CASE AUTH/2614/7/13

HEALTH PROFESSIONAL v ALLERGAN

Market Research

A health professional and ex Allergan employee complained about market research on injecting botulinum toxins that his wife, a nurse, was asked to participate in.

The complainant noted that the market research asked the recipient to answer questions on all three commercially available botulinum toxins which were referred to by brand name and not their non-proprietary names. The material presented information on a hypothetical, single use, prefilled syringe to be launched shortly and presented calculations on savings to be made through switching to it from a competitor botulinum toxin. Payment for completing the study was a £65 shopping voucher or a cheque.

The complainant assumed that the work had been commissioned by Galderma which marketed Azzalure. The complainant alleged that repeated use of a pharmaceutical company's brand name in material, commissioned by that company, constituted promotion of that product and so the material should carry the prescribing information for that product. The complainant noted that in the market research survey this was not so, in breach of the Code.

The identity of the commissioning pharmaceutical company was not clear from the documentation. The agency confirmed that it was Allergan. Allergan marketed Botox and Vistabel. The complaint was thus taken up with Allergan.

The detailed response from Allergan is given below.

The Panel noted that the complainant had assumed the market research had been commissioned by Galderma, which marketed Azzalure. Whilst the complaint primarily referred to Azzalure it also mentioned other botulinum toxins including Botox and Bocouture [marketed by Merz Pharma]. On being notified of the respondent company, the complainant stated that some of his points should, therefore, be read in context. Allergan was asked to respond to the alleged breaches in relation to its products. The Panel thus considered the complaint on this basis.

The Panel noted Allergan's submission that the purpose of the research was to evaluate the potential opportunity of a ready-to-use neurotoxin (NTX); its value to the facial aesthetic market and to the company. The objectives included exploring reactions etc to new ready-to-use NTXs given potential differences in manufacturing company, available forms, duration of effect and price. To accomplish the stated objectives factors including company/brand were presented to participants systematically to assess market impact. The Panel noted Allergan's late submission that, contrary to its initial statement that Allergan Inc was not researching or developing a R2U toxin, it had entered into a licensing agreement with a Korean company, Medytox to develop and, if approved, commercialize certain NTX products including a potential liquid-injectable product.
The market research asked 120 UK participants about their typical monthly activity regarding cosmetic patients, which brands of NTX they were aware of (Vistabel/Botox, Neuronox, Bocouture, Azzalure, other) and whether if newer, easier to dose/use NTXs became available, they would expand their practice to treat more facial cosmetic patients. The survey continued by asking participants about facial injection locations; choice of brands (Vistabel/Botox, Bocouture, Azzalure) and number of units typically used. Respondents were asked to rate currently available products on a scale of 1 to 6 according to eleven parameters such as 'Does not diffuse outside of targeted tissue', 'Is a brand I can trust' and 'Has excellent overall efficacy'. The market research then presented a series of product profiles sequentially. Each product profile was introduced thus 'Now we would like to show you a potential profile of a new ready-to-use neurotoxin product. Please take a moment to thoroughly read the information. As you read the description please note that this may or may not be the actual profile at launch, but is based on the most recent information on the product available. However, for this research please assume that the information is accurate and that the product will perform as described'. Detailed profiles for Azzalure ready-to-use syringe, Vistabel/Botox ready-to-use vial, Product X (eg Neuronox, Medytox) ready-to-use vial, and Product Z (eg Neuronox, Medytox) a not ready-to-use vial followed. In addition, an alternative profile for Azzalure as a ready-to-use vial was provided and introduced thus: 'Now we would like to get your opinion about an alternative configuration of this new product. The description of this new product that you initially read is only one way this product could be configured in the market and several product attributes could be different'.

Each product profile listed, *inter alia*, the manufacturer, indication, configuration, dosing forms and strengths, duration of effect, dosing and administration, safety/adverse events and the list price. The profiles for products X and Z referred to an established Korean manufacturer and that 'Clinical studies have demonstrated non-inferiority to Vistabel/Botox and no significant difference in the safety profiles'. Participants were then asked about their possible use of the product based on the description. Subsequent questions were based on comparative tables whereby the potential profiles of these 'new product/s' were compared with currently available products. A Vistabel/Botox ready-to-use syringe was mentioned. It was not introduced with a standalone profile although such details appeared

in subsequent comparative tables. The final question asked participants which NTX presentation would be of greatest value to their practice: a ready-to-use vial, current vial requiring reconstitution or a ready-to-use syringe.

The Panel did not accept Allergan's submission that it was made clear that participants were providing feedback on hypothetical scenarios. In its view the phrase 'a potential profile' implied that some features might relate to a prospective product. This was compounded by the provision of a detailed product profile to include the list price and the phrase 'please note that this may or may not be the actual profile at launch'. There was no reference to the wholly hypothetical nature of the profiles in the introduction to the market research. In addition, the Panel noted that the profile of the Azzalure ready-to-use vial was introduced as 'an alternative configuration of this new product' and the product description was not 'the only way this product could be configured in the market and several product attributes could be different'. In the Panel's view this description implied that a product or closely similar product would become available.

The Panel was concerned that when participants were asked to rate products from 'would perform very poorly' to 'would perform very well' in relation to a number of features, the first quantities listed for Vistabel/Botox ready-to-use vial and ready-to-use syringe were 'Would have excellent overall efficacy' and 'Would be able to count on the brand to deliver patient satisfaction'. The corresponding question for Azzalure ready-to-use syringe listed the lower impact statements 'Brand would be profitable to my practice' and 'Would be a brand I trust' as the first and second statements respectively. Excellent overall efficacy and patient satisfaction were lower down the list.

Overall the Panel considered that the market research went beyond its stated objectives and would solicit interest in the botulinum toxins cited including ready-to-use toxins and was promotional in this regard. Participants were asked to assume that the ready-to-use products would become available and state how likely they would be to use them. The Panel considered that insofar as the market research promoted the botulinum toxins cited it also promoted Vistabel/Botox. If this were not so then the effect would be for companies to cite a number of products as a means of avoiding the restrictions in the Code. The Panel considered that as the material promoted Botox and Vistabel relevant prescribing information should have been included; as it was not, a breach of the Code was ruled which was upheld on appeal by Allergan.

The complainant alleged that the material was presented as a 'study' and was clearly market research and not a 'study'. The complainant alleged that repeated use of its prescription only medicine's brand name within this market research by the pharmaceutical company constituted disguised promotion. The complainant further stated that presenting the material as a 'study', paying the participant for completing the market research and presenting arguments aiding a 'switch' from each of the other branded products to Azzalure constituted disguised promotion.

The Panel noted its general comments above and that it considered that as the market research survey promoted Vistabel/Botox, the survey's promotional nature was disguised. A breach of the Code was ruled which was upheld on appeal by Allergan.

The Panel did not, however, consider that the material advocated a switch as alleged and ruled no breach of the Code.

The Panel noted its ruling above and thus considered that the payment of £65 was contrary to requirements of the Code and a breach was ruled which was upheld on appeal by Allergan.

The complainant was concerned that nurses had been targeted to participate in the market research. The indications for all botulinum toxins were the same and Section 4.2 of the Azzalure summary of product characteristics (SPC) read 'Azzalure should only be administered by physicians with appropriate qualifications and expertise in this treatment and having the required equipment'. The complainant submitted that solicited feedback from nurses was therefore solicited feedback from an out of licence group of individuals. The complainant stated that mention of the brand name, Azzalure, comprised 'promotion' and consequently solicited feedback from an out of licence audience on a product referred to by its brand name constituted out of licence promotion.

Lastly, the complainant was concerned that the use of the brand name and a presentation of the product carrying the Azzalure brand name which was not yet available on the market constituted pre-licence promotion.

The Panel noted the complainant's reference to Azzalure in relation to the alleged breach of the Code. The Panel noted, as above, that it was considering this complaint in relation to Vistabel/ Botox. Vistabel/Botox were indicated for the temporary improvement in the appearance of moderate to severe vertical lines between the eyebrows seen at frown (glabellar lines), in adults <65 years old when the severity of these lines had an important psychological impact for the patient. In addition, Botox had non-cosmetic indications. Each SPC stated that Vistabel/Botox should only be administered by physicians with appropriate qualifications and expertise in the treatment and use of the required equipment. The Panel also noted in a document issued by the MHRA it was noted general cosmetic use was outside the licensed indication of Botox and Vistabel and that for cosmetic use, these medicines could be administered by an appropriate practitioner or anyone acting in accordance with the directions of an appropriate practitioner. An appropriate practitioner was defined as a doctor, a dentist or, subject to certain limitations, *inter alia*, a nurse or pharmacist.

The Panel noted the complainant's concern about the participation of nurses. The Panel was

also particularly concerned that some nurses were selected to participate because they were recommended for participation by nurse colleagues. The Panel noted the market research had been sent *inter alia* to 30 aesthetic nurse injectors. It had also been sent to 30 non injectors all of whom were physicians who would consider a facial aesthetic practice. In addition 40 non-core respondents had received the material including those in ophthalmology and gynaecology and emergency medicine.

The Panel noted that the market research solely covered cosmetic use of the products. Question 1 stated that some questions might refer to uses for all NTXs which were currently not authorized indications. Participants were referred to the prescribing information of each product as to licensed indications. Question 1 referred to the injection of forehead lines, glabellar lines, crows feet, bunny lines, under eyes and lateral eyebrows. The Panel considered that the market research therefore covered the unlicensed use of Vistabel and Botox.

The Panel noted its finding above that the material was promotional and its comments on the products' licensed indications above and the role and participation of aesthetic nurse injectors. The Panel considered that the provision of the material to aesthetic nurse injectors therefore, promoted Botox/ Vistabel for an unlicensed indication as alleged. A breach of the Code was ruled which was upheld on appeal by Allergan.

The Panel noted that the material presented detailed information on and solicited interest in a Botox ready-to-use, single-use vial and syringe. Neither medicine had a licence and thus the Panel considered that they were each promoted contrary to the Code and a breach was ruled which was upheld on appeal by Allergan.

The Panel noted Allergan's late disclosure that it had entered into a licensing agreement with a Korean company, Medytox, to develop and, if approved, commercialize certain NTX products including a potential liquid injectable product. The Panel noted that the products in question were in the mid stages of development. The Panel considered that the survey was, nonetheless, promotional for these unlicensed products referred to in the survey as products X and Z. Comparative claims for both products vs Vistabel/Botox were included. A breach of the Code was ruled which was upheld on appeal by Allergan.

The Panel noted its rulings above and considered that high standards had not been maintained. A breach of the Code was ruled which was upheld on appeal by Allergan. Overall, the Panel was very concerned about the market research. The Panel noted its comments about the promotional nature of the material which had been circulated to 120 UK health professionals. The Panel considered that to pay health professionals to participate in a promotional activity brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled.

The Panel noted its rulings and comments above. The Panel was especially concerned that, in the first instance, it had received incorrect and misleading information. In response to the Panel's question 'Is Allergan Inc researching/developing a ready-to-use neurotoxin?', the company had unambiguously stated that it was not. Allergan subsequently disclosed relevant and contrary information about the activity of Allergan Inc. Allergan had not fully explained why its two submissions were contradictory. In addition the Panel was concerned that the market research was promotional and solicited interest in, *inter alia*, unlicensed medicine/s. Participants had been paid for their time. The Panel noted that the Authority had previously been concerned about the activity of Allergan and market research in Case AUTH/2274/10/09. Taking all the circumstances into account, the Panel reported Allergan to the Code of Practice Appeal Board under Paragraph 8.2 of the Constitution and Procedure for it to consider whether to impose further sanctions.

On appeal by Allergan the Appeal Board noted its submission that when it made its first submission, no-one in the UK knew anything of the Allergan Inc/Medytox deal. As such negotiations were commercially very sensitive, known only to a limited number of very senior employees in the parent organization. As soon as the deal was made public, Allergan had updated the Panel. The Appeal Board noted that market research would often inform commercial decisions but that when conducting such research on the potential of new products, companies had to be extremely careful not to be seen to promote a medicine before the grant of a marketing authorization. In the Appeal Board's view the impact of market research on the participants was important and in that regard it noted that the complainant had considered that the survey at issue was promotional. Nonetheless, the Appeal Board considered that the survey had set out to answer some legitimate business questions and although noting its rulings above, the Appeal Board did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was reserved as a sign of particular censure. No breach of Clause 2 was ruled. The appeal on this point was successful.

In relation to the Panel's report, the Appeal Board noted its rulings above, and in particular the ruling of no breach of Clause 2, and considered that no further action was required.

A health professional and ex Allergan employee complained about market research on injecting botulinum toxins that his wife, a nurse, was asked to participate in.

The complainant noted that the market research asked the recipient to answer questions on all three commercially available botulinum toxins which were referred to by brand name and not their non-proprietary names. The material highlighted the lower price of Azzalure (abobotulinumtoxin A, marketed by Galderma (UK) Ltd) compared with Botox (onabotulinumtoxin A, marketed by Allergan Ltd) and Bocouture (incobotulinumtoxin A, marketed by Merz Pharma UK Ltd). It presented information

on a hypothetical, single use, prefilled syringe to be launched shortly and presented calculations on savings to be made through switching to it from a competitor botulinum toxin. Payment for completing the study was £65 in the form of a shopping voucher for use on the high street or internet, or a cheque.

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The identity of the commissioning pharmaceutical company was not clear from the documentation. The agency confirmed that it was Allergan. Allergan marketed Botox and Vistabel. The complaint was thus taken up with Allergan. When notified of this the complainant was extremely surprised as it did not, in his view, make sense as the positioning of the Galderma product was so positive. The complainant confirmed that he was an ex-employee of Allergan. Given that the responsible company was not Galderma, the complainant stated that some of the points in his complaint might need to be read in context.

When writing to Allergan, the Authority asked it to respond in relation to Clauses 2, 9.1 and 18.1 in addition to 3.1, 3.2, 4.1, and 12.2 cited by the complainant.

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1 Prescribing Information

COMPLAINT

The complainant alleged that the material repeatedly used the brand names of three marketed toxins with some pages containing three to four mentions; there appeared to be no attempt to use the non-proprietary name. The complainant stated that a single attempt to identify the product using the brand name was standard in genuine market research. The complainant assumed that the work had been commissioned by Galderma which marketed Azzalure. The complainant alleged that repeated use of a pharmaceutical company's brand name in material, commissioned by that company, constituted promotion of that product and so the material should carry the prescribing information for that product. The complainant noted that in the market research survey this was not so, and he alleged a breach of Clause 4.1.

RESPONSE

Allergan explained that the purpose of the market research was to evaluate the potential opportunity of a ready-to-use (R2U) neurotoxin (NTX). To assess what value a R2U NTX might bring to both the facial aesthetic market and the company it had commissioned market research to better understand the potential size of that opportunity in a number of markets, including the UK. A R2U NTX reduced the need for reconstitution and thus offered ease of administration and increased patient turnaround. These potential new products could be offered by Allergan or a competitor.

Specific research objectives were to:

- Explore physician reactions, perceptions, and receptivity to new R2U products given potential differences in:
  - manufacturing company
  - available forms (vial vs syringe)
  - duration of effect
  - price
- Identify areas of particular strength/shortcoming given currently available options

Understand how a R2U option would impact perceptions of Botox

- Estimate potential demand for a new R2U NTX, including when:
  - it was the only new R2U NTX in the market
  - it was one of two R2U NTXs in the market (assessing order of entry impacts by brand)
  - a low cost NTX was available
- Assess the degree to which an R2U option increased the number of:
  - physicians/injectors interested in/performing facial cosmetic injections
  - units/ml used per patient
  - sites injected per treatment.

To accomplish the central objectives of the research a market evolution discrete choice framework was used. Using this framework the following factors were presented to participants in a systematic fashion to assess market impact:

- manufacturing company/brand
- form
- order of entry
- duration of effect
- price.

Data on current number of patients treated with NTXs in selected areas of the face, including typical mls used in each area, were collected as a baseline reference against which to evaluate changes.

New products were introduced to participants, varying selected characteristics (as outlined in the discrete choice design) and evaluations collected. Participants were then asked to estimate usage across brands (new and current); the allocations were collected at the patient level. Usage, in terms of sites injected and average mls per site, was collected 'outside' of the discrete choice exercise.

A 25-minute online survey was chosen to accomplish the objectives.

The sample comprised of current injectors (physicians and aesthetic nurse injectors) and non-injectors (physicians only) distributed across specialty and representative of the target population. The sample size was chosen as sufficient for the primary purpose of this research (estimation of market potential for new R2U products). The sampling and quantification specific to the UK, along with the screening criteria to qualify to participate in the research was provided.

The physicians were all part of a market research panel who had agreed to be invited to, and participate in, market research.

The majority of nurse injectors were recruited from market research panels. However, as it was difficult to recruit the required number of nurse injectors, those UK nurses who completed the survey were asked to refer other nurses. Eight out of thirty UK nurse respondents were recruited this way and consent to participate in market research was obtained before they were invited to participate in the market research survey. All respondents who came in via the survey link saw the landing page with the terms and conditions that 'opt in' the respondent to participate in market research. The terms and conditions outlined everything that participation in market research entailed and how their responses/data would be used.

ESOMAR (the essential organisation for encouraging, advancing and elevating market research worldwide) and the British Healthcare Business Intelligence Association (BHBIA) recruiting guidelines for market research were followed by all parties involved.

As was standard practice, respondents were offered an appropriate honorarium (£65) to compensate them for their time and feedback.

Allergan enclosed a copy of the contact email invitation and the survey screenshots which included screening questions. The first page of the survey made it clear that participants were participating in a market research survey.

Allergan submitted that the market research was conducted properly and in accordance with the BHBIA Legal and Ethical Guidelines for Healthcare Market Research. The market research material was examined by two final signatories registered with the PMCPA, in line with Section 9.10 of the BHBIA Guidelines and the supplementary information to Clause 14.3. It was considered to be appropriately conducted market research, non-promotional, and therefore did not contravene the Code. As this material was examined, there was no certificate.

Allergan submitted that the following points had been considered and confirmed the appropriate, non-promotional nature of the market research.

There was a clear valid objective to the research which was clear to the potential participants.

Participants comprised of current injectors (physicians and aesthetic nurse injectors) and non-injectors (physicians) distributed across specialty and representative of the target population. The numbers selected from each specialty grouping was small; the largest group size was 40 and covered a very broad range of specialties. Allergan provided details of the 120 respondents.

The sample size was chosen as sufficient for the primary purpose of this research (estimation of market potential for new R2U products).

It was an entirely on-line market research activity. The email and survey screen had been provided and Allergan submitted that these were not promotional in appearance.

Products and brand names were included in this market research. However, given the objective of the research (as described above) it was essential that these were included to achieve the objective of the research. This use of brand names in the research was in line with Section 9.4.1 of the BHBIA Guidelines and did not constitute disguised promotion.

Questions regarding the R2U products were constructed within a market evolution discrete choice framework. The factors to be assessed were presented to participants in a systematic fashion to assess market impacts. When applicable, it was made clear to the participants that they were providing feedback on hypothetical scenarios and potential new products profiles which might (or might not) be the actual profile at launch. At the start of the survey some general questions were asked. It was clearly flagged that some questions might refer to uses for NTXs which were currently not authorized indications. The content of the research was in line with Sections 9.6 and 9.7 of the BHBIA Guidelines and did not constitute disguised promotion.

In response to the specific allegation Allergan acknowledged that products and brand names had been included in the market research but stated that it was essential that these were included to achieve the objective of the research. This use of brand names in the research was in line with Section 9.4.1 of the BHBIA Guidelines and did not constitute disguised promotion. The content did not constitute promotional material or require prescribing information for any of the products mentioned. Allergan denied a breach of Clause 4.1.

In response to a question from the Panel, Allergan submitted that Allergan Inc was not researching/developing a R2U NTX. The purpose of this research was to understand the impact an R2U NTX might have on the market and to help shape future strategy. In relation to the Panel's question about other companies' activities in this regard, Allergan stated that according to www.clinicaltrials.gov there were two studies, one of which was active (but not recruiting) and the other which had completed. Both of these studies were with Dysport R2U (marketed by Ipsen Ltd). The former in cervical dystonia and the latter in glabellar lines.

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Subsequent to the Panel's consideration of this matter, but before it had finalized its rulings, Allergan wrote to the Authority about a recent financial announcement. It stated that Allergan Inc had just announced that it had entered into a licensing agreement with Medytox, a biopharmaceutical company based in Korea. The licensing agreement granted Allergan exclusive rights worldwide, outside of Korea, to develop and, if approved, commercialize certain NTX products, including a potential liquid-injectable product. The close of this transaction was contingent on obtaining certain government approvals. At this time, Allergan anticipated that the transaction would be completed in late 2013 or early 2014. The NTX products included in this

licensing agreement were currently in the mid-stages of development. Allergan stated that it was unaware of this information when it responded previously but considered it should make the Authority aware of this new development.

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PANEL RULING

The Panel noted that the complainant had assumed the market research had been commissioned by Galderma, which marketed Azzalure. Whilst the complaint primarily referred to Azzalure it also mentioned other botulinum toxins including Botox and Bocouture. When notified of the respondent company, the complainant stated that some of his points should, therefore, be read in context. Allergan was asked to respond to the alleged breaches in relation to its products. The Panel thus considered the complaint on this basis.

The Panel noted that the market research had been undertaken in a number of markets including the UK. The Panel noted that the use of the market research in the UK had to comply with the UK Code.

The Panel noted Allergan's submission that the market research was in line with the BHBIA Legal and Ethical Guidelines for Healthcare Market Research. The Panel's role was to consider the complaint in relation to the ABPI Code. It had no role in deciding whether the survey was in line with the BHBIA Guidelines.

Only Clause 12.2 of the Code specifically mentioned market research and it required that market research activities, clinical assessments, post-marketing surveillance and experience programmes, post-authorization studies (including those that were retrospective in nature) and the like must not be disguised promotion. They must be conducted with a primarily scientific or educational purpose. The supplementary information to Clause 12.2 referred to the BHBIA Guidelines. The Panel considered that market research had to be conducted for a bona fide purpose. If market research was ruled to be disguised promotion contrary to Clause 12.2, any payment was likely to be in breach of Clause 18.1. In addition, the company should be mindful of the impression created by the invitation to participate in the survey and by the description of any payment.

The Panel noted Allergan's submission that the purpose of the research was to evaluate the potential opportunity of a R2U NTX; its value to the facial aesthetic market and to the company. The objectives included exploring reactions etc to new R2U NTXs given potential differences in manufacturing company, available forms, duration of effect and price. To accomplish the stated objectives factors including company/brand were presented to participants in a systematic fashion to assess market impact. The Panel noted Allergan's submission that, contrary to its initial statement that Allergan Inc was not researching or developing a R2U toxin, it had entered into a licensing agreement with a Korean company, Medytox to develop and, if approved, commercialize certain NTX products including a potential liquid-injectable product.

The market research questioned the 120 UK participants about their typical monthly activity regarding cosmetic patients, which brands of NTX they were aware of (Vistabel/Botox, Neuronox, Bocouture, Azzalure, other) and whether if newer, easier to dose/use NTXs became available, they would consider expanding their practice to treat more facial cosmetic patients. The survey continued by asking participants about facial injection locations; choice of brands (Vistabel/Botox, Bocouture, Azzalure) and number of units typically used. Questions about variation of dilution levels and use of saline applied to Vistabel and Botox only. Respondents were asked to rate currently available products on a scale of 1 to 6 according to eleven parameters such as 'Does not diffuse outside of targeted tissue', 'Is a brand I can trust' and 'Has excellent overall efficacy'. The market research then presented a series of product profiles sequentially. Each product profile was introduced thus 'Now we would like to show you a potential profile of a new ready-to-use neurotoxin product. Please take a moment to thoroughly read the information. As you read the description please note that this may or may not be the actual profile at launch, but is based on the most recent information on the product available. However, for this research please assume that the information is accurate and that the product will perform as described'. Detailed profiles for Azzalure R2U syringe, Vistabel/Botox R2U vial, Product X (eg Neuronox, Medytox) R2U vial, and Product Z (eg Neuronox, Medytox) a not ready-to-use vial followed. In addition, an alternative profile for Azzalure as a R2U vial was provided and introduced thus: 'Now we would like to get your opinion about an alternative configuration of this new product. The description of this new product that you initially read is only one way this product could be configured in the market and several product attributes could be different'.

Each product profile listed, *inter alia*, the manufacturer, indication, configuration, dosing forms and strengths, duration of effect, dosing and administration, safety/adverse events and the list price. The profiles for products X and Z included statements that the manufacturer was an established Korean manufacturer and that 'Clinical studies have demonstrated non-inferiority to Vistabel/Botox and no significant difference in the safety profiles'. Questions were then asked about the participants' possible use of the product based on the description. Subsequent questions were based on comparative tables whereby the potential profiles of these 'new product/s' were compared with currently available products. A Vistabel/Botox R2U syringe was mentioned. It was not introduced with a standalone profile although such details appeared in subsequent comparative tables. The final question asked participants which NTX presentation would be of greatest value to their practice: a R2U vial, current vial requiring reconstitution or a R2U syringe.

The Panel noted that market research was a legitimate business activity which, to comply with the Code, must not be disguised promotion. The Panel did

not accept Allergan's submission that it was made clear that participants were providing feedback on hypothetical scenarios. In its view the phrase 'a potential profile' did not make it sufficiently clear that the profile was purely hypothetical and implied that at the very least some features might relate to a prospective product. This was compounded by the provision of a detailed product profile to include the list price and the phrase 'please note that this may or may not be the actual profile at launch'. There was no reference to the wholly hypothetical nature of the profiles in the introduction to the market research. In addition, the Panel noted that the profile of the Azzalure R2U vial was introduced as 'an alternative configuration of this new product' and the product description was not 'the only way this product could be configured in the market and several product attributes could be different'. In the Panel's view this description implied that a product or closely similar product would become available.

The Panel was concerned that in relation to a question which required participants to rate a product from 'would perform very poorly' to 'would perform very well' in relation to a number of features, the first quality listed for Vistabel/Botox R2U vial and subsequently Vistabel/Botox R2U syringe was 'Would have excellent overall efficacy', followed by 'Would be able to count on the brand to deliver patient satisfaction'. The corresponding question for Azzalure R2U syringe listed the lower impact statements 'Brand would be profitable to my practice' and 'Would be a brand I trust' as the first and second statements respectively. Excellent overall efficacy and patient satisfaction were the fourth and final statements respectively.

The Panel considered that the cumulative effect of the points mentioned above was that the market research went beyond its stated objectives and would solicit interest in the botulinum toxins cited including R2U toxins and was promotional in this regard. Participants were asked to assume that the R2U products would become available and state how likely they would be to use them. The Panel considered that insofar as the market research promoted the botulinum toxins cited it also promoted Vistabel/ Botox. If this were not so then the effect would be for companies to cite a number of products as a means of avoiding the restrictions in the Code. The Panel considered that as the material promoted Botox and Vistabel relevant prescribing information should have been included; as it was not, a breach of Clause 4.1 was ruled.

APPEAL BY ALLERGAN

Allergan noted the Panel had noted its submission that the market research was in line with the BHBIA Legal and Ethical Guidelines for Healthcare Market Research. The Panel however stated that its role was to consider the complaint in relation to the Code and not to decide whether the survey was in line with the BHBIA Guidelines. Only Clause 12.2 of the Code specifically mentioned market research and it required that market research activities and the like must not be disguised promotion. Market research must be conducted with a primarily scientific or educational purpose. The supplementary information to Clause 12.2 did however refer to the BHBIA Guidelines.

Allergan did not contest that it was the Panel's role to consider the complaint in relation to the Code, more specifically Clause 12.2 in this instance, and that it had no role in deciding whether the survey was in line with the BHBIA Guidelines. Allergan was not asking the Panel to consider whether the survey was in line with the BHBIA Guidelines, but rather whether the survey was in line with Clause 12.2 of the Code.

Allergan noted that Clause 12.2 was the only reference in the Code to 'market research', and in itself it provided no guidance as to what criteria should be applied to ensure that market research complied with Clause 12.2 and was not disguised promotion. Disguised promotion was not defined in the Code. The only clue to this question lay in the supplementary information to Clause 12, which stated 'Attention is drawn to the Legal & Ethical Guidelines for Healthcare Market Research produced by the British Healthcare Business Intelligence Association in consultation with the ABPI'.

Allergan submitted that the Code therefore specifically invited readers to consider the guidelines set out in the BHBIA Code, developed in consultation with the ABPI and so presumably endorsed by it, to help determine whether market research complied with Clause 12.2. It was thus reasonable and proper for Allergan to take these guidelines into account when it designed market research, and it was likewise reasonable and proper for the Panel to consider them when determining whether market research complied with Clause 12.2. To Allergan's knowledge, there were no other available reference guidelines that had been endorsed by the ABPI in the UK, and so this was the only reference on which to rely. Allergan therefore considered the guidelines, as recommended by the supplementary information, when it designed its market research, and now invited the Panel to likewise consider them when it determined whether or not the market research was in line with Clause 12.2.

Allergan submitted that the BHBIA Guidelines aimed to provide clear, comprehensive and explicit best practice guidelines on the execution of primary and secondary healthcare market research within an up-to-date legal and ethical framework. These had been produced by the BHBIA and endorsed by the ABPI (Section 1a) as noted above. The guidelines drew heavily on the Code, the Market Research Society's Code of Conduct and the ICC/ESOMAR International Code of Marketing & Social Research Practice (Section 1c). The Guidelines were designed to:

- set standards for the design, execution and use of market research
- encourage best practice
- provide an industry-sponsored guide for sound and ethical market research
- compliment other relevant professional codes of conduct
- incorporate the impact of relevant legislation and industry guidelines.

Market research attempted to generate understanding and knowledge about a market place and 'consumer or physician' behaviour within it, by gaining information (data) from specific samples of 'consumers or physicians' and extrapolating results to the population as a whole.

Allergan submitted that market research was scientifically-conducted research where the identity of respondents, and all personal data they gave to the researchers, were kept confidential and could not be disclosed or used for any non-research purpose. Market research was not a commercial communication or a selling opportunity.

Allergan submitted that the market research was thus conducted appropriately and in accordance with BHBIA Guidelines to ensure it complied with Clause 12.2 of the Code. The market research material was examined by two signatories registered with the PMCPA, to ensure compliance with Clause 12.2 of the Code. This was also in line with Section 9.10 of the BHBIA Guidelines and the supplementary information to Clause 14.3. It was considered to be conducted for a bona fide reason, was non-promotional and therefore did not contravene the Code.

Allergan submitted that it was evaluating the potential opportunity of a R2U NTX. To assess what need and perceived value an R2U NTX might bring to facial aesthetic health professionals and the company, Allergan commissioned market research to better understand the potential size of that opportunity in a number of markets, including the UK. A R2U NTX reduced the need for reconstitution and thus offered ease of administration and increased patient turnaround. These potential new products could be offered by Allergan or a competitor and, in addition to differences in the market heritage that a manufacturing company could bring to a new R2U product, there were also likely to be differences in the form (vial/syringe), size of the offering (10, 20 and 30 units) due to potential wastage and cost with a single use syringe, duration of effect and price of any product brought to market.

Allergan submitted that Allergan Inc knew that Azzalure/Dysport was being researched/ developed for a R2U formulation; two relevant trials were listed on www.clinicaltrials.gov.

Allergan submitted that the initial market research by Allergan Inc into R2U formulations started in January 2013 with research being fielded in the US and then expanded to other markets. UK field work took place between 13 May and 19 June. Market research and healthcare compliance teams involved in the review, conduct and initial response to the complaint did not know about a Medytox deal until it was publicly announced on 25 September 2013 by Allergan Inc and this information was shared accordingly with the Panel on 1 October. Allergan noted that the material was reviewed and approved for UK use on 26 April 2013.

Allergan submitted that the key objective of the market research at issue was to understand if Allergan Inc should pursue a R2U vial and/or syringe either via internal development or by in-licensing and what impact a competitor R2U vial and/or syringe would have on its current market share. Allergan wanted to:

- Explore physician reactions, perceptions, and receptivity to potential new R2U products given potential differences in manufacturing company, available forms (vial vs syringe), duration of effect and price
- Identify areas of particular strength/shortcoming given currently available options
- Estimate potential demand for a new R2U NTX, including when:
  - Azzalure/Dysport launched first and was the only new R2U NTX in the market
  - Azzalure/Dysport launched first and there were two R2U NTXs in the market — either BOTOX R2U or South Korean R2U (assesses order of entry impacts, given branding)
  - Azzalure/Dysport launched first and there were three R2U NTXs in the market — Botox R2U and South Korean R2U alternating which was the second entrant (assesses order of entry impacts, given branding)
  - A low cost NTX from a South Korean company launched fourth
- Assess the degree to which an R2U option increased the number of:
  - Practitioners interested in performing facial cosmetic injections#
  - Patients being treated

The market research included practitioners who currently practiced in cosmetic medicine.

Allergan submitted that Allergan Inc knew that the Korean manufacturer (Medytox) had a liquid/ R2U formulation in early development but when the market research was conducted, the fact that a potential commercial deal might be possible was not known by any of the corporate head office market research team nor by anyone in the UK office.

Allergan noted that the Panel was concerned that it was not made clear that participants were providing feedback on hypothetical scenarios. In its view the phrase 'a potential profile' did not make it sufficiently clear.

Allergan submitted that the respondents saw the following:

> '*Now we would like* to show you a *potential profile of a new* ***ready-to use*** neurotoxin product. Please take a moment to thoroughly read the information. As you read the description please note that this *may or may not be the actual profile at launch*, but is based on the most recent information on the product available'. (Italics added for emphasis).

Allergan submitted that respondents saw this statement multiple times in the survey and the use of 'potential' and 'at launch' was sufficient to make them aware that these were hypothetical scenarios. At multiple points in the survey, respondents were told that:

> 'Questions refer to uses for all neurotoxins which are currently not authorised indications. Please

always refer to the prescribing information of each product as to licensed indications.'

Allergan noted that the Panel was concerned that in relation to questions which required participants to rate potential product attributes, higher and lower impact statements were ordered preferentially for different products. Allergan submitted that unfortunately this was not apparent in the screen shots of the survey provided to the Panel, but respectively for Q11, Q28b and Q39b these were randomised lists to prevent bias so that every respondent potentially saw a different order of attributes. The original screenshots provided were what one respondent would have seen with the online survey – they would not see the programming flow of the questionnaire such as question skips, randomisation, etc. In reality the responses for these questions were randomised lists to prevent bias so that every respondent potentially saw a different order of attributes. The programmer notes for the questionnaire, clearly stated that these responses should be randomized. This was clear in the final questionnaire document.

Allergan submitted that in line with BHBIA Guidelines, Section 9.4.1, respondents were exposed to a balanced number of brand names so no one brand was seen more than another.

> 'A specific product needs to be referenced e.g. in brand tracking. If possible, include other brand names, as comparators, to blind the subject's identity and so reduce the risk of promotion',

Given the points noted above, Allergan submitted that this was not promotional activity, that required prescribing information and thus it did not breach Clause 4.1.

COMMENTS FROM THE COMPLAINANT

The complainant stated that although he had initially, wrongly thought that Galderma had commissioned the market research, the principles of the complaint still stood against Allergan which had commissioned the market research and was thus responsible for the way in which it was conducted.

APPEAL BOARD RULING

The Appeal Board noted that market research was a legitimate business activity which, to comply with Clause 12.2 of the Code, must not be disguised promotion.

The Appeal Board noted that the market research at issue had originated in the US. Allergan UK was instructed by its parent company in the US, Allergan Inc, to implement the market research in the UK after what Allergan's representatives described as appropriate geographical modifications.

The Appeal Board noted Allergan's submission that the purpose of the research was to evaluate the potential effect of new R2U NTXs given potential differences in manufacturing company, available forms (vial vs syringe), duration of effect and price. The market research questioned the 120 UK participants about their typical monthly activity regarding cosmetic patients, which brands of NTX they were aware of (Vistabel/Botox, Neuronox, Bocouture, Azzalure, other) and whether if newer, easier to dose/use NTXs became available, they would consider expanding their practice to treat more facial cosmetic patients.

The Appeal Board noted one question of the survey which concerned a 'Vistabel/BOTOX Ready-to-use VIAL' stated 'Now we would like to show you a potential profile of a new ready-to-use neurotoxin product. Please take a moment to thoroughly read the information. As you read the description please note that this may or may not be the actual profile at launch, but is based on the most recent information on the product available. However, for this research, please assume that the information is accurate and that the product will perform as described'. This page went on to list product name, manufacturer, product description, indication, product configuration, dosing forms and strengths, duration of effect, dosing and administration, safety/AEs [adverse events] and list price per 50 units. Similar pages were also included for Azzalure New Syringe and Neuronox (product X RTU and Product Z, a not ready-to-use vial). The Appeal Board noted that under 'Dosing Forms and Strengths' it stated 'preservative-free 0.9% Sodium Chloride Injection USP'. The Appeal Board noted that USP was the abbreviation of 'United States Pharmacopoeia', and considered that this should have been modified for the UK audience.

The Appeal Board was concerned about the use of brand names in the market research survey in question. These were used for hypothetical formulations of existing medicines. The Appeal Board queried why these were necessary as they could have been named A,B or C etc. In that regard the Appeal Board noted that Neuronox was denoted as product X or Y depending on its configuration and yet it was still considered necessary to name its manufacturer and include product names. The Appeal Board also questioned whether it was necessary to mock up a hypothetical unlicensed profile of an existing medicine in such detail in the market research in question.

The Appeal Board did not accept Allergan's submission that it was made clear that participants were providing feedback on hypothetical scenarios. In this regard the phrase 'this may or may not be the actual profile at launch' implied that it was not a question of 'if' the product was to be launched but 'when'.

The Appeal Board considered that some of the questions and information were in effect promotional claims for example, stating that the Vistabel/Botox R2U vial 'Allows for flexibility and does not require reconstitution' and the use of coloured text which differentiated new products from existing products.

The Appeal Board considered that the market research would solicit interest in the botulinum toxins cited including R2U toxins and it was promotional in this regard. The Appeal Board considered that as the

material promoted Botox/Vistabel relevant prescribing information should have been included; as it was not, the Appeal Board upheld the Panel's ruling of a breach of Clause 4.1. The appeal on this point was unsuccessful.

2 Disguised promotional activity and payment

COMPLAINT

The complainant alleged that the material was presented as a 'study' and was clearly market research and not a 'study'. The complainant alleged that repeated use of its prescription only medicine's brand name within this market research by the pharmaceutical company constituted disguised promotion. The complainant further stated that presenting the material as a 'study', paying the participant for completing the market research and presenting arguments aiding a 'switch' from each of the other branded products to Azzalure constituted disguised promotion in breach of Clause 12.2.

RESPONSE

Allergan noted its general comments above at point 1. The complainant believed that the market research had been commissioned by another company whose brand was mentioned in the survey, and that the survey promoted this particular product. Whilst Allergan submitted that it could not comment on the alleged promotion of that product, it strongly disagreed that the market research was disguised promotion. The use of the term 'study' in the contact email was appropriate, the term 'study' and 'survey' were used interchangeably in the BHBIA Guidelines. Once participants clicked the link to the 'study', they were taken straight to the introductory screen of the survey which made it clear that it was a marketing research survey.

It was made clear to the participants that they were providing feedback on hypothetical scenarios and potential new products profiles which might (or might not) be the actual profile at launch. At the start of the survey some general questions were asked and it was clearly flagged that some questions might refer to uses for NTXs which were currently not authorized indications. The content of the research was in line with Sections 9.6 and 9.7 of the BHBIA Guidelines and did not constitute disguised promotion. Allergan denied a breach of Clause 12.2.

Noting the additional clauses cited by the Authority, Allergan submitted that the reimbursement offered (£65) was a reasonable compensation for the service provided. It was at a low level, proportionate to the time involved and appropriate to the respondent type and nature of the task. Allergan submitted that this sum would not be an inducement to prescribe, supply, administer, recommend buy or sell any of the products mentioned in the market research. Allergan denied a breach of Clause 18.1.

PANEL RULING

The Panel noted its general comments above at point 1 and that it considered that as the market research survey promoted Vistabel/Botox, the survey's promotional nature was disguised. A breach of Clause 12.2 was ruled.

The Panel did not, however, consider that the material advocated a switch as alleged. The Panel noted its comment above that the material solicited an interest in botulinum toxins including R2U vials and syringes but did not consider that it went beyond such solicitation and positively advocated a switch. In this regard, the complainant had cited Clause 12.2 of the Code and the Panel ruled no breach of that Clause accordingly.

The Panel noted its ruling above of a breach of Clause 12.2. The supplementary information to Clause 18.1, Payment to Individuals, stated that any payment for an activity ruled, *inter alia*, in breach of Clause 12.2 is likely to be viewed as an unacceptable payment. The Panel thus considered that the payment of £65 was contrary to requirements of Clause 18.1 and a breach of that Clause was ruled.

APPEAL BY ALLERGAN

Allergan submitted that the Panel considered that as the market research survey promoted Vistabel/Botox, its promotional nature was disguised. The Panel considered the payment of £65 was contrary to the requirements of the Code as the ruling of a breach of Clause 12.2 would lead to the breach of Clause 18.1.

Allergan submitted that the first screen shot of survey stated:

> 'Thank you for agreeing to participate in this survey. It is a 25 minute *marketing research* survey that we are conducting with a wide range of physician specialties. Your individual answers and identity will be kept confidential. Your opinions will be combined with those provided by others in order to make the best decisions possible. This *survey* is brought to you by [named agency], an independent marketing research firm.' (Italics added for emphasis).

Allergan submitted that it was thus clear from the outset as to the nature of the activity. The use of study in the contact email was also appropriate, as 'study' and 'survey' were used interchangeably in the BHBIA Guidelines. Once the link to the 'study' was clicked it took the participant directly to the introductory screen of the survey which made clear this was a marketing research survey as noted above.

Allergan submitted that the reimbursement of £65 was a reasonable compensation for the service provided. It was at a low level, proportionate to the time involved (25 minutes) and appropriate to the respondent type and nature of the task. This sum would not be an inducement to prescribe one or the other product. The Panel as such did not consider that the material advocated a switch as alleged by the complainant. BHBIA Guidelines, Section 8.24 stated as follows:

> 'Reimbursement (sometimes referred to as an incentive) is any benefit given to a respondent to

encourage their participation in a MR study and should be:
- Kept to a minimum level;
- Proportionate to the amount of their time involved;
- Appropriate to the respondent type and the nature of the task(s).'

Allergan noted that the Panel had noted that the complainant had assumed that the market research was commissioned by Galderma, which marketed Azzalure and that the survey promoted this product. By this, Allergan understood that the Panel had ruled Allergan in breach of Clause 12.2 of the Code for undertaking disguised promotion of a competitor product. Certainly, no complainant had alleged that the market research was disguised promotion of an Allergan product. Allergan queried how it could be found in breach of designing market research that promoted a competitor's product when this would clearly never have been its intention. Allergan had been found in breach of the Code for conducting disguised promotion of a product that competed with its product, subject to a complaint by someone who did not identify Allergan as the promoter, and in circumstances where Allergan clearly would not have had any intention to do so. No complaint had ever been received that Allergan had conducted some form of disguised promotion, and no evidence had been brought to the Panel's attention to suggest that the market research was regarded as disguised promotion, and so Allergan did not understand how the Panel could have reached this conclusion.

Allergan submitted that the complainant alleged and the Panel was concerned about the over use of brand names in the market research survey. Allergan had not used non-proprietary names because there were no differentiating non-proprietary names for the various marketed NTX products in the UK. This could be verified from the respective SPCs of the three products (Vistabel, Bocouture and Azzalure) in the UK. In addition, the various marketed NTX products each had unique characteristics and dosing. To prevent confusion between products it was important to allow respondents to distinguish between brands. The prime objective of the study was to understand the hypothetical use of a R2U vial or syringe for each branded toxin in addition to the current vial.

Furthermore, Allergan submitted that an analysis of the questionnaire provided counts for the number of times each brand appeared associated with a hypothetical or potential new product at each question. The noted questions and counts were:

- Q11. Azzalure was always presented first and was seen by n = 119; no other brands presented at this point.

The Vistabel/Botox brand was presented either second or third, depending on the market scenario selected for the respondent and rotated with the Products X and Z (Medytox / Neuronox branded product):

- Q28b. 60 respondents saw Vistabel before seeing the products X or Z
- Q39b. 59 respondents saw Vistabel after the products X or Z.

Thus, Allergan submitted that looking across both Q28b and Q39b, the Vistabel/Botox brand was presented 119 times, the same number of times as the Azzalure brand and the Korean brand product. Therefore, it was appropriate to use brand names in the survey to allow respondents to correctly respond without confusion. Additionally respondents were exposed to a balanced number of brand names so no one brand was seen more than another. This was further supported by BHBIA Guidelines which stated that brand names could be used when this was essential to the objectives of the research. Section 9.4.1 stated:

'Avoid unnecessary or repeated use of brand names, use 'Product X' unless:
- Reaction to the name or its visual representation is an objective;
- Use of a name is essential to the interpretation of the stimulus, and this is in turn, essential to the study objectives;
- A specific product needs to be referenced e.g. in brand tracking. If possible, include other brand names, as comparators, to blind the subject's identity and so reduce the risk of promotion.'

Allergan submitted that an objective of the survey was to model potential future market scenarios so respondents had to see brand names multiple times. These scenarios that were being determined were:

- Azzalure/Dysport launches first and is the only new R2U NTX in the market
- Azzalure/Dysport launches first and there are two R2U NTX in the market – either Botox R2U or South Korean R2U (assesses order of entry impacts, given branding)
- Dysport launches first and there are three R2U NTX in the market – Botox R2U and South Korean R2U alternating which is the second entrant (assesses order of entry impacts, given branding)
- A low cost NTX from a South Korean company launches fourth.

Allergan submitted that for the research methodology to model all potential scenarios respondents had to see a total of nine product combinations. The methodology used was a discrete choice modeling technique which was typically used to study physician future demand and to predict their responses to a number of hypothetical situations, enabling researchers to forecast the impact of a range of factors such as pricing, product development, and demand etc.

Allergan submitted that this methodology relied on presenting multiple scenarios to respondents to collect sufficient information to build a predictive model. For a discrete choice model, the choice set must meet the following key requirements:

- The set of alternatives must be exhaustive, meaning that the set included all possible alternatives. This requirement implied that the person necessarily chose an alternative from the set.

- The alternatives must be mutually exclusive, meaning that choosing one alternative meant not choosing any other alternatives. This requirement implied that the person chose only one alternative from the set.
- The set must contain a finite number of alternatives.

Allergan submitted the nature of methodology, in the absence of any differentiation with molecule/generic names, required using brand names. Therefore it was appropriate to use brand names in the survey multiple times to allow the survey objectives to be met.

Allergan submitted that the market research questioned 119 UK participants. Sample selection was aimed to represent different specialty groups including dermatologists, plastic/cosmetic surgeons, aesthetic medicine doctors and nurses practising in the cosmetic area. Aesthetic medicine doctors included medical doctors of any primary speciality and dentists practising cosmetic medicine/injecting NTXs. Based on the primary and desk research undertaken by Allergan Inc third party suppliers to determine number of injectors by specialty groups, it showed that this group included a number of different primary specialties including general practitioners.

Allergan submitted that in total, the sample represented 2% of the neurotoxins' cosmetic injector universe, and the sample size only allowed it to analyse results for the total sample (n=119) in a statistically meaningful way, predicting validity of responses with an error margin of up to +/- 9.02% (at 95% confidence interval), but not for different injector groups mentioned above. Considering these factors, a sample of 119 was not unnecessarily large for the objectives of the research. Allergan provided details of the estimated total number of NTX injectors in the UK by speciality group and the percentage of each group included in the survey.

Allergan noted that the BHBIA Guidelines in Section 7b on sample size stated:

- 7.2 The size of the sample must be limited to that necessary to achieve only the objectives of the MR and should be consistent with the nature of the MR undertaken.
- 7.3 There are no fixed guidelines on sample size; this will vary by objective, universe size, analysis requirements, and the level of statistical confidence required. However, if the universe is 800, a sample of 400 could be deemed excessive.
- 7.4 If the sample size is unnecessarily large, the MR may be misconstrued as 'disguised promotion'.

Allergan submitted that as noted above, the survey methodology was discrete choice which required a robust sample to allow study statisticians to build models to simulate the market. Based on the screening methodology all respondents that entered into the survey must be seeing and treating cosmetic patients. Additionally all nurses and physician non-injectors that were not interested in providing aesthetic treatments were screened out. This ensured that all participants were legitimate potential users of NTXs for aesthetic purposes independent of their specialty focus. Therefore it was appropriate to the size of the sample collected across respondent groups to meet the objective of the survey.

Given the points noted above, Allergan did not consider that this was disguised promotion and the payment unacceptable. The company denied breaches of Clauses 12.2 and 18.1.

COMMENTS FROM THE COMPLAINANT

Please see the complainant's comments above (point 1).

APPEAL BOARD RULING

The Appeal Board noted its general comments above at point 1 and that it considered that as the market research survey promoted Vistabel/Botox, the survey's promotional nature was disguised. The Appeal Board upheld the Panel's ruling of a breach of Clause 12.2. The appeal on this point was unsuccessful.

The Appeal Board noted its ruling above of a breach of Clause 12.2. The supplementary information to Clause 18.1, Payment to Individuals, stated that any payment for an activity ruled, *inter alia*, in breach of Clause 12.2 was likely to be viewed as an unacceptable payment. The Appeal Board thus considered that the payment of £65 was contrary to requirements of Clause 18.1 and the Appeal Board upheld the Panel's ruling of a breach of that clause. The appeal on this point was unsuccessful.

3 OUT OF LICENCE PROMOTION

COMPLAINT

The complainant was concerned that nurses had been targeted to participate in the market research. The indications for all botulinum toxins were the same and Section 4.2 of the Azzalure SPC read 'Azzalure should only be administered by physicians with appropriate qualifications and expertise in this treatment and having the required equipment'. The complainant submitted that solicited feedback from nurses was therefore solicited feedback from an out of licence group of individuals. The complainant stated that mention of the brand name, Azzalure, comprised 'promotion' and consequently solicited feedback from an out of licence audience on a product referred to by its brand name constituted out of license promotion in breach of Clause 3.2.

Lastly, the complainant was concerned that the use of the brand name and a presentation of the product carrying the Azzalure brand name which was not yet available on the market constituted pre-licence promotion in breach of Clause 3.1.

RESPONSE

Allergan stated that nurse injectors were selected to participate in the survey so that, together, the respondents reflected the range of specialties of the target population in the UK which might use a R2U NTX.

The legislation surrounding the administration of injectable medicines (such as NTX's) in cosmetic procedures was outlined briefly in a document issued by the MHRA (Frequently asked questions [FAQ]: Supply and administration of Botox, Vistabel, Dysport and other injectable medicines outside their licensed uses such as in cosmetic procedures – November 2012). The MHRA had stated that injectable medication for cosmetic procedures such as NTXs might be: self-administered; administered by an appropriate practitioner (eg doctor, dentist, independent nurse prescriber) or administered by anyone in accordance with the directions of an appropriate practitioner eg a nurse. The prescriber (eg a doctor, dentist or an independent nurse prescriber) had a responsibility to the patient for whom he/she provided a prescription.

Allergan submitted that the selection of nurse injectors to participate in the market research was thus appropriate. More importantly, the market research was not a promotional activity, and therefore did not promote in a manner inconsistent with the SPC and it was not in breach of Clause 3.2.

Allergan submitted that finally, as the market research survey was not promotional it did not agree that it promoted a presentation of a product prior to the grant of its marketing authorisation.

It was made clear to the participants that they were providing feedback on hypothetical scenarios and potential new products profiles which might (or might not) be the actual profile at launch. The content of the research was in line with Sections 9.6 and 9.7 of the BHBIA Guidelines and did not constitute disguised promotion. Therefore, the research was not in breach of Clause 3.2.

In summary, Allergan stated that this market research was conducted properly and in accordance with BHBIA Guidelines. The market research material was examined by two final signatories registered with the PMCPA, in line with Section 9.10 of the BHBIA Guidelines and the supplementary information to Clause 14.3 of the Code. Allergan considered that the survey was appropriately conducted, non-promotional, market research. Allergan denied any breach of the Code including Clauses 9.1 and 2.

PANEL RULING

The Panel noted that the complainant referred to Azzalure in relation to the alleged breach of Clause 3.2. The Panel noted its comment above about the basis upon which it was considering this complaint; namely in relation to Vistabel/Botox. The Panel noted that Section 4.1, Therapeutic Indications, of the Vistabel/Botox SPCs stated that they were indicated for the temporary improvement in the appearance of moderate to severe vertical lines between the eyebrows seen at frown (glabellar lines), in adults <65 years old when the severity of these lines had an important psychological impact for the patient. In addition, Botox had non-cosmetic indications. Section 4.2 of each SPC required that Vistabel/ Botox should only be administered by physicians with appropriate qualifications and expertise in the treatment and use of the required equipment. The Panel also noted that the MHRA FAQ document cited by Allergan noted general cosmetic use was outside the licensed indication of Botox and Vistabel. Further, the document noted that for cosmetic use, these medicines could be administered by an appropriate practitioner or anyone acting in accordance with the directions of an appropriate practitioner. An appropriate practitioner was defined as a doctor, a dentist or, subject to certain limitations, *inter alia*, a nurse or pharmacist.

The Panel noted the complainant's concern about the participation of nurses. The Panel was also particularly concerned that some nurses were selected to participate because they were recommended for participation by nurse colleagues. The Panel noted the market research had been sent, *inter alia*, to 30 aesthetic nurse injectors. It had also been sent to 30 non injectors all of whom were physicians who would consider a facial aesthetic practice. In addition 40 non-core respondents had received the material including those in ophthalmology and gynaecology and emergency medicine.

The Panel noted that the market research solely covered cosmetic use of the products. Question 1 stated that some questions might refer to uses for all NTXs which were currently not authorized indications. Participants were referred to the prescribing information of each product as to licensed indications. Question 1 referred to the injection of forehead lines, glabellar lines, crows feet, bunny lines, under eyes and lateral eyebrows. The Panel considered that the market research therefore covered the unlicensed use of Vistabel and Botox.

The Panel noted the requirements in the Code for market research as set out above at point 1. Bona fide market research should always be non-promotional. The Panel noted its finding at point 1 that the material was promotional and its comments on the products' licensed indications above and the role and participation of aesthetic nurse injectors. The Panel considered that the provision of the material to aesthetic nurse injectors therefore, promoted Botox/Vistabel for an unlicensed indication as alleged. A breach of Clause 3.2 was ruled.

The Panel noted that it had to consider the allegation about the pre-licence promotion of Azzalure in relation to, *inter alia*, Botox. The Panel noted that the material presented detailed information on and solicited interest in a Botox R2U, single-use vial and syringe. Neither medicine had a licence and thus the Panel considered that they were each promoted contrary to Clause 3.1. A breach of that clause was ruled.

The Panel noted Allergan's disclosure that it had entered into a licensing agreement with a Korean company, Medytox, to develop and, if approved, commercialize certain NTX products including a potential liquid injectable product. The Panel noted that the products in question were in the mid stages of development. The Panel considered that the survey was, nonetheless, promotional for these unlicensed products referred to in the survey

as products X and Z. Comparative claims for both products vs Vistabel/Botox were included. A breach of Clause 3.1 was ruled.

The Panel noted its rulings above and considered that high standards had not been maintained. A breach of Clause 9.1 was ruled. Overall, the Panel was very concerned about the market research. The Panel noted its comments about the promotional nature of the material which had been circulated to 120 UK health professionals. The Panel considered that to pay health professionals to participate in a promotional activity brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled.

The Panel noted its rulings and comments above. The Panel was especially concerned that, in the first instance, it had received incorrect and misleading information. In response to the Panel's question 'Is Allergan Inc researching/developing a ready-to-use neurotoxin?', the company had unambiguously stated that it was not. Allergan subsequently disclosed relevant and contrary information about the activity of Allergan Inc. Allergan had not fully explained why its two submissions were contradictory. In addition the Panel was concerned that the market research was promotional and solicited interest in, *inter alia*, unlicensed medicines. Participants had been paid for their time. The Panel noted that the Authority had previously been concerned about the activity of Allergan and market research in Case AUTH/2274/10/09. Taking all the circumstances into account, the Panel decided to report Allergan to the Code of Practice Appeal Board under Paragraph 8.2 of the Constitution and Procedure for it to decide whether the imposition of further sanctions was appropriate.

APPEAL BY ALLERGAN

Allergan noted the Panel's concern about the participation of nurses and non injectors in the market research activity and that the market research covered the unlicensed use of Botox and Vistabel.

Allergan submitted that nurse injectors were one of the groups selected to ensure distribution of respondents across a range of specialties reflective of the target population in the UK which might use a R2U NTX. This was based on the primary and desk research undertaken by Allergan Inc third party suppliers to determine the number of injectors by specialty groups. It showed that this group included a number of different primary specialties including general practitioners.

Allergan again noted that the legislation surrounding the administration of injectable medicines (such as NTXs) in cosmetic procedures was outlined in the MHRA FAQ document which stated that injectable medicine for cosmetic procedures such as NTXs might be: self-administered; administered by an appropriate practitioner (e.g. doctor, dentist, independent nurse prescriber) or administered by anyone in accordance with the directions of an appropriate practitioner eg a nurse.
Allergan reiterated that the appropriate practitioner (eg a doctor, dentist or an independent nurse prescriber) who prescribed the NTX had a responsibility to the patient for whom he/she had provided a prescription. Therefore, the selection of nurse injectors to participate in the market research was appropriate.

Allergan submitted that the Panel had noted that the MHRA FAQ document stated that the general cosmetic use was outside the licensed indication of Botox and Vistabel. For cosmetic use, these medicines could be administered by an appropriate practitioner or anyone acting in accordance with the directions of an appropriate practitioner. An appropriate practitioner in the MHRA FAQ document was defined as a doctor, dentist or, subject to certain limitations, a nurse or pharmacist.

Allergan submitted that an objective of the survey was to ascertain the likelihood of aesthetic injectors using a R2U NTX (replace usage from the current version that required reconstitution) and to find out if non-neurotoxin aesthetic providers would use NTXs if one that required no reconstitution was available in the future. Allergan submitted that based on the screening methodology all respondents entered into the survey must have seen and treated cosmetic patients. Additionally all nurses and physician non-injectors that were not interested in providing aesthetic treatments were screened out. This ensured that all participants in the survey were legitimate potential users of NTXs for aesthetic purposes independent of their specialty focus.

Allergan submitted that to help find additional aesthetic nurse injectors, identified nurses were asked to refer potential candidates for the research. Only eight nurses out of 29 who participated in the survey were recruited through referral. However all respondents had to go through the screening criteria to enter the survey. Therefore, it was appropriate to use the respondent groups in the survey as they all currently treated aesthetic patients in their practice and could have opted out of the survey.

Allergan submitted that the current injectors of NTXs were screened into the survey if they met the following criteria:

- Must be a physician, nurse practitioner, physician assistant or registered nurse
- More than 75% of clinical practice time spent seeing patients (screener question 6)
- Must typically see at least 10 patients a month for cosmetic consultants and/or treatment
- Must personally inject at least 2 patients per typical month with a NTX for cosmetic consultation and/or treatment
- Must know about Vistabel or Botox
- Nurse injectors who indicated that they were not interested in providing aesthetic treatments in their practice were screened out.

Moreover current non-injectors of NTX were screened into the survey if they met the following criteria:

- Must be a physician – excluded all nurse

practitioners, physician assistants or registered nurses from the non-user sample
- More than 75% of clinical practice time spent seeing patients
- Must typically see at least 10 patients a month for cosmetic consultants and/or treatment – must see at least 10 patients matching this criteria
- Must not currently inject patients with NTX for cosmetic treatment
- Must know about Vistabel or Botox
- Physicians who indicated that they were not interested in providing aesthetic treatments in their practice were screened out.

Allergan submitted that questions which related to current usage were only asked of current injectors and they were warned that:

> 'Some questions may refer to uses for all neurotoxins which are currently not authorised indications. Please always refer to the prescribing information of each product as to licensed indications.'

These questions were only asked to understand if a R2U syringe was made available, what size would be most appropriate for further development as this related to the cost of the product and wastage as a R2U syringe would not be suitable for multiple uses. The intent was never to solicit off-label usage of NTXs for off-label indications. Therefore, it was appropriate to the objective of the survey to collect usage data from current users of NTXs.

Given the points noted above, Allergan did not consider that the market research was out of licence promotion and it denied breaches of Clauses 3.1 and 3.2.

Allergan noted that the Panel was very concerned about the market research and that it had received incorrect and misleading information.

Allergan was extremely disappointed that despite sharing all the information as soon as it was available, the Panel considered that it had received contradictory information. Allergan informed the Panel as soon as an announcement about a possible licensing agreement become public and known to staff in the UK. The reviewers were aware that the research was designed to help the company make strategic business decisions about whether or not to develop an R2U formulation in-house or as it transpired consider entering into such an in-licensing agreement with a third party. However they were not aware of the potential or actual Medytox deal until this was announced on 25 September 2013 with an internal communication to all Allergan employees.

Allergan again noted that it knew that Azzalure/Dysport was being researched/developed for a R2U formulation. According to www.clinicaltrials.gov there were two studies, a Phase III trial in cervical dystonia which was active (but not recruiting) and a completed Phase II trial in glabellar lines. Both of these studies were with Dysport RU. This information was the basis of a potential strategic business decision and in order to help make that informed choice, market research was conducted. The same information was duly shared with the Panel.

As noted above, initial market research into R2U formulations started in January 2013 with research in the US which was expanded to other markets. The material was reviewed and approved for use in UK on 26 April. UK field work took place between 13 May and 19 June. Allergan personnel involved in review, conduct and response to the complaint did not know about the Medytox deal until it was publicly announced on 25 September by Allergan Inc; this information was accordingly shared with the Panel on 1 October.

Allergan submitted that due to the sensitive financial nature of these business in-licensing and/or acquisition deals and their potential impact on the value and stock prices, the information was kept confidential and limited to a core group of Allergan Inc senior executives. Many times the business intelligence and market research teams were asked to provide information and data to support business decision making without knowing the exact nature of any potential business deal. Frequently, as a result of the information gathered, the deals might not be reached. This was a usual business practice and not limited to Allergan or the pharmaceutical industry.

Allergan submitted that at least one of the formulations was not hypothetical as it knew that Dysport/Azzalure was in development and currently in Phase III. It noted however that none of the products were currently available and were not likely to be in the near future. The market research was designed to seek opinions on products that might reasonably be expected to be available in the future. Allergan Inc aimed to assess the potential of a product which still had to enter late phase clinical studies. The intent was to establish the need for strategic future acquisition or partnering or in-house development and required the use of different brand names to effectively assess if the availability of specific brands in a R2U format would differ depending on the specific brand and timing of entry in the market. It was certainly not promotional in intent from Allergan and even the complainant initially considered the survey was commissioned by Galderma for Azzalure.

Allergan submitted that data on the current number of patients treated with NTXs in selected areas of the face, including typical volume used in each area, were collected as a baseline reference against which to evaluate changes.

Allergan outlined the survey design and the composition and size of the sample. Allergan submitted that all the physicians were part of a market research panel of physicians who had agreed to receive solicitations for, and participate in, market research. The numbers selected from each specialty grouping was small; the largest group size was 67 (aesthetic medicine doctors) and covered a

very broad range of specialties based on previous research and available data.

Twenty one of the nurse injectors were recruited from market research panels however, due to the difficulty in recruiting the required number, those UK nurses who completed the survey were asked to refer other nurses. Eight UK nurse respondents were thus recruited through referral and consent to participate in market research was obtained before they were invited to participate. All respondents who came in via the survey link saw the landing page with the terms and conditions that 'opt in' the respondent to participate in market research. The terms and conditions page outlined everything that participation in market research entailed and how their responses/data would be used.

Allergan submitted that, as stated above, it was essential that brand names were included in this market research in order to achieve the specific objective. This use of brand names in the research was in line with Section 9.4.1 of the BHBIA Guidelines and did not constitute disguised promotion as noted below:

9.4.1 **Avoid unnecessary or repeated use of brand names**, use 'Product X' unless:
- Reaction to the name or its visual representation is an objective;
- Use of a name is essential to the interpretation of the stimulus, and this is in turn, essential to the study objectives;
- A specific product needs to be referenced eg in brand tracking. If possible, include other brand names, as comparators, to blind the subject's identity and so reduce the risk of promotion.

Allergan submitted that the questions regarding the R2U products were constructed within a market evolution discrete choice framework. The factors to be assessed were presented to participants in a systematic fashion to assess market impacts. When applicable, it was made clear to the participants that they were providing feedback on hypothetical scenarios and potential new products profiles which might (or might not) be the actual profile at launch. The survey started with some general questions. It was clearly stated that some questions might refer to uses for NTXs which were currently not authorized indications. The content of the research was in line with Sections 9.2 and 9.3 of the BHBIA Guidelines and did not constitute disguised promotion as noted below:

9b Disguised Promotion
Instrument and stimulus design
9.2 **No attempt must be made to influence respondents' opinions or behaviours through the design of the questionnaire, the guide, or the stimulus materials.** This is often referred to as 'disguised promotion', 'selling under the guise of' or 'sugging'. The ABPI Code of Practice 2011 states within Clause 12.2 that: 'MR activities … must not be disguised promotion'.

Impact of the MR
9.3 **Respondents must not be expected, or asked, to make any commitment to change their attitudes or behaviour as a result of the MR**. However, it is reasonable to ask respondents whether a change could hypothetically be possible. This questioning may well be required in new product or sales aid testing e.g. If this product was available and performed as described, would you…..?

Given the points noted above, Allergan did not consider that the rulings of a breach of Clause 2 and 9.1 and the report to the Appeal Board was warranted.

Allergan submitted that since 2009 it had gone beyond the Code requirements to have market research examined including review and approval by two signatories. This check primarily ensured that any proposal was genuine market research, was not promotional and adhered to the relevant Code and industry requirements. Allergan believed this was the case here.

Allergan was very disappointed that its attempt to show complete transparency by providing the Panel with a corporate press release as soon as it became available, had been misinterpreted.

Allergan submitted that this was a piece of genuine market research, it was not promotional and that high standards had been maintained. Allergan denied any breach of the Code.

COMMENTS FROM THE COMPLAINANT

The complainant referred to his comments at point 1 above.

APPEAL BOARD RULING

The Appeal Board noted its finding at point 1 that the material was promotional. The Appeal Board noted that the Allergan representatives could not confirm that the 29 nurses who took the survey were prescribers and suggested that some might administer under the direction of a doctor.

The Appeal Board noted and agreed with the Panel's concerns and comments on the products' licensed indications and the role and participation of aesthetic nurse injectors and decided that the survey promoted Botox/Vistabel for an unlicensed indication as alleged. The Appeal Board upheld the Panel's ruling of a breach of Clause 3.2. The appeal on this point was unsuccessful.

The Appeal Board noted that the material presented detailed information on and solicited interest in an Azzalure and Botox R2U, single-use vial and syringe. Neither medicine had a licence and thus the Appeal Board considered that this promoted the Botox R2U, single use vial and syringe contrary to Clause 3.1, and the Appeal Board upheld the Panel's ruling of a breach of that clause. The appeal on this point was unsuccessful.

The Appeal Board noted Allergan's disclosure that it had entered into a licensing agreement with a South Korean company, Medytox, to develop and, if approved, commercialize certain NTX products including a potential liquid injectable product. The survey was promotional for these unlicensed products referred to in the survey as products X and Z. Comparative claims for both products vs Vistabel/ Botox were included. The Appeal Board upheld the Panel's ruling of a breach of Clause 3.1. The appeal on this point was unsuccessful.

The Appeal Board noted that Allergan UK was instructed to undertake the market research by its US parent company. In the Appeal Board's view, when Allergan examined the survey before use it should have changed it to ensure compliance with the Code.

The Appeal Board noted its rulings above and considered that high standards had not been maintained and it upheld the Panel's ruling of a breach of Clause 9.1. The appeal on this point was unsuccessful.

The Appeal Board noted Allergan's submission that when it made its first submission, no-one in the UK knew anything of the Allergan Inc/Medytox deal. As such negotiations were commercially very sensitive, they were only known to a limited number of very senior employees in the parent organization. As soon as the deal was made public, Allergan had updated the Panel on the position. The Appeal Board noted that market research would often inform commercial decisions but that when conducting such research on the potential of new products, companies had to be extremely careful not to be seen to promote a medicine before the grant of a marketing authorization. In the Appeal Board's view the impact of market research on the participants was important and in that regard it noted that the complainant had considered that the survey at issue was promotional. Nonetheless, the Appeal Board considered that the survey had set out to answer some legitimate business questions and although noting its rulings above, the Appeal Board did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was reserved as a sign of particular censure. No breach of Clause 2 was ruled. The appeal on this point was successful.

With regard to the Panel's report to the Appeal Board in accordance with Paragraph 8.2 of the Constitution and Procedure, the Appeal Board noted its rulings above, and in particular the ruling of no breach of Clause 2, and considered that no further action was required.

Complaint received **4 July 2013**

Case completed **25 January 2014**