MERZ/DIRECTOR v ALLERGAN

Breaches of undertaking

Merz alleged that, by again making disparaging, misleading and unbalanced claims about the comparative potency/clinical efficacy of its own products Vistabel/Botox (onabotulinumtoxinA) vs that of Bocouture/Xeomin (incobotulinumtoxinA), Allergan had breached undertakings given in previous cases. Merz marketed Bocouture/Xeomin.

The matters were taken up with the Director acting as the complainant as the PMCPA was responsible for ensuring compliance with undertakings.

Merz submitted that the claims at issue were consistent with previous breaches of undertaking, most recently Case AUTH/2460/11/11 together with Cases AUTH/2183/11/08 and AUTH/2346/8/10. These cases clearly demonstrated a flagrant disregard for the Code and associated sanctions. Merz alleged that Allergan's actions in Cases AUTH/2487/3/12 and AUTH/2489/3/12 were covered by the same undertakings as in the previous cases.

In Case AUTH/2487/3/12 the material at issue was an article in Cosmetic News, March 2012. The article 'Dosages for botulinum toxins are not interchangeable says study' was written as if it were an Allergan press release. At issue in Case AUTH/2489/3/12 was a substantially similar article in the International Journal of Aesthetic and Anti-Ageing Medicine (PRIME), a UK-based publication, March 2012, entitled 'BTX-A [botulinum toxin A] Dosing Not Interchangeable'.

The articles summarised Moers-Carpi *et al* (2011), (a poster presented at a European meeting in September 2011) that was the subject of the breach of undertaking in Case AUTH/2460/11/11. This was a non-peer reviewed poster authored by two Allergan employees and a third author. The articles made claims about the potency of Vistabel compared with Bocouture – a comparison which had been the subject of Cases AUTH/2460/11/11 and AUTH/2346/8/10 – with the intention of implying that Bocouture was less potent than Vistabel.

Merz considered that the design of Moers-Carpi *et al* was open to significant question; there was no control arm and unmatched doses of each product were used (20 units of Vistabel, 30 units of Bocouture) making potency comparison difficult. In Case AUTH/2460/11/11 the Panel concluded that the use of Moers-Carpi *et al* data alone did not reflect the balance of evidence and Merz alleged that this was also the case with the two articles in question. The data had not been used in the context of the summaries of product characteristics (SPCs) recommendations for either product of the same starting dose of 20U. Additionally the data was not contextualised, there was no reference to the regulatory approved study data (Sattler *et al* 2010) which demonstrated non-inferiority between the two medicines at a 1:1 dosing conversion ratio.

Merz noted that the articles also did not refer to Carruthers *et al* (2005) which compared Botox in eighty females with moderate to severe glabellar frown lines at the doses of 10U, 20U, 30U and 40U. The study demonstrated that Botox showed no measurable clinical difference between 20U and 30U; the authors concluded that there 'were no statistically significant differences among the three higher-dose groups'. It was postulated that in most patients 20U was sufficient to saturate the local nerve endings so that additional dosing had little or no incremental clinical effect.

In summary Merz noted that Allergan had been ruled in breach for suggesting that Xeomin (the same pharmaceutical product as Bocouture) was less potent than Botox (the same pharmaceutical product as Vistabel) in Case AUTH/2183/11/08. Following this Allergan gave an undertaking not to use this or similar claims. This undertaking was breached twice in Cases AUTH/2335/7/10 and AUTH/2346/8/10 and Allergan gave yet another undertaking. In Case AUTH/2460/11/11 Allergan was again ruled in breach of an undertaking relating to product potency claims in relation to Bocouture. Within only one month of the outcome of Case AUTH/2460/11/11, Allergan had briefed a third party to promote the same unbalanced data that it was not able to promote directly.

Merz was concerned that Allergan was relentless in its pursuit of the message that the Bocouture and Xeomin units were less potent than the Vistabel and Botox units against all the clinical evidence and the view of the Medicines and Healthcare products Regulatory Agency (MHRA) and the wider European regulators. Furthermore, Merz had been able to comment on an article in the March issue of Cosmetic News up until 23 February which was some time after the ruling for Case AUTH/2460/11/11.

The detailed response from Allergan is given below.

The Panel noted that Allergan had been notified of the outcome of Case AUTH/2460/11/11 on 26 January 2012, four days before it sent a press release about the Moers-Carpi *et al* (2011) data to Cosmetic News and PRIME; the subsequent articles were published in the March edition of the journals. In Case AUTH/2460/11/11, Allergan was again ruled to have breached undertakings with regard to claims about the relative potency of its botulinum toxin vs that of the Merz product. One of the matters at issue was about the emphasis given to the Moers-Carpi *et al* results in the relative absence of other data. Allergan accepted the rulings and signed the relevant undertaking on 3 February 2012; there was no reference in the undertaking to any other material already in press. The Panel noted the submission from Merz that it had been given up until 23 February to comment on an article

which was to be published in the March editions of Cosmetic News and PRIME. Allergan submitted that after it had sent the press release on 30 January, it had not had any further contact with the journals or been offered the chance to comment on the articles. The Panel noted that Allergan's PR agency had provided the press release following its contact with the editor of Cosmetic News and PRIME (30 January) in the period when Allergan, having received the notification of the Panel's rulings of breaches in Case AUTH/2460/11/11 (26 January) and report to the Code of Practice Appeal Board, would be deciding whether to accept or appeal those rulings (due 3 February). The Panel also noted that the press release was examined and signed on 25 January which was whilst Allergan was awaiting the outcome of Case AUTH/2460/11/11.

The Panel noted that complaints about articles in the press were judged on the information provided by the pharmaceutical company or its agent to the publisher/journalist and not on the content of the article itself. The articles at issue reproduced large sections of Allergan's press release. The press release was headed 'New study provides further evidence that dosing for botulinum toxins are not interchangeable'; the sub-heading read 'Head to head study launched at international aesthetics congress further reinforces need for awareness of the different doses for two botulinum toxin type A products'. The press release ended with a quotation from one of the authors of Moers-Carpi *et al*, an Allergan employee; 'We are pleased to see further evidence for the efficacy of Vistabel and consider that this study provides further clarity that Vistabel and the Merz unit doses are not interchangeable in clinical practice'.

The Panel noted that in Case AUTH/2460/11/11 both parties had submitted more information than above. The Panel thus noted elements of its rulings in that case.

In addition it noted that in Case AUTH/2346/8/10 Allergan had been ruled in breach of its undertaking given in Case AUTH/2183/11/08 in that an impression was given that Botox was more potent than Xeomin and this was inconsistent with the SPCs and available clinical data. Breaches of the Code including Clause 2 were ruled.

Turning to the cases now at issue, Cases AUTH/2487/3/12 and AUTH/2489/3/12, the Panel noted that the press release in question (Date of preparation Dec 2011) was itself undated. It had been examined by Allergan on 25 January 2012 according to the certificate. The press release was only about the Moers-Carpi *et al* data. The results of that study had not been set within the context of the recommended doses for Vistabel and Bocouture according to their SPCs, the statement in the Bocouture SPC that comparative clinical study results suggested that Bocouture and the comparator product containing conventional botulinum toxin type A complex (900kD) [Botox/ Vistabel] were of equal potency and the clinical results of Sattler *et al* which showed that 24 units of Bocouture/Xeomin was non-inferior to 24 units of Botox/Vistabel in the treatment of glabellar lines.

The Panel did not consider that the discussion of Moers-Carpi *et al*, in isolation, in the press release represented the balance of the evidence with regard to the relative efficacy of Vistabel and Bocouture. In the Panel's view, the press release implied that in order to achieve the same clinical outcome in the treatment of glabellar lines, 20 units of Vistabel was needed vs 30 units of Bocouture, ie unit for unit, Bocouture was less potent than Vistabel. In that regard the Panel considered that the press release was sufficiently similar to the point at issue in Cases AUTH/2346/8/10 and AUTH/2460/11/11 for it to be covered by the undertaking in Case AUTH/2346/8/10. Thus the press release now at issue breached an undertaking previously given. A breach of the Code was ruled in each case. These rulings were appealed by Allergan.

The Panel noted that an undertaking was an important document and that Allergan's successive breaches of undertaking were such as to bring discredit upon and reduce confidence in the pharmaceutical industry. The Panel ruled a breach of Clause 2 which was appealed by Allergan.

The Panel was concerned that Allergan stated that it had reviewed the press release in relation to the outcome of Cases AUTH/2335/7/10 and AUTH/2346/8/10 and that the press release had been sent out when Allergan would be considering whether to appeal yet another breach of undertaking ruled by the Panel in Case AUTH/2460/11/11. Given the seriousness of the situation, the Panel considered that Allergan should have taken urgent action and considered not using the press release until it had decided whether to appeal Case AUTH/2460/11/11, particularly as the form of undertaking required withdrawal of any similar material. Allergan could have contacted the editor of both journals following its provision of the undertaking in Case AUTH/2460/11/11. However, the Panel noted that the press release was used on 30 January and that the undertaking was dated 3 February. Thus Allergan had not breached its undertaking in Case AUTH/2460/11/11 and no breach of the Code was ruled in each case. These rulings were not appealed.

Notwithstanding the fact that in Case AUTH/2460/11/11 Allergan had been reported to the Code of Practice Appeal Board, the Panel once again decided firstly in Case AUTH/2487/3/12 and subsequently in Case AUTH/2489/3/12 to report the company to the Appeal Board in accordance with Paragraph 8.2 of the Constitution and Procedure. The continued breaches of undertaking raised serious questions about the company's procedures and commitment to complying with the Code. The Panel noted that in Case AUTH/2460/11/11 the Appeal Board had required an audit of Allergan's procedures in relation to the Code to be carried out by the Authority and had also decided that the company should be publicly reprimanded for successive breaches of its undertakings.

In considering the appeals the Appeal Board noted that Moers-Carpi *et al* demonstrated in a head-to-head comparison that 20 units of Vistabel was as effective as 30 units of Bocouture in the treatment of glabellar lines. The Appeal Board noted, however,

that the recommended starting dose for both products according to their SPCs was 20 units and it thus queried the choice of doses. The Appeal Board noted Allergan's submission on this point. Moers-Carpi *et al* did not examine the efficacy of the starting dose of Bocouture and whether this dose would have achieved the same clinical result as 30 units. In that regard the Appeal Board noted that once muscle saturation had occurred, any increase in dose would not produce any increase in effect.

The Appeal Board considered that the press release at issue gave an accurate account of Moers-Carpi *et al*. Given that both study medicines were botulinum toxins, the Appeal Board considered that many clinicians would assume that the difference in dosing to achieve a similar therapeutic effect meant that Vistabel (20 units) was more potent than Bocouture (30 units). In that regard the Appeal Board noted the following quotation from the press release: 'We are pleased to see further evidence for the efficacy of Vistabel and consider that this study provides further clarity that Vistabel and the Merz unit doses are not interchangeable in clinical practice'.

The Appeal Board noted that the press release did not refer to the relative potency of Vistabel and Bocouture but nonetheless, in its view, the inevitable implication was that Bocouture, unit for unit, was less potent than Vistabel. In the Appeal Board's view, in this particular context, ie a direct comparison of two botulinum toxins dosed in units, clinicians might well take efficacy and potency to mean one and the same. The discussion of Moers-Carpi *et al* in isolation in the press release did not represent the balance of the evidence with regard to the relative efficacy of Vistabel and Bocouture. Given the implied claim that Bocouture was less potent than Vistabel, the Appeal Board considered that the press release was sufficiently similar to the point at issue in Cases AUTH/2346/8/10 and AUTH/2460/11/11 for it to be covered by the undertaking in Case AUTH/2346/8/10. Thus the press release now at issue breached a previous undertaking. The Appeal Board upheld the Panel's rulings. The Appeal Board further considered that Allergan's successive breaches of undertaking was such as to bring discredit upon and reduce confidence in the pharmaceutical industry. The Appeal Board upheld the Panel's rulings of breaches of Clause 2. The appeals were unsuccessful.

The Appeal Board noted that it was important for the reputation of the pharmaceutical industry that companies understood the importance of their undertakings and took the necessary action to comply with them. The Appeal Board questioned Allergan's conduct and attitude in this regard and decided that the company should be publicly reprimanded for its successive failures to comply with its undertakings. These two cases taken together represented the fourth breach of undertaking. Allergan's conduct was completely unacceptable. The Appeal Board also decided, in accordance with Paragraph 11.3 of the Constitution and Procedure, to require an audit of Allergan's procedures in relation to the Code to be carried out by the Authority. The audit should be conducted at the same time as the re-audit required in Case AUTH/2460/11/11 which was scheduled to take place in August 2012. On receipt of the audit report the Appeal Board would consider whether further sanctions were necessary including pre-vetting of promotional material.

On receipt of the August 2012 audit report the Appeal Board was disappointed at the lack of progress demonstrated. However the company appeared to have taken action including setting time frames for the bulk of the processes and work to be completed by the end of 2012. The Appeal Board was concerned that the amendments to some of the standard operating procedures (SOPs) had not been finalized. The Appeal Board noted that there were plans to significantly change the company structure and the interim country manager would be replaced in 2013. A UK medical director was due to be appointed. The Appeal Board considered that Allergan should be re-audited in January 2013 at which point it expected there to be significant improvement.

Upon receipt of the January 2013 audit report, the Appeal Board noted that although Allergan had made progress, further improvement was necessary. The Appeal Board noted that one key change in senior personnel would take place shortly and another in due course. Given that further improvement was required, the Appeal Board considered that Allergan should be re-audited in September 2013. Upon receipt of the next audit report, the Appeal Board would decide whether further sanctions were necessary.

Upon receipt of the September audit report, the Appeal Board noted that Allergan had made progress since the re-audit in January. The company had undergone four audits since April 2012. It was important that the progress shown in the September 2013 audit was continued and maintained. Every opportunity should be taken for improvement. The Appeal Board noted that Allergan needed to ensure that it updated its processes in good time to reflect the 2014 Code and that relevant staff were trained on the new Code. Allergan provided details of its plans to implement the recommendations in the audit report. On the basis that this work was completed, the Appeal Board decided that no further action was required.

Merz Pharma UK Ltd alleged that Allergan UK Limited had breached undertakings given in previous cases in relation to the promotion of Vistabel/Botox (onabotulinumtoxinA). Merz marketed Bocouture/Xeomin (incobotulinumtoxinA).

The matters were taken up with the Director acting as the complainant as the PMCPA was responsible for ensuring compliance with undertakings.

COMPLAINT

Merz stated that again Allergan had made disparaging, misleading and unbalanced claims about the comparative potency/clinical efficacy of Bocouture/Xeomin and Vistabel/Botox.

The claims at issue were consistent with previous breaches of undertaking, most recently

Case AUTH/2460/11/11 together with Cases AUTH/2183/11/08 and AUTH/2346/8/10. These cases clearly demonstrated a pattern of behaviour by Allergan that showed a flagrant disregard for the Code and associated sanctions. Merz considered that Allergan's actions in this case were covered by the same undertakings as in the previous cases. A breach of Clause 25 was alleged.

The material at issue in Case AUTH/2487/3/12 was an article in Cosmetic News, March 2012. The article 'Dosages for botulinum toxins are not interchangeable says study' was written as if it were an Allergan press release. Its tone and style together with the direct quotations from Allergan employees clearly inferred that this was a promotional statement provided by Allergan. It therefore fell under Clause 1.2 as an 'activity undertaken by a pharmaceutical company or with its authority'.

The material at issue in Case AUTH/2489/3/12 was an article in the International Journal of Aesthetic and Anti-Ageing Medicine (PRIME) March 2012. Merz submitted that as this was a UK-based publication with many of its readers in the UK, it was covered by the Code. The article entitled 'BTX-A Dosing Not Interchangeable' was written as if it were an Allergan press release (and was substantially similar to what Merz considered was another breach of undertaking (Case AUTH/2487/3/12) in the March 2012 edition of Cosmetic News). Merz stated that the tone and style of the article together with the direct quotations from Allergan employees clearly inferred that this was a promotional statement provided by Allergan. It therefore fell under Clause 1.2 as an 'activity undertaken by a pharmaceutical company or with its authority'.

Merz noted that the articles summarised Moers-Carpi *et al* (2011) (a poster presented at the 7th European Masters in Anti-Aging Medicine (EMAA), September 2011) that was the subject of the breach of undertaking in Case AUTH/2460/11/11. This was a non-peer reviewed poster authored by two Allergan employees together with a third author. The articles made claims about the potency of Vistabel compared with Bocouture – a comparison which had been the subject of Cases AUTH/2460/11/11 and AUTH/2346/8/10 – building the case with the intention of implying that Bocouture was less potent than Vistabel.

Merz considered that the design of this study was open to significant question as there was no control arm and unmatched doses of each product were used, making potency comparison difficult. In Case AUTH/2460/11/11 the Panel concluded that the use of Moers-Carpi *et al* data alone did not reflect the balance of evidence and Merz alleged that this was also the case with the Cosmetic News and PRIME articles in question. The data had not been used in the context of the summaries of product characteristics (SPCs) recommendations for either product of the same starting dose of 20U. Additionally the data was not contextualised, there was no reference to the regulatory approved study data (Sattler *et al* 2010) which demonstrated non-inferiority between the two medicines at a 1:1 dosing conversion ratio.

Merz noted that the articles in Cosmetic News and PRIME did not refer to the established position by Carruthers *et al* (2005) which compared four doses of Botox in eighty females with moderate to severe glabellar frown lines at the doses of 10U, 20U, 30U and 40U. The study demonstrated that Botox showed no measurable clinical difference between 20U and 30U; the authors concluded that there 'were no statistically significant differences among the three higher-dose groups'. It was postulated that in most patients 20U was sufficient to saturate the local nerve endings so that additional dosing had little or no incremental clinical effect.

Merz alleged that the crafting of both articles, the selective use of data and what could only be a deliberate omission of the clearly established regulatory position to imply reduced potency/ effectiveness of Bocouture compared with Vistabel was both cynical and clearly in breach of previous multiple undertakings made by Allergan.

In summary Merz noted that Allergan had been ruled in breach for suggesting that Xeomin (the same pharmaceutical product as Bocouture) was less potent than Botox (the same pharmaceutical product as Vistabel) in Case AUTH/2183/11/08. Following this Allergan gave an undertaking not to use this or similar claims. This undertaking was breached twice in Cases AUTH/2335/7/10 and AUTH/2346/8/10 and Allergan gave yet another undertaking. In Case AUTH/2460/11/11 Allergan was again ruled in breach of an undertaking relating to product potency claims in relation to Bocouture. Within only one month of the outcome of Case AUTH/2460/11/11, Allergan had briefed a third party to promote the same unbalanced data that it was not able to promote directly.

Merz was concerned that Allergan was relentless in its pursuit of the message that the Bocouture and Xeomin units were less potent than the Vistabel and Botox units against all the clinical evidence and the view of the Medicines and Healthcare products Regulatory Agency (MHRA) and the wider European regulators. Furthermore, in Case AUTH/2487/3/12 Merz noted that it was able to comment on an article in the March issue of Cosmetic News up until 23 February. The publication had thus not gone to press by this date which was some time after the ruling for Case AUTH/2460/11/11. Merz insisted on a corrective statement in the publication to help to rectify the clearly misleading statements that had previously been published.

In Case AUTH/2487/3/12 Merz identified an article in Cosmetic News that was a verbatim quotation of the one at issue in Case AUTH/2489/3/12. It would be reasonable to conclude that both articles had come from the same Allergan press release. In Case AUTH/2489/3/12 Merz additionally submitted that furthermore Allergan had repeatedly demonstrated that it had no intention to complying with undertakings. In Case AUTH/2460/11/11 Allergan was reported to the Code of Practice Appeal Board. Merz believed that full and fair competition was healthy but it was important to ensure that physicians received accurate and truthful information and were able to make informed decisions about products.

When writing to Allergan, the Authority asked it to respond in relation to Clause 2 in addition to Clause 25 cited by Merz.

RESPONSE

Allergan stated that Moers-Carpi *et al* was presented at the 7th EMAA Congress (held in Paris, September 30-1 October 2011) and also at the International Master Course on Aging Skin (IMCAS) Congress (held in Paris, 26-29 January 2012). A press release regarding the new study was drafted for use at EMAA. However, the press release was not finalised and was not used at EMAA. Subsequently, the draft press release was finalised and approved (examined) on Zinc (UK/0762/2011).

The press release covered the presentation of the new study at EMAA. The clear message from the title and the text was that unit doses of botulinum toxins, as with all biologicals, were not interchangeable. There was no suggestion or implication of sub-potency of the Merz toxin.

Allergan considered the presentation of this new study at a scientific congress was a newsworthy event. These new data from a large (n=220) randomised, double blind, peer reviewed equivalence study directly challenged the hypothesis that botulinum toxins were interchangeable at a 1:1 dose ratio. The study compared 20 units of Vistabel with 30 units of Bocouture. The basis for this study was the investigators' clinical experience of the relative effectiveness of the different products in clinical practice, the differences seen in the different reference LD50 assays and the different dose ranging data that were available.

Allergan submitted that these data were not inconsistent with the findings of the Merz non-inferiority studies or indeed the Bocouture SPC. The study confirmed that unit doses of botulinum toxins were not interchangeable. The study clearly challenged the basis for any claims of equivalence or a 1:1 conversion ratio made by Merz.

Allergan noted that subsequent to EMAA, Moers-Carpi *et al* re-presented their data at IMCAS. Allergan's PR agency contacted the editors of Cosmetic News and PRIME on 30 January, following IMCAS, and provided a copy of the press release (UK/0762/2011). Neither the agency nor Allergan's PR team had any further correspondence or calls with either journal on this matter or received any page proofs. Neither Allergan nor its PR agency were offered the chance to comment on the articles. An email chain to confirm the history of the events outlined above was provided.

Allergan did not consider it had breached its undertakings given in Cases AUTH/2335/7/10 and AUTH/2346/8/10. It provided a press release covering the details of a new study with a clear message of non-interchangeability not sub-potency of Merz toxin. The press release was reviewed with the above cases in mind and wording was amended to remove reference to potency. Data from a new study was provided with a clear take away message of non-interchangeability.

Regarding Case AUTH/2460/11/11, Allergan informed the PMCPA of its intention not to appeal the rulings on 3 February 2012.

Allergan accepted that there were a number of areas for improvement with respect to the handling of press releases and interactions with its PR agency. Allergan had instigated further training and a review of procedures regarding review, approval and release of press and media materials.

Allergan denied breaches of Clauses 25 and 2.

PANEL RULING

The Panel noted that Allergan had been notified of the outcome of Case AUTH/2460/11/11 on 26 January 2012, four days before it sent a press release about the Moers-Carpi *et al* (2011) data to Cosmetic News and PRIME; the subsequent articles were published in the March edition of the journals. In Case AUTH/2460/11/11, Allergan was again ruled to have breached undertakings with regard to claims about the relative potency of its botulinum toxin vs that of the Merz product. One of the matters at issue was specifically about the emphasis given to the Moers-Carpi *et al* results in the relative absence of other data. Allergan accepted the rulings of breaches of the Code and signed the relevant undertaking on 3 February 2012; there was no reference in the undertaking to any other material that could not be withdrawn due to the passing of copy deadlines. The Panel noted the submission from Merz in Case AUTH/2487/3/12 that it had been given up until 23 February to comment on an article which was to be published in the March edition of Cosmetic News. Allergan submitted that after it had sent the press release on 30 January, it had not had any further contact with Cosmetic News and PRIME or been offered the chance to comment on the articles. The Panel noted that Allergan's PR agency had provided the press release following its contact with the editors of Cosmetic News and PRIME (30 January) in the period when Allergan, having received the notification of the Panel's rulings of breaches in Case AUTH/2460/11/11 (26 January) and report to the Code of Practice Appeal Board, would be deciding whether to accept or appeal those rulings (due 3 February). The Panel also noted that the press release was examined and signed on 25 January which was whilst Allergan was awaiting the outcome of a relevant complaint, Case AUTH/2460/11/11.

The Panel noted that complaints about articles in the press were judged on the information provided by the pharmaceutical company or its agent to the publisher/journalist and not on the content of the article itself. The articles which appeared in the March editions of Cosmetic News and PRIME reproduced large sections of Allergan's press release. The press release was headed 'New study provides further evidence that dosing for botulinum toxins are not interchangeable'; the sub-heading read 'Head to head study launched at international aesthetics congress further reinforces need for awareness of the different doses for two botulinum toxin type A products'. The press release ended with a quotation from one of the authors of Moers-Carpi *et al*, an Allergan employee; 'We are pleased

to see further evidence for the efficacy of Vistabel and consider that this study provides further clarity that Vistabel and the Merz unit doses are not interchangeable in clinical practice'.

The Panel noted that in Case AUTH/2460/11/11 both parties had submitted more information than above. The Panel thus noted the following paragraph from its ruling in point 1 of that case:

> 'The Panel noted that there appeared to be no standard assay method for the two [botulinum toxin] preparations. The SPCs for Botox/Vistabel referred to Allergan Units/vial and the Bocouture/Xeomin SPCs referred to LD50 units per vial. The Xeomin SPC stated that due to differences in the LD50 assay, these units were specific to Xeomin and were not interchangeable with other botulinum toxin preparations. All of the SPCs stated that as the botulinum toxin units differed from product to product, doses recommended for one product were not interchangeable with those for another. The Bocouture SPC, however, stated that comparative clinical study results suggested that Bocouture and the comparator product containing conventional botulinum toxin type A complex (900kD) [Botox/Vistabel] were of equal potency. The Xeomin 50 units SPC contained the equivalent statement but added 'when used with a dosing conversion ratio of 1:1'. In this regard the Panel noted that Sattler *et al* (2010) demonstrated the non-inferiority of 24 units each of Bocouture/Xeomin (n=277) to Botox/Vistabel (n=93) in the treatment of glabellar frown lines. The SPCs for Bocouture and Vistabel stated identical recommended unit doses for the treatment of moderate to severe glabellar frown lines, ie five injections each of 4 units. The Bocouture SPC stated that the dose might be increased to up to 30 units if required by the individual needs of the patient.'

The Panel also noted that a representative's use of copies of the Moers-Carpi *et al* poster had been at issue in point 2 of Case AUTH/2460/11/11. The Panel thus noted the following relevant paragraphs from its ruling on that matter:

> 'The Panel noted that the Vistabel sales aid (ref UK/0775/2011) provided by Allergan as the only promotional item that referred to Moers-Carpi *et al* was entitled 'Not all toxins are Vistabel'. The front cover included the statement 'Vistabel unit doses are not interchangeable with other preparations of botulinum toxins'. One page in the sales aid was headed 'Head-to-head data review of glabellar lines' beneath which was boxed text with a very brief description of Sattler *et al* and a more detailed description of Moers-Carpi *et al*. Subsequent pages of the sales aid detailed the results of Moers-Carpi *et al* with the use of a bar chart and graph. The back page of the material included the claim 'A recently conducted equivalence study confirms that unit doses of Vistabel and Merz toxin are not interchangeable in clinical practice' which was referenced to Moers-Carpi *et al*. There was no reference on the back page to the Sattler *et al* non-inferiority study which showed that 24 units of Bocouture/Xeomin was non-inferior to 24 units of Botox/Vistabel in the treatment of glabellar lines. There was no mention of the statement in the Bocouture SPC that clinical data suggested equal potency.
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> There was no complaint about the sales aid. However, the Panel considered it was relevant to the allegation that the customer was left with the message that Bocouture did not possess the same clinical potency per unit as Vistabel.
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> The Panel noted that the Moers-Carpi *et al* poster was not available for representatives to distribute; if customers asked for a copy the representatives had to ask medical information to send a copy or receive a copy themselves in a sealed envelope for onward transmission to the customer. Allergan had acknowledged that three customers had asked the representative for a copy of the poster. In that regard the Panel noted Allergan's submission that the requests were unsolicited. In the Panel's view, the emphasis on the Moers-Carpi *et al* data within the sales aid meant that any request for a copy of the poster which was prompted by a representative's discussion of that data was a solicited request for the poster.
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> The Panel noted that it was impossible to know what the representative had said to any of the three customers about the poster or whether the representative had used the sales aid. However, the Panel considered that, given the content of the sales aid, on the balance of probabilities, the representative had used the Moers-Carpi *et al* poster to inform the health professional that in order to achieve the same clinical outcome in the treatment of glabellar lines 20 units of Vistabel was needed vs 30 units of Bocouture ie unit for unit, Bocouture was less potent than Vistabel.'

The Panel noted that in Case AUTH/2346/8/10 Allergan had been ruled in breach of its undertaking given in Case AUTH/2183/11/08 in that an impression was given that Botox was more potent than Xeomin and this was inconsistent with the product SPCs and available clinical data. Breaches of Clauses 2, 9.1 and 25 were ruled.

Turning to the cases now at issue, Cases AUTH/2487/3/12 and AUTH/2489/3/12, the Panel noted that the press release in question (UK/0762/2011 Date of preparation Dec 2011) was itself undated. It had been examined on 25 January 2012 according to the Zinc certificate. The press release was only about the Moers-Carpi *et al* data. The results of that study had not been set within the context of the recommended doses for Vistabel and Bocouture according to their SPCs, the statement in the Bocouture SPC that comparative clinical study results suggested that Bocouture and the comparator product containing conventional botulinum toxin type A complex (900kD) [Botox/Vistabel] were of equal potency and the clinical results of Sattler *et al* which showed that 24 units of Bocouture/Xeomin was non-inferior to 24 units of Botox/Vistabel in the treatment of glabellar lines.

The Panel did not consider that the discussion of Moers-Carpi *et al*, in isolation, in the press release represented the balance of the evidence with regard to the relative efficacy of Vistabel and Bocouture. In the Panel's view, the press release implied that in order to achieve the same clinical outcome in the treatment of glabellar lines, 20 units of Vistabel was needed vs 30 units of Bocouture, ie unit for unit, Bocouture was less potent than Vistabel. In that regard the Panel considered that the press release was sufficiently similar to the point at issue in Cases AUTH/2346/8/10 and AUTH/2460/11/11 for it to be covered by the undertaking in Case AUTH/2346/8/10. Thus the press release now at issue breached an undertaking previously given. A breach of Clause 25 was ruled in each case. These rulings were appealed by Allergan.

The Panel noted that an undertaking was an important document and that Allergan's successive breaches of undertaking was such as to bring discredit upon and reduce confidence in the pharmaceutical industry. The Panel ruled a breach of Clause 2 in each case. These rulings were appealed by Allergan.

The Panel was concerned that Allergan stated that it had reviewed the press release in relation to the outcome of Cases AUTH/2335/7/10 and AUTH/2346/8/10 and that the press release had been sent out during the time Allergan would be considering whether to appeal yet another breach of undertaking ruled by the Panel in Case AUTH/2460/11/11. Given the seriousness of the situation, the Panel considered that Allergan should have taken urgent action and considered not using the press release until it had decided whether to appeal Case AUTH/2460/11/11, particularly as the form of undertaking required withdrawal of any similar material. Allergan could have contacted the editors of Cosmetic News and PRIME following its provision of the undertaking in Case AUTH/2460/11/11. However, the Panel noted that the press release was used on 30 January and that the undertaking was dated 3 February. Thus Allergan had not breached its undertaking in Case AUTH/2460/11/11 and no breach of Clause 25 was ruled in each case. These rulings were not appealed.

The Panel noted that in case AUTH/2487/3/12, Merz had requested that Allergan publish a corrective statement to help rectify the misleading impression given in the March edition of Cosmetic News. Corrective statements were a sanction available only to the Code of Practice Appeal Board.

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The Panel noted its rulings in this case that Allergan had again breached its undertaking with regard to claims about the relative potency of its botulinum toxin vs that of the Merz product. Cases AUTH/2346/8/10 and AUTH/2460/11/11 had been ruled in breach of Clauses 2, 9.1 and 25. Notwithstanding the fact that in Case AUTH/2460/11/11 Allergan had been reported to the Code of Practice Appeal Board, the Panel once again decided firstly in Case AUTH/2487/3/12 and subsequently in Case AUTH/2489/3/12 to report the company to the Appeal Board in accordance with Paragraph 8.2 of the Constitution and Procedure. The continued breaches of undertaking raised serious questions about the company's procedures and commitment to complying with the Code. The Panel noted that in Case AUTH/2460/11/11 the Appeal Board had required an audit of Allergan's procedures in relation to the Code to be carried out by the Authority and had also decided that the company should be publicly reprimanded for successive breaches of its undertakings.

APPEAL BY ALLERGAN

Allergan noted that the Panel had ruled that it had breached the undertaking given in Case AUTH/2346/8/10 following publication of two articles based on its press release.

By way of background, Allergan reiterated that Moers-Carpi *et al* was presented at the 7th EMAA Congress in October 2011 and at the IMCAS Congress in January 2012.

Allergan submitted that it had originally drafted a press release about the Moers-Carpi *et al* study with the intention of issuing it in connection with EMAA. However, the press release was not finalised in time and so it was subsequently issued in connection with IMCAS, although it erroneously referenced EMAA. Allergan submitted that the intention of the study and the press release, as evidenced by the clear message from the title and the text of the release, was that unit doses of botulinum toxins were not interchangeable, a point strongly made in the labels of all approved botulinum toxins. There was no suggestion or implication of sub-potency of the Merz toxin, as this was not the intention of the release.

Allergan reiterated that the launch of this study at EMAA was newsworthy. These new data from a large (n=220), randomised, double blind, peer reviewed equivalence study directly challenged Merz's claim that botulinum toxins were interchangeable at a 1:1 dose ratio. The study compared 20 units of Vistabel with 30 units of Bocouture. The basis for this study was the investigators' clinical experience of the relative effectiveness of the different products in clinical practice, the differences seen in the different reference LD50 assays and the different dose ranging data that was available.

Allergan further reiterated that these data were not inconsistent with the findings of the Merz non-inferiority studies or the SPC for Bocouture at the time (dated 29 June 2010). In fact, the only thing with which the study was inconsistent was the claim that the products were equivalent or interchangeable at a 1:1 dose ratio. While not revealed to the PMCPA, Merz had known for some time that this language would be removed from the posology section of its label but continued to rely upon that language. However, the updated Bocouture SPC (dated 6 March 2012) had removed the language and was thus not inconsistent with the conclusion of Moers-Carpi *et al*. The study confirmed that unit doses of botulinum toxins were not interchangeable and clearly challenged the basis for any claims by Merz of equivalence or a 1:1 conversion ratio.

Dr Moers-Carpi presented the study and its conclusions at IMCAS. Allergan again noted that its PR agency (CCA) contacted the editor of Cosmetic News on 30 January, following IMCAS, and provided a copy of the press release. Neither CCA nor Allergan had any further correspondence or calls with Cosmetic News on this matter and they did not receive any page proofs. Neither Allergan nor CCA were offered the chance to comment on the article. The email chain to confirm the history of the events outlined above was provided.

Allergan again submitted that it had not breached its undertakings with respect to Case AUTH/2346/8/10 (or Case AUTH/2335/7/10). Allergan provided a press release covering the details of a new study with a clear message of non-interchangeability, not sub-potency of Merz's toxin.

Allergan submitted that the press release was intended to announce an important new and newsworthy study which shed further light on what should have been an incontrovertible fact, that unit doses of botulinum toxin type A products were not interchangeable.

Allergan submitted that its goal was not to state or imply sub-potency. Indeed, claiming or implying that it took 30 units of Xeomin to get 20 units of Botox efficacy was not only not its goal in the study or press release, but was inconsistent with its view on this matter which it had stated throughout this, and other cases. These products were not interchangeable, regardless of dose conversion ratio. They had separate profiles, they were separate products and had different efficacy and safety margins all of which were indication specific. They acted differently. The last thing Allergan wanted was a fixed dose ratio implied regarding these products. Allergan submitted that its press release was clear in that regard and the study, and quotation from the lead investigator and Dr Fulford-Smith, confirmed that unit doses of botulinum toxins were not interchangeable.

Allergan submitted that the presentation of Moers-Carpi *et al* without reference to either the Bocouture SPC or the Merz non-inferiority study (Sattler *et al*) was not unbalanced. This study and the claims made by Allergan were not inconsistent or out of line with any of the other available data from Merz, Allergan or Ipsen/Galderma. All the available data, including Moers-Carpi *et al*, confirmed that unit doses were not interchangeable. This new study was not designed to, and could not be used to, establish a fixed dose conversion between products.

In Allergan's view, the Panel had accepted the concept that there was an established 1:1 conversion ratio between Botox/Vistabel and Xeomin/Bocouture and in this regard had been misled by Merz.

Allergan knew that changes to the Bocouture and Xeomin 50U SPCs were approved on 6 March 2012 following Allergan's communication to the Pharmacovigilance Working Party (PhVWP) highlighting the potential patient safety concerns with the Bocouture and Xeomin 50U SPC wording. A summary of these changes was provided. However, in summary, in the Bocouture SPC any reference to equal potency had been removed. In Section 4.2 of the Xeomin 50U SPC the statement regarding 1:1 dosing ratio had been removed. Section 5.1 of the SPC still contained information regarding its non-inferiority studies but this was specifically in relation to patients with blepharospasm or cervical dystonia. As previously established, non-inferiority studies did not support claims of equivalence.

Allergan submitted that it had not undertaken this appeal lightly; it understood the serious nature of its position, especially given the very recent PMCPA audit. Allergan was completely committed to compliance with the Code and understood that it had to address significant issues with respect to process, integration and teamwork, resources and training. Allergan further accepted that there were a number of areas for improvement with respect to the handling of press releases and interactions with its PR agency. Allergan had instigated further training and a review of its procedures regarding review, approval and release of press and media materials.

However, Allergan did not believe that it had breached its undertaking by implying or stating that Merz's toxins were sub-potent. Allergan had provided information on a new study which reflected the balance of evidence and the clearly established fact that unit doses of botulinum toxin type A products were not interchangeable.

Allergan did not accept the Panel's ruling of breaches of Clauses 2 and 25.

COMMENTS FROM MERZ

Merz noted that in Case AUTH/2183/11/08 the Panel ruled that, on the balance of probabilities, an Allergan representative had claimed that there was a difference in potency between Botox and Xeomin, which was inconsistent with the guidance on prescribing in the respective SPCs. The Panel also found that the supporting promotional material examined was misleading and unsubstantiated and did not support the rational use of medicine. The Panel determined that the training materials issued in association with the promotional material did not maintain high professional standards.

Merz noted that in Case AUTH/2460/11/11 the Panel again reached a similar conclusion, that the selective use of data to convey a message of sub-potency of Xeomin/Bocouture to Botox/Vistabel (in the form of the Moers-Carpi *et al* data) did not reflect the balance of evidence and was misleading. Specifically the data had not been used in the context of the SPC recommendations for either product with the same starting dose of 20 units. Additionally the data had not been contextualised without reference to the regulatory approved study data (Sattler *et al*) which demonstrated non-inferiority between the two medicines at a 1:1 dosing ratio. Allergan was notified of this view on 26 January 2012.

On 30 January Allergan issued a press release announcing new data which demonstrated that 20 units of Vistabel were equivalent to 30 units of Xeomin. Merz alleged that the new data was the

same data by Moers-Carpi *et al* subject of the ruling in Case AUTH/2460/11/11, it was again selectively presented without context. The Panel ruled in Cases AUTH/2487/3/12 and AUTH/2489/3/12 regarding the press release that:

- The results of the study had not been set within the context of the recommended doses for Vistabel and Bocouture according to the SPCs
- The Panel did not consider that the discussion of Moers-Carpi *et al*, in isolation in the press release represented the balance of evidence with regard to the relative efficacy of Vistabel and Bocouture
- In the Panel's view the press release 'implied that Bocouture was less potent than Vistabel'. In this regard that Panel considered that the press release was sufficiently similar to the point at issue in Cases AUTH/2460/11/11 and AUTH/2346/8/10
- In addition, the Panel referred to the serial breaches in Cases AUTH/2335/7/10, AUTH/2346/8/10, AUTH/2460/11/11 and the seriousness of the situation associated with the lack of urgent action taken by the company with respect to these new cases

Whilst Merz accepted that because it had not signed the undertaking in Case AUTH/2460/11/11 until 3 February Allergan had avoided a breach of this undertaking by a technicality, Merz fully supported the Panel's ruling that the persistent use of isolated data out of context and in conflict with the regulatory head-to-head clinical studies and SPC dosage guidance, was in breach of the undertaking given in Case AUTH/2183/11/08.

Merz noted that Xeomin/Bocouture and Botox/Vistabel had been compared at a 1:1 dose conversion ratio across numerous indications, in large registration standard studies designed with advice from the regulatory authorities. In these studies Xeomin/Bocouture had consistently been found to be non-inferior to Botox/Vistabel at a 1:1 dose conversion ratio with no significant differences being observed between any of the primary and secondary efficacy variables measured.

Merz submitted that it was an inconvenient truth for Allergan that a 1:1 ratio made switching from Botox/Vistabel to Xeomin/Bocouture relatively straightforward and cost comparisons more obvious. This represented a clear commercial threat for Allergan.

Allergan stated its position on the 1:1 conversion ratio very clearly in its appeal when it stated;

> 'These products were not interchangeable, regardless of the conversion ratio. They had separate profiles, they were separate products and had different efficacy and safety margins all of which were indication specific. They acted differently. The last thing Allergan wanted was a fixed dose ratio implied regarding these products.'

Merz took this statement point by point and submitted the following:

1 *'these products were not interchangeable, regardless of the conversion ratio'* – Merz submitted that Xeomin/Bocouture had been demonstrated non-inferior to Botox/Vistabel at a 1:1 dosing ratio, and this was reflected in the product SPC dosing guidance (the fact that units of potency were product specific was inconsequential to this comparison).

2 *'They had separate profiles, they were separate products and had different efficacy and safety margins all of which were indication specific'* – Merz submitted that Xeomin/Bocouture and Botox/Vistabel had consistently been shown to have comparable efficacy and similar safety profiles with no significant difference between onset of action, peak effect, duration of effect and diffusion through muscle being observed across all indications assessed (Sattler *et al*, Roggenkamper *et al*, 2006, Benecke *et al* 2009, Jost *et al* 2005).

3 *'They acted differently. The last thing Allergan wanted was a fixed dose ratio implied regarding these products'* – Merz noted that both Xeomin/Bocouture and Botox/Vistabel were botulinum toxin type A, they both originated from the same Hall strain of Clostridium botulinum and they both blocked cholinergic transmission at the neuromuscular junction by inhibiting the release of acetylcholine. This similarity was reinforced by the near identical descriptions of their mode of action in Section 5.1 of their respective SPCs.

Merz stated that what could be observed by Allergan's conduct, and was very clearly articulated in its appeal, was that it could not accept 'a fixed dose ratio being implied regarding these products'. One could presume it would represent an unacceptable commercial threat.

Merz alleged that in the face of this compelling clinical data Allergan had sought to leverage a statement indicating that the different products had different assays to assess their preclinical potency and elevate it to a level above that of the dosing guidance in the respective SPC's and the robust clinical data on which that guidance was issued. Merz was confident that this was not the objective of the PhVWP in the drafting of the 'units of potency' statement that botulinum toxin products should be rendered incomparable in the clinical setting.

Allergan's argument that the phase IV Moers Carpi *et al* data, co-authored by an employee of Allergan, challenged the validity of previous head-to-head comparisons was flawed. Moers Carpi *et al* demonstrated that there was no benefit in using a higher dose of Bocouture (30 units) vs a lower dose of Botox (20 unit) which was why both products had an initial dose recommendation of 20 units. As the dosing arms were not matched, no useful comparison of potency could be made. Or to put it another way, if a man could drown in 10 feet of one brand of mineral water as quickly as he could in 20 feet of another brand of mineral water did that make the first brand of mineral water twice as dangerous

or beyond comparison? No, it did not. To draw out Allergan's conclusion it had used the finding of the paper to communicate that toxins were not interchangeable it was a fair challenge to ask how they interpreted the findings of its paper (Curruthers *et al*) which found no significant difference between 20 and 30 units of Botox in treating glabellar frown lines.

In Allergan's appeal it submitted that Moers Carpi *et al* directly challenged Merz's claim that botulinum toxins were interchangeable at a 1:1 dose ratio. Merz alleged that it did not. Used in isolation it represented the most recent in a series of breaches of undertaking which it appeared should not stop until Allergan accepted that Xeomin/Bocouture had been demonstrated non-inferior to Botox/Vistabel at a 1:1 dosing ratio. Allergan was on record in its appeal that it would not accept this fact.

Allergan stated that Merz had withheld pending changes in the Bocouture SPC to the Panel and implied that the recent changes in the wording of the SPC might be associated with the Moers-Carpi *et al* data. Merz submitted that the matter at hand should be assessed against the position at the time of the breach, without mitigation for future events but was happy to address the matter.

Merz stated that it was common following the approval of a new product licence in Europe, for regulatory harmonisation to occur. Following the pan-European approval of the 50U Xeomin vial throughout 2011, an updated SPC for Xeomin and Bocouture was developed in conjunction with the regulators. The final version was approved by the MHRA over a month after the release of Allergan's press briefing document on Moers-Carpi *et al* and implemented by Merz within a week of receipt.

Merz stated that as a result of the harmonisation process the Xeomin statement of 1:1 comparable potency was moved from Section 4.2 (Posology and method of administration) to Section 5.1 (Pharmacodynamic properties) of the SPC where a clearer reference to the comparative studies was made. At the same time the more appropriate use of the term 'efficacy', rather than 'potency' was used to describe the study data.

Merz noted that Section 4.2 of the revised Xeomin 50 unit SPC (March 2012 revision) stated: '… Study results also suggest that Xeomin and this comparator product [Botox] have a similar efficacy and safety profile in patients with blepharospasm or cervical dystonia when used in a dosing conversion ratio of 1:1 …'.

Merz stated that the harmonisation process was on-going and would result in further SPC updates for Xeomin 100 unit and Bocouture 50 unit. Merz submitted that Moers Carpi *et al* did not feature in its discussions with the MHRA on this matter. Similarly Merz did not believe that the body of data on this matter had changed, that the respective SPCs still reflected the clinical situation and that the SPCs still supported the 1:1 dosing schedule in their dosing guidance.

In summary, Merz supported the Panel's rulings and its approach to ensuring compliance to previous undertakings.

APPEAL BOARD RULING

The Appeal Board noted that the press release at issue had to be considered in relation to the statements which were in the Merz SPCs (Bocouture and Xeomin 50U) when it was issued and not those subsequently approved on 6 March 2012. All the SPCs for botulinum toxins included a statement that botulinum toxin units were not interchangeable from one product to another.

The Appeal Board noted that Moers-Carpi *et al* demonstrated in a head-to-head comparison that 20 units of Vistabel was as effective as 30 units of Bocouture in the treatment of glabellar lines. The Appeal Board noted, however, that the recommended starting dose for both products according to their SPCs was 20 units and it thus queried the choice of doses. The Appeal Board noted Allergan's submission on this point. Moers-Carpi *et al* did not examine the efficacy of the starting dose of Bocouture and whether this dose would have achieved the same clinical result as 30 units. In that regard the Appeal Board noted that once muscle saturation had occurred, any increase in dose would not produce any increase in effect.

The Appeal Board considered that the press release gave an accurate account of Moers-Carpi *et al*. Given that both study medicines were botulinum toxins, the Appeal Board considered that many clinicians would assume that the difference in dosing to achieve a similar therapeutic effect meant that Vistabel (20 units) was more potent than Bocouture (30 units). In that regard the Appeal Board noted the following quotation from the press release: 'We are pleased to see further evidence for the efficacy of Vistabel and consider that this study provides further clarity that Vistabel and the Merz unit doses are not interchangeable in clinical practice'.

The Appeal Board noted that the press release did not refer to the relative potency of Vistabel and Bocouture but nonetheless, in its view, the inevitable implication was that Bocouture, unit for unit, was less potent than Vistabel. In the Appeal Board's view, in this particular context, ie a direct comparison of two botulinum toxins dosed in units, clinicians might well take efficacy and potency to mean one and the same. The discussion of Moers-Carpi *et al* in isolation in the press release did not represent the balance of the evidence with regard to the relative efficacy of Vistabel and Bocouture. Given the implied claim that Bocouture was less potent than Vistabel, the Appeal Board considered that the press release was sufficiently similar to the point at issue in Cases AUTH/2346/8/10 and AUTH/2460/11/11 for it to be covered by the undertaking in Case AUTH/2346/8/10. Thus the press release now at issue breached a previous undertaking. The Appeal Board upheld the Panel's rulings of breaches of Clause 25. The Appeal Board further considered that Allergan's successive breaches of undertaking was such as to bring discredit upon and reduce confidence in the pharmaceutical industry. The Appeal Board upheld

the Panel's rulings of breaches of Clause 2. The appeals were unsuccessful.

The Appeal Board noted that it was important for the reputation of the pharmaceutical industry that companies understood the importance of their undertakings and took the necessary action to comply with them. The Appeal Board questioned Allergan's conduct and attitude in this regard and decided that the company should be publicly reprimanded for its successive failures to comply with its undertakings. These two cases taken together represented the fourth breach of undertaking. Allergan's conduct was completely unacceptable. The Appeal Board also decided, in accordance with Paragraph 11.3 of the Constitution and Procedure, to require an audit of Allergan's procedures in relation to the Code to be carried out by the Authority. The audit should be conducted at the same time as the re-audit required in Case AUTH/2460/11/11 which was scheduled to take place in August 2012. On receipt of the audit report the Appeal Board would consider whether further sanctions were necessary including pre-vetting of promotional material.

FURTHER APPEAL BOARD CONSIDERATION

Although the Appeal Board was disappointed, on receipt of the August 2012 audit report, at the lack of progress demonstrated, the company appeared to have taken action including setting time frames for the bulk of the processes and work to be completed by the end of 2012. The Appeal Board was concerned that the amendments to some of the standard operating procedures (SOPs) had not been finalized. The Appeal Board noted that there were plans to significantly change the company structure. The Appeal Board considered that Allergan should be re-audited in January 2013 at which point it expected there to be significant improvement.

Upon receipt of the January 2013 audit report, the Appeal Board noted that although Allergan had made progress, further improvement was necessary. The Appeal Board noted that one key change in senior personnel would take place shortly and another in due course. Given that further improvement was required, the Appeal Board considered that Allergan should be re-audited in September 2013. Upon receipt of the next audit report, the Appeal Board would decide whether further sanctions were necessary.

Upon receipt of the September audit report, the Appeal Board noted that Allergan had made progress since the re-audit in January. The company had undergone four audits since April 2012. It was important that the progress shown in the September 2013 audit was continued and maintained. Every opportunity should be taken for improvement. The Appeal Board noted that Allergan needed to ensure that it updated its processes in good time to reflect the 2014 Code and that relevant staff were trained on the new Code. Allergan provided details of its plans to implement the recommendations in the audit report. On the basis that this work was completed, the Appeal Board decided that no further action was required.

Complaint received (Case AUTH/2487/3/12)	**6 March 2012**
Complaint received (Case AUTH/2489/3/12)	**12 March 2012**
Appeal Board Consideration	**28 June, 11 October 2012, 6 March, 15 October 2013**
Undertakings received	**17 July 2012**
Interim case report first published	**2 December 2012**
Case completed	**15 October 2013**