ALLERGAN/DIRECTOR v MERZ

Alleged breach of undertaking

Allergan complained about the promotion of Bocouture (botulinum toxin type A) by Merz Pharma UK at the FACE Conference and Exhibition, in June 2012. The materials at issue were the Merz exhibition stand and a leavepiece. As the complaint involved an alleged breach of undertaking, it was taken up by the Director without the need for prior inter-company dialogue, as it was the Authority's responsibility to ensure compliance with undertakings. Allergan supplied Botox (botulinum toxin type A).

The exhibition stand, headed 'Merz Aesthetics, Your partner in facial aesthetics', featured a photograph of a vial of Bocouture and a vial of Botox side-by-side. To the right of the photograph was the claim 'According to comparative clinical studies [Sattler *et al* 2010] Bocouture vs Botox: Comparable efficacy, 1:1 Clinical Conversion Ratio'. Below the photograph, in less prominent font, was the statement 'Unit doses recommended for Bocouture are not interchangeable with those for other preparations of botulinum toxin' which was referenced to the Bocouture summary of product characteristics (SPC), March 2012. Below a thick, blue horizontal line was reference to Bocouture's use in the temporary improvement of moderate to severe glabellar frown lines. The front cover of the leavepiece was similar to the exhibition stand.

Allergan alleged that the items at issue and overall campaign had clearly been designed to lead the prescriber to conclude that Bocouture and Botox were interchangeable in terms of potency units and that they delivered equivalent results in clinical practice.

Allergan considered that the visual was clearly designed to emphasise a direct 1:1 equivalence/conversion of the two products and the overall message taken away by a health professional was that Bocouture and Botox were equally potent and could be converted at a ratio of 1:1.

The current Bocouture summary of product characteristics (SPC) (updated on 6 March 2012) stated: 'Unit doses recommended for Bocouture are not interchangeable with those for other preparations of Botulinum toxin'. There was no reference to equal potency. The Xeomin 50U SPC still contained information regarding its non-inferiority studies (in Section 5.1, Pharmacodynamic properties) but this was in relation to patients with blepharospasm or cervical dystonia. Non-inferiority studies did not support claims of equivalence. The SPC for Botox 50, 100 and 200 units stated: 'Botulinum toxin units are not interchangeable from one product to another. Doses recommended in Allergan units are different from other botulinum toxin preparations'.

Allergan submitted that the promotion by Merz of this 1:1 clinical conversion ratio between Bocouture and Botox was of significant concern. No 'dosing conversion' occurred or should be implied from the non-inferiority study conducted by Merz (Sattler *et al*). The direct medical impact was that a significant patient safety risk existed with prescribers encouraged to transfer information from one label to another product.

Allergan noted the ruling in Case AUTH/2270/10/09 that the results of a non-inferiority study could not be used to claim equivalence. Merz's submission in that case was that it had no data to support a claim that Xeomin was equivalent to Botox. Allergan considered this was still so, Merz had not published any new clinical data that supported a claim of equivalence for either Xeomin or Bocouture. Therefore, Allergan alleged the visuals which implied equivalence/equipotency and the claim of a '1:1 Clinical Conversion Ratio' between Bocouture and Botox (ie equivalence) were a breach of the undertaking given in Case AUTH/2270/10/09.

The detailed response from Merz is given below.

The Panel noted that Case AUTH/2270/10/09 concerned a complaint from Allergan that Merz's claim that Xeomin was 'At least as effective as Botox with a similar safety profile' without appropriate context and qualification did not accurately reflect the available evidence and was misleading. Allergan had submitted that to claim 'At least as effective as', Merz needed further evidence to confirm equivalent efficacy and clinically relevant superiority. The claim at issue was referenced to two non-inferiority studies. The Panel had considered that there was a difference between showing non-inferiority and showing comparability and that the claim that Xeomin was 'At least as effective as Botox' did not reflect the available evidence. It implied possible superiority of Xeomin and was misleading as alleged and breaches of the Code were ruled. Following an appeal by Merz, the Appeal Board noted Merz's submission that it had no data upon which to claim that Xeomin was equivalent to Botox. The Appeal Board's view was that the claim 'At least as effective as' not only implied equivalence but also possible superiority which was misleading. The claim could not be substantiated by the available data and the Panel's rulings were upheld.

The Panel noted that there was still no data to show whether Bocouture/Xeomin was equivalent to Botox/Vistabel. As when the ruling in Case AUTH/2270/10/09 was made, there were still only non-inferiority studies which showed that the medicines were no worse than each other by a clinically acceptable pre-specified margin.

Turning to the present case, the Panel noted that the material now at issue was different to that at issue in Case AUTH/2270/10/09 where the comparison at issue had been between Xeomin and Botox; the comparison now at issue was between Bocouture and Botox. Bocouture and Xeomin, however, were the same product but with different indications.

The Panel did not agree with Allergan's position that the materials in question implied that Bocouture and Botox were equivalent in clinical practice. The Panel considered that the material at issue was very different to that at issue in Case AUTH/2270/10/09 which featured the claim, 'At least as effective as Botox with a similar safety profile'.

The Panel noted that, for the temporary improvement of moderate to severe glabellar frown lines, the initial dose for both Bocouture and Botox was 20U. Sattler *et al* compared the effect of 24 units of each medicine in the treatment of glabellar frown lines and showed that Bocouture was non-inferior to Botox. The materials now at issue featured the reasonably prominent claim 'Comparable efficacy' which in the opinion of the Panel meant that neither the bullet point that followed, '1:1 Clinical Conversion Ratio', nor the depiction of the adjacent vials implied equipotence or clinical equivalence as alleged. Given the common understanding of 'comparable' the Panel did not consider that the materials were caught by the undertaking given in Case AUTH/2270/10/09 which applied to claims of equivalence and possible superiority. The Panel thus ruled no breaches of the Code including Clause 2. These rulings were unsuccessfully appealed by Allergan.

Allergan Limited complained about the promotion of Bocouture (botulinum toxin type A) by Merz Pharma UK Ltd at the FACE Conference and Exhibition, in June 2012. The materials at issue were the Merz exhibition stand (ref 1149/MER/MAY/2012/JH) and a leavepiece (ref 1080/BOC/FEB/2012/JH) given to delegates. As the complaint involved an alleged breach of undertaking, it was taken up by the Director without the need for prior inter-company dialogue, as it was the Authority's responsibility to ensure compliance with undertakings. Allergan supplied Botox (botulinum toxin type A).

The exhibition stand, headed 'Merz Aesthetics, Your partner in facial aesthetics', featured a photograph of a vial of Bocouture and a vial of Botox side-by-side. To the right of the photograph was the claim 'According to comparative clinical studies [Sattler *et al* 2010] Bocouture vs Botox: Comparable efficacy, 1:1 Clinical Conversion Ratio'. Below the photograph, in small font, was the statement 'Unit doses recommended for Bocouture are not interchangeable with those for other preparations of botulinum toxin' which was referenced to the Bocouture summary of product characteristics (SPC), March 2012. Below a thick, blue horizontal line was reference to Bocouture's use in the temporary improvement of moderate to severe glabellar frown lines.

The front cover of the leavepiece had the same heading as the exhibition stand and similarly featured a photograph of a vial of Bocouture and a vial of Botox, side-by-side and the claim as stated above referenced to Sattler *et al*. Below the photograph was a thick blue horizontal line and beneath that was the statement as above referenced to the Bocouture SPC, February 2012 together with reference to Bocouture's use in the temporary improvement of moderate to severe glabellar frown lines.

COMPLAINT

Allergan alleged that the items at issue and overall campaign had clearly been designed to lead the prescriber to conclude that Bocouture and Botox were interchangeable in terms of potency units and that they delivered equivalent results in clinical practice.

Allergan noted that Merz had used the claim '1:1 Clinical Conversion Ratio' alongside a visual of a Bocouture and Botox vial standing side-by-side. The visual was clearly designed to emphasise a direct 1:1 equivalence/conversion of the two products. The claim 'According to comparative clinical studies' was included. Less prominently and in smaller font was the statement 'Unit doses recommended for Bocouture are not interchangeable with those for other preparations of Botulinum toxin' taken from the Bocouture SPC.

Allergan considered that the overall message taken away by a health professional was that Bocouture and Botox were equally potent and could be converted at a ratio of 1:1.

The current Bocouture SPC (updated on 6 March 2012) stated:

> 'Unit doses recommended for Bocouture are not interchangeable with those for other preparations of Botulinum toxin'.

Allergan stated that the UK Bocouture SPC (and that of Merz's product Xeomin 50U (botulinum toxin type A)) was changed following Allergan's communication to the Pharmacovigilance Working Party (PhVWP) highlighting the potential patient safety concerns with wording in the Bocouture 50U and Xeomin 50U SPCs. In the Bocouture SPC any reference to equal potency had been removed.

Allergan further stated that the statement regarding 1:1 dosing ratio in Section 4.2 of the Xeomin 50U SPC, Posology and method of administration, had been removed. The Xeomin 50U SPC still contained information regarding its non-inferiority studies (in Section 5.1, Pharmacodynamic properties) but this was in relation to patients with blepharospasm or cervical dystonia. As previously established, non-inferiority studies did not support claims of equivalence.

The SPC for Botox 50, 100 and 200 units stated:

> 'Botulinum toxin units are not interchangeable from one product to another. Doses recommended in Allergan units are different from other botulinum toxin preparations'.

Allergan submitted that the promotion by Merz of this 1:1 clinical conversion ratio between Bocouture and Botox was of significant concern. No 'dosing conversion' occurred or should be implied from the non-inferiority study conducted by Merz with its toxin (Sattler *et al*). The direct medical impact was that a significant patient safety risk existed with prescribers encouraged to transfer information from one label to another product.

Allergan noted that the PMCPA ruled in Case AUTH/2270/10/09 that the results of a non-inferiority study could not be used to claim equivalence. Merz's own submission in that case was that it had no data to support a claim that Xeomin was equivalent to Botox. Allergan considered this was still the case and Merz had not published any new clinical data that supported a claim of equivalence for either Xeomin or Bocouture. Therefore, Allergan considered the visuals which implied equivalence/equipotency and the claim of a '1:1 Clinical Conversion Ratio' between Bocouture and Botox (ie equivalence) were a breach of the undertaking given in Case AUTH/2270/10/09 and as such were in breach of Clause 25.

RESPONSE

Merz noted that in Case AUTH/2270/10/09 it was found in breach of the Code for claiming that Xeomin was 'At least as effective as Botox with a similar safety profile'. The Panel considered that the claim implied possible superiority of Xeomin vs Botox which was not supported by the available data. The breach was upheld upon appeal.

Merz submitted that Bocouture had been demonstrated to have similar efficacy and tolerability to Botox when used with a 1:1 dosing conversion ratio. The use of non-inferiority studies to make this point, (specifically that of similar efficacy at a fixed dosing ratio), had been reviewed by the Panel in Case AUTH/2357/9/10 regarding the promotion of Pradaxa. The Panel ruled that the claim '…efficacy and safety comparable to…' was substantiated by the non-inferiority studies referenced. This was taken to appeal and the Appeal Board further reinforced that comparable did not imply equivalence. Merz did not consider that the term used in the exhibition panel or leavepiece now at issue (ie comparable efficacy) was interchangeable with or implied equivalence which, as previously established, was not a general term but had a very specific meaning. As such Merz considered these claims were sufficiently different to the original case not to be considered a breach of Clause 25.

Furthermore Merz noted that in Case AUTH/2496/4/12, claims of 'Equipotent' or 'Equal Potency' were ruled on by the Panel in the context of Case AUTH/2270/10/09 and no breach of Clause 25 was found. The term, 'comparable' conferred even less likelihood of implied superiority than 'equipotent'.

Merz submitted that subsequent to these rulings, two articles about the use of toxins in clinical practice had been published recently in peer reviewed publications (Jandhyala 2012 and Prager *et al* 2012). Both studies compared the authors' up-to-date experiences of using Botox and Bocouture in a large number of patients. The authors' conclusions were consistent with the claims of comparable efficacy. Merz therefore considered that the items in question were also not in breach of Clauses 9.1 or 2.

Finally, Merz submitted that the material at issue had already been withdrawn following an internal review of promotional material based on the undertaking (signed 27 June 2012) to comply with the Panel's ruling in Case AUTH/2496/4/12.

PANEL RULING

The Panel noted that Case AUTH/2270/10/09, concerned a complaint from Allergan that the claim by Merz that Xeomin was 'At least as effective as Botox with a similar safety profile' without appropriate context and qualification did not accurately reflect the available evidence and was misleading. Allergan had submitted that to make the claim 'At least as effective as', Merz needed further evidence to confirm equivalent efficacy and clinically relevant superiority. The claim at issue was referenced to Benecke *et al* (2005) and Roggenkamper *et al* (2006) both of which were non-inferiority studies. The Panel had considered that there was a difference between showing non-inferiority and showing comparability and that the claim that Xeomin was 'At least as effective as Botox' did not reflect the available evidence. It implied possible superiority of Xeomin and was misleading as alleged and breaches of the Code were ruled. Following an appeal by Merz, the Appeal Board noted Merz's submission that it had no data upon which to claim that Xeomin was equivalent to Botox. The Appeal Board stated that in its view, the claim 'At least as effective as' not only implied equivalence but also possible superiority which was misleading. The Appeal Board did not consider that the claim could be substantiated by the available data and the Panel's rulings were upheld.

The Panel noted that there was still no data to show whether Bocouture/Xeomin was equivalent to Botox/Vistabel. As when the ruling in Case AUTH/2270/10/09 was made, there were still only non-inferiority studies which showed that the medicines were no worse than each other by a clinically acceptable pre-specified margin.

Turning to the present case, the Panel noted that the material now at issue was different to that at issue in Case AUTH/2270/10/09. In Case AUTH/2270/10/09 the comparison at issue had been between Xeomin and Botox; the comparison now at issue was between Bocouture and Botox. Bocouture and Xeomin, however, were the same product but with different indications – Bocouture was indicated for the temporary improvement in the appearance of glabellar frown lines whilst Xeomin was for the symptomatic treatment of blepharospasm, cervical dystonia and post-stroke spasticity of the upper limb.

The Panel did not agree with Allergan's position that the materials in question implied that Bocouture and

Botox were equivalent in clinical practice. The Panel considered that the material at issue was very different to that at issue in Case AUTH/2270/10/09 which featured the claim, 'At least as effective as Botox with a similar safety profile'.

The Panel noted that, for the temporary improvement of moderate to severe glabellar frown lines, the initial dose for both Bocouture and Botox was 20U. Sattler *et al* compared the effect of 24 units of each medicine in the treatment of glabellar frown lines and showed that Bocouture was non-inferior to Botox. The materials now at issue featured the reasonably prominent claim 'Comparable efficacy' which in the opinion of the Panel meant that neither the bullet point that followed, '1:1 Clinical Conversion Ratio', nor the depiction of the adjacent vials implied equipotence or clinical equivalence as alleged. Given the common understanding of 'comparable' the Panel did not consider that the materials were caught by the undertaking given in Case AUTH/2270/10/09 which applied to claims of equivalence and possible superiority. The Panel thus ruled no breach of Clause 25. The Panel consequently ruled no breach of Clauses 9.1 and 2.

APPEAL BY ALLERGAN

Allergan appealed the Panel's ruling of no breach of Clause 25. It noted that Merz had used the claim '1:1 Clinical Conversion Ratio' alongside a visual of a Bocouture and Botox vial standing side-by-side which it considered clearly emphasised a direct 1:1 equivalence/conversion of the two products. The phrase 'According to comparative clinical studies' was included, as well as the statement 'Comparable efficacy'. Less prominently and in smaller font was the SPC statement 'Unit doses recommended for Bocouture are not interchangeable with those for other preparations of botulinum toxin'.

Allergan alleged that the take away message would be that the products were equivalent, interchangeable and could be converted 1:1.

The current SPC for Bocouture (which was updated on 6 March 2012) stated:

> **'Unit doses recommended for Bocouture are not interchangeable with those for other preparations of Botulinum toxin'.**

Allergan stated that changes to the UK Bocouture and Xeomin 50U SPCs were approved after Allergan had highlighted to the PhVWP the potential patient safety concerns with the previous wording. Any reference to 'equal potency' had been removed from the Bocouture SPC.

Allergan further stated that in Section 4.2 of the Xeomin 50U SPC the statement regarding 1:1 dosing ratio had been removed; Section 5.1 still contained information regarding its non-inferiority studies but this was in relation to patients with blepharospasm or cervical dystonia. As previously established, non-inferiority studies did not support claims of equivalence.

The SPCs for Botox 50, 100 and 200 units stated:

> **'Botulinum toxin units are <u>not interchangeable from one product to another</u>. Doses recommended in Allergan units are different from other botulinum toxin preparations'.**

Allergan alleged that the promotion of a '1:1 Clinical Conversion Ratio' between Bocouture and Botox was a source of significant concern. No 'dosing conversion' occurred or should be implied from the non-inferiority study conducted by Merz with its toxin (Sattler *et al*). The direct medical impact was that a significant patient safety risk existed with prescribers encouraged to transfer information from one label to another product.

Allergan noted that the PMCPA ruled in Case AUTH/2270/10/09 that the results of a non-inferiority study could not be used to claim equivalence. Merz's submission in that case was that it had no data to support a claim that Xeomin was equivalent to Botox. As acknowledged by Merz in Case AUTH/2496/4/12, this was still the case and Merz had not published any new clinical data that supported a claim of equivalence for Bocouture (or Xeomin). Therefore, Allergan alleged that any claim which implied clinical equivalence and interchangeability must be in breach of the undertaking made in Case AUTH/2270/10/09.

Allergan alleged that the overall impression given by the materials at issue was sufficiently similar with regard to a claim for 'equivalence' to be covered by the undertaking given in Case AUTH/2270/10/09. The insertion of the 'reasonably prominent' claim 'Comparable efficacy' did not negate the overall impression given by the visual and the accompanying claim of a 1:1 clinical conversion ratio.

Allergan alleged that Merz clearly intended to convey a message of equivalence and interchangeability even though it had been clearly established that there was no new data to support this message and the updates to the Bocouture and Xeomin SPCs in March 2012. As stated by the Appeal Board in Case AUTH/2496/4/12, implying the products were clinically equivalent and hence interchangeable was contrary to statements in the SPCs and raised possible patient safety concerns.

Allergan alleged that the two recent articles cited by Merz in its response did not support a claim of clinical equivalence, as already acknowledge by Merz. Jandhyala was discussed in Case AUTH/2496/4/12; this mixed treatment comparisons meta-analysis included only one head-to-head study (Sattler *et al*).

Allergan noted that Prager *et al* was a retrospective analysis of daily practice in treatment of the upper face. 1256 patient charts were reviewed demonstrating use of the Merz toxin (88%), the Allergan toxin (10.4%) and Ipsen toxin (1.6%) in the treatment of the glabellar frown lines (48.3%), lateral periorbital wrinkles (27.4%) and/or horizontal

forehead lines (24.4%). Overall, no statistically significant differences between the Merz and Allergan products were found for any of the parameters measured. A validated patient satisfaction scale had not been used in this study, instead a yes/no assessment captured patient satisfaction. In the analysis, the data were actually pooled and analyzed as a whole under the term 'upper face'. No data was provided to show the doses administered to each region. It was inappropriate to draw conclusions on clinical efficacy when there had only been data gathered on patient satisfaction and time to re-injection.

In conclusion, Allergan submitted that the overall impression given by the materials at issue was sufficiently similar with regard to a claim for 'equivalence' to be covered by the undertaking given in Case AUTH/2270/10/09. The insertion of the 'reasonably prominent' claim 'Comparable efficacy' did not negate the overall impression given by the visual and the accompanying claim of a 1:1 clinical conversion ratio.

Allergan noted that the PMCPA had ruled in Case AUTH/2270/10/09 that the results of a non-inferiority study could not be used to claim equivalence. Merz's own submission in that case, in Case AUTH/2496/4/12 and confirmed in Case AUTH/2516/6/12, was that it had no data to support a claim that Xeomin/Bocouture was equivalent to Botox. This was still the case and Merz had not published any new clinical data that supported a claim of equivalence.

Therefore, Allergan alleged that the visuals which implied equivalence/equipotency and the claim of a '1:1 Clinical Conversion' between Bocouture and Botox (ie equivalence) breached the undertaking given in Case AUTH/2270/10/09 and were thus in breach of Clause 25.

COMMENTS FROM MERZ

Merz noted that in Case AUTH/2270/10/09 Allergan had complained about the use of the claim 'At least as effective as Botox with a similar safety profile'. The Panel had ruled that this was misleading since it implied 'possible superiority' of Xeomin vs Botox which was not supported by the available data at the time. The breach was upheld upon appeal.

Merz submitted that its consistent interpretation of the undertaking given in Case AUTH/2270/10/09 was aligned to that of the Panel, ie that it sought to ensure that there was no implied superiority in promotional campaigns and accordingly all materials were developed with this in mind. Merz took undertakings seriously and its consistent intent was to comply with this. When the Medicines and Healthcare products Regulatory Agency (MHRA) approved Bocouture (June 2010) with an SPC which stated 'equal potency' there was still no implied superiority in any Merz promotional materials. Despite very consistent promotional campaigns for Bocouture there was no challenge from the date of publication of Case AUTH/2270/10/09 (January 2010) until the complaint now in hand (15 June 2012). This therefore suggested that the interpretation of this undertaking was consistently shared not only by Merz and the Panel but also by Allergan.

Turning to the case now at issue (Case AUTH/2515/6/12) the Panel's summary was clear: 'Given the common understanding of 'comparable' the Panel did not consider that the materials were caught by the undertaking … which applied to claims of equivalence and possible superiority'.

Merz noted that the interpretation of the Case AUTH/2270/10/09 undertaking by it, the Panel (and arguably Allergan) had been recently broadened (after more than two years) in Case AUTH/2496/4/12. The Panel originally ruled no breach of the Code with regard to an alleged breach of undertaking in Case AUTH/2270/10/09 which related to comparisons between Bocouture/Xeomin and Botox/Vistabel, concluding that since there was no implied superiority it could not constitute a breach of undertaking. The ruling was appealed and the Appeal Board (July 2012) overturned the Panel ruling, stating that 'although the claim at issue was not the same as that in Case AUTH/2270/10/09, it was sufficiently similar with regard to a claim for "equivalence" for it to be covered by the undertaking previously given.' This new interpretation and the timing of it was important in the current case.

As a result of this new interpretation Merz was found in breach of Clause 2. The Code was clear that Clause 2 was a sign of particular censure and was reserved for such circumstances. Examples included (but were not limited to) '… prejudicing patient safety and/or public health, excessive hospitality, inducements to prescribe, inadequate action leading to a breach of undertaking, promotion prior to the grant of a marketing authorization, conduct of company employees/agents that falls short of competent care and multiple/cumulative breaches of a similar and serious nature in the same therapeutic area within a short period of time'. Whilst this list was not exhaustive it did not capture any activity under review in the current case. Once the original undertaking was signed all future promotional materials were carefully developed to avoid the original interpretation of implied superiority, (ie adequate action was taken) and therefore the absolute intent of Merz was to faithfully comply with the undertaking.

Merz supported the Panel's ruling that the claim 'at least as effective as' which implied superiority was significantly different from the claims at issue which related to 'comparable efficacy'. As such this was not a breach of undertaking. Since the materials in question pre-dated the findings of Case AUTH/2496/4/12 Merz could not have knowingly breached the undertaking and therefore could not be considered to have breached Clause 9.1. Nor could this intent to faithfully comply with the undertaking be considered to bring discredit upon the pharmaceutical industry.

FINAL COMMENTS FROM ALLERGAN

Allergan noted the Panel's ruling in Case AUTH/2270/10/09 that the results of a non-inferiority study could not be used to claim equivalence. Merz's own submission in that case was that it had no data to support a claim that Xeomin was equivalent to Botox. As acknowledged by Merz in Case AUTH/2496/4/12, this was still the case and Merz had not published any new clinical data that supported a claim of equivalence for Bocouture (or Xeomin).

The ruling in Case AUTH/2270/10/09 by the Panel and then by the Appeal Board was not only in relation to an implied claim of 'superiority' as Merz continued to believe but also in relation to 'comparability' and 'equivalence'. The summary of the case made the ruling very clear as follows: 'The Panel considered that there was a difference between showing non-inferiority to showing comparability. The Panel considered on the basis of the data the claim that Xeomin was "At least as effective as Botox" did not reflect the available evidence. It implied possible superiority of Xeomin as alleged and was misleading. Breaches of the Code were ruled'. Upon appeal by Merz the Appeal Board noted that both parties agreed that Benecke *et al* and Roggenkamper *et al* were non-inferiority studies that showed that Xeomin was no worse than Botox by a pre-specified margin (delta) that was clinically acceptable. The Appeal Board noted Merz's submission that it had no data upon which to make the claim that Xeomin was equivalent to Botox. In the Appeal Board's view the claim 'At least as effective' not only implied equivalence but also possible superiority which was misleading. The Appeal Board did not consider that the claim could be substantiated by the available data. The Appeal Board upheld the Panel's ruling of breaches of the Code.

Therefore, Allergan submitted that any claim which implied clinical equivalence and interchangeability must breach the undertaking given in Case AUTH/2270/10/09.

Allergan submitted that the overall impression given by the materials at issue was sufficiently similar with regard to a claim for 'equivalence' to be covered by the undertaking given in Case AUTH/2270/10/09. The insertion of the 'reasonably prominent' claim 'Comparable efficacy' did not negate the overall impression given by the visual and the accompanying claim of a 1:1 clinical conversion ratio.

Allergan disagreed with Merz's view that the insertion of the words 'Comparable efficacy' constituted 'adequate action' to comply with the undertaking given in Case AUTH/2270/10/09 and in that regard Allergan referred to the above summary of that case where a clear distinction between non-inferiority and comparability was highlighted.

Allergan submitted that Merz clearly intended to convey a message of equivalence and interchangeability despite the fact that it had been clearly established there was no new data to support this message and despite the updates to the Bocouture and Xeomin SPCs in March 2012. As stated by the Appeal Board in Case AUTH/2496/4/12, implying the products were clinically equivalent and hence interchangeable was contrary to statements in the SPCs and raised possible patient safety concerns.

In Case AUTH/2270/10/09 the Panel ruled that the results of a non-inferiority study could not be used to claim equivalence. Merz's own submission in that case, in Case AUTH/2496/4/12 and confirmed in Case AUTH/2516/6/12, was that it had no data to support a claim that Xeomin/Bocouture was equivalent to Botox. This was still the case and Merz had not published any new clinical data that supported a claim of equivalence.

Allergan thus submitted that the visuals which implied equivalence/equipotency and the claim of a '1:1 Clinical Conversion' between Bocouture and Botox, (ie equivalence) breached the undertaking given in Case AUTH/2270/10/09 and as such were in breach of Clause 25 and consequently Clauses 9.1 and 2.

APPEAL BOARD RULING

The Appeal Board noted its ruling in Case AUTH/2270/10/09 which stated that:

> 'The Appeal Board noted Merz's submission at the appeal that it had no data upon which to make the claim that Xeomin [Bocouture] was equivalent to Botox. In the Appeal Board's view the claim 'At least as effective as' not only implied equivalence but also possible superiority which was misleading. The Appeal Board did not consider that the claim could be substantiated by the available data. The Appeal Board upheld the Panel's ruling of breaches of Clauses 7.2 and 7.3.'

The Appeal Board noted that the undertaking in that case related to claims of implied equivalence and/or superiority. The Appeal Board considered that in the case now in question, Case AUTH/2515/6/12, there was clearly no claim for implied superiority of Bocouture vs Botox. The issue to be considered was, did the material overall suggest that the two medicines were equivalent?

The Appeal Board noted that the material, which was used at an aesthetics meeting, featured the image of a vial of Bocouture and Botox side-by-side together with the claims 'Comparable efficacy' and '1:1 Clinical Conversion Ratio'. The Appeal Board noted that the study cited in support of the claims was Sattler *et al* which showed that in the treatment of glabellar lines, 24 units of each medicine produced comparable clinical results; the response rates supported the non-inferiority of Bocouture to Botox.

In the Appeal Board's view 'Comparable efficacy' did not imply equivalence. Overall the Appeal Board considered that the material at issue was sufficiently

different to that at issue in Case AUTH/2270/10/09 for it not to be covered by the undertaking given in that case. The Appeal Board upheld the Panel's ruling of no breach of Clause 25, and consequently the rulings of no breach of Clause 2 and 9.1. The appeal was thus unsuccessful.

Complaint received	**15 June 2012**
Case completed	**11 October 2012**