and only suggested the products were of equal potency, based on a non-inferiority study. Case AUTH/2270/10/09 had established that equivalence or equal potency could not be claimed from a non-inferiority study.

Finally, scientific debates by their nature involved different parties, typically with opposing views, stating their case in order that the audience could assess the balance of evidence and draw their own conclusions. Although these scientific debates presented pharmaceutical companies with significant challenges they remained of particular interest to clinicians attending such conferences. Allergan submitted that it was legitimate, in the context of a scientific debate, balanced not only with opposing data but also contextualised with recently available clinical data from Moers-Carpi, to present the two slides containing the Hunt data. Allergan denied that it had breached its undertaking and thus Clause 25 of the Code. It also denied breaches of Clauses 2 and 9.1.

FINAL COMMENTS BY MERZ

Merz stated that whilst Allergan might have sought approval by the FACE congress organiser for its presentation, Merz was sure that the organiser did not have the necessary Code expertise to determine the promotional or non-promotional nature of any activity undertaken by a pharmaceutical company. Merz would be disappointed to learn that Allergan had abdicated responsibility for this decision to the FACE organiser. Merz noted that Allergan had stated that it believed that its presentation was fair and balanced. Merz alleged that data from Hunt et al was presented that supposedly directly compared Xeomin with Botox. However, it did not include a very large data set showing non-inferiority of Xeomin to Botox in over 700 patients and did not mention the statement in section 4.2 of the Bocouture SPC that suggested equal potency of the two products.

Merz alleged that the slide which cited Hunt et al and Dressler et al (which was dismissed by the presenter and Allergan) and the subsequent slide of only the Hunt et al together with the presenter’s words left no doubt that the message was that Xeomin was less potent than Botox. The conclusion from this in vitro data was not supported by the large clinical trials that Allergan were aware of at the time of the presentation and therefore its presentation was not a fair and balanced representation of the available data.

Merz noted that promotional material had to be up-to-date and reflect the available data. Bocouture was granted a marketing authorization on 29 June and the Bocouture SPC was available when the presentation was delivered and therefore was of direct relevance to this case. Allergan’s suggestion that it did not know that Bocouture was being launched was difficult to believe as the Merz stand at the conference launched Bocouture and was erected by 8am; one stand separated the Merz stand from the Allergan stand. Materials available on the stand included a Bocouture leavepiece and SPC. The stand was visited by a number of Allergan employees in the morning of 2 July prior to the presentation in the afternoon. That the presenter was not aware of the imminent launch of Bocouture when he prepared the presentation was not relevant as it was licensed when the presentation was given. The Code required all material to be up-to-date. This presentation was not up-to-date when it was delivered.

Merz alleged that the fact that the source of the data behind the Bocouture SPC was not available to Allergan was not relevant as the wording of the SPC was available and represented the regulator’s view of the data and should have been represented.

Merz alleged that again Allergan mentioned the Moers-Carpi data which was a very small off-label study the conclusions of which were only partly reported by Allergan. The use of this data in this way was questioned by the Panel in this case as not representing of the totality of clinical data, which it did not, but was selected to support Hunt et al.

APPEAL BOARD RULING

The Appeal Board noted from slide 1 that the title of Allergan’s presentation was ‘Pharmacology, diffusion and potency of Botulinum Toxins’. Slide 1 also listed the various botulinum toxins available from the three manufacturers. Slide 3 of the presentation showed a number of vials of different sizes and was headed ‘Are they all the same?’. Beneath the picture of the vials was the second question

‘Are they non-interchangeable – Structure?Unit potency? Stability? Diffusion characteristics? Clinical performance?’. The last slide had the same heading and picture of vials below which was now the statement ‘They are non-interchangeable. Differences in: Structure, Unit potency, Stability, Diffusion characteristics, Clinical performance’.

The Appeal Board noted that Merz had drawn attention to slides 12 and 13 of the presentation. These were headed ‘Differences in LD50 assays’ and ‘Xeomin potency’. Slide 10 made it clear that the products were different ‘… and non-interchangeable potency units are specific’. Slide 11 was headed ‘Reasons for potency differences’ with the sub headings ‘Intrinsic differences in product characteristics’ and ‘Differences in LD50 assays’.

The Appeal Board noted that the presentation had included data from the small (n=12) Moers-Carpi study which was a split-face comparison of Vistabel and Xeomin in the forehead region of healthy volunteers. The results presented were those which showed a statistically significant advantage for Vistabel [Botox] vs Xeomin when brow position was assessed by digital photography. The results of the patients’ own evaluation of therapy, however, were not included; these showed no difference between the products.

The Appeal Board noted that the Bocouture [Xeomin] SPC stated in Section 4.2 that ‘Comparative clinical study results suggest that Bocouture and the comparator product containing conventional Botulinum toxin type A complex (900KD) [ie Botox] are of equal potency’. The Appeal Board noted that the relevant data was an unpublished non-inferiority study which Allergan had received from Merz on 27 July after the meeting in question.

The Appeal Board did not accept Allergan’s submission that the inclusion of the Dressler et al and Moers-Carpi studies meant that the presentation was substantially different to the materials (a product monograph and an objection handler) at issue in Case AUTH/2183/11/08.

Overall, the Appeal Board considered that the presentation had implied that Xeomin was less potent than Botox using, inter alia, the same data, ie Hunt et al, as that at issue in Case AUTH/2183/11/08. The Appeal Board considered that the presentation breached the undertaking given in that case and ruled a breach of Clause 25. In that regard high standards had not been maintained. A breach of Clause 9.1 was ruled. The appeal on both points was successful.

The Appeal Board noted that an undertaking was an important document. The Appeal Board considered that Allergan’s conduct was such as to bring discredit upon and reduce confidence in the pharmaceutical industry. The Appeal Board ruled a breach of Clause 2. The appeal on this point was successful.

The Appeal Board noted that Allergan had initially considered that the presentation was not promotional and had reviewed it in that context. That the presentation was non-promotional had been rejected by the Panel. The Appeal Board was concerned that Allergan’s initial view regarding the status of the presentation showed a lack of understanding although at the appeal hearing the company made it clear that it now accepted that the presentation was promotional.

Complaint received 21 July 2010

Case completed 6 December 2010