CASE AUTH/2274/10/09

CONSULTANT NEUROLOGIST v ALLERGAN

Marketing survey

A consultant neurologist complained about a survey headed 'Neurology Pharmaceutical Survey' sent by a market research agency which consisted of two pages of 22 questions and sub-questions. Nine questions, ie all but one, on page 2 related to the use of botulinum toxin injections. Six of the questions specifically referred to the use of botulinum toxin injections for the treatment of primary headache or migraine.

The accompanying letter from the agency described the survey as a marketing study on the management of primary headache and migraine conditions. It was being carried out on behalf of a pharmaceutical company which had a specific interest in individual clinicians' treatment practice in this therapy area. The letter further stated that as this was a marketing study as opposed to a market research study participants would be identifiable to the company commissioning the research. A cheque for £35 was included.

The identity of the commissioning pharmaceutical company was not clear from the documentation. The agency confirmed that it was Allergan. Allergan marketed Botox (botulinum toxin). Botox was not licensed for the treatment of primary headache or migraine.

The complainant provided a copy of the material at issue, together with part of a poster of the more successful trial presented at the recent International Headache Society (IHS) meeting in Philadelphia (Dodick *et al* 2009). The complainant found it hard to believe that 'marketing study' was not a means of assembling large numbers of willing users of the medicine before the National Institute for Health and Clinical Excellence (NICE) had established whether the modest (though mathematically significant) improvement over the effect of placebo was cost-effective.

The complainant queried whether Allergan (through its agent) had strayed over the boundaries of honest promotion.

The detailed response from Allergan is given below.

The Panel noted Allergan's submission that the purpose of the survey was to seek information and opinion from senior health professionals actively involved in the management of primary headache and migraine. The information gained would ensure that Allergan's communications were effectively targeted. Allergan did not argue that the survey was market research outside the scope of the Code but described it as a marketing survey as the participants would be identified to the company. Allergan had examined the survey in relation to the requirements of the Code as non promotional material.

The Panel noted that most of the questions on page 2 of the survey referred to the use of botulinum toxin injections. Six of the questions referred to the use of such injections for the treatment of primary headache or migraine. One question asked which was the respondent's preferred brand and named each botulinum toxin injection brand available in the UK. Another question similarly named all the brands. None of the botulinum toxin injections currently marketed were licensed for the treatment of primary headache or migraine. Question 19a asked 'Are you currently aware of the use of botulinum toxins for any type of primary headache or migraine?'. Question 22 asked clinicians to choose which one of four statements best described their usage intentions of botulinum toxins for headaches/migraine assuming that such a use was officially approved. The third statement read 'I am not interested in trying botulinum toxins for headache/migraine patients, neither injecting them or referring them, unless they become a very common and successful treatment for headache/migraine'. The Panel considered that the nature of the questions and the survey's broad distribution to over 800 clinicians was such that it went beyond merely seeking information and opinion from senior clinicians actively involved in the management of primary headache and migraine conditions as submitted by Allergan. The questions would stimulate interest in the use of botulinum injections for an unlicensed indication. In the Panel's view the survey was a marketing tool which was subject to the Code.

The Panel noted the complainant's primary concern regarding the lack of NICE guidance about the use of botulinum toxins to treat primary headache or migraine but noted that providing the relevant marketing authorization had been granted medicines could be promoted before NICE guidance on their use had been issued. Similarly, the promotion of medicines did not have to be in accordance with any such guidance. In this regard the Panel did not consider that Allergan had failed to maintain high standards as alleged. No breach of the Code was ruled.

The Panel noted that the complainant had also made a broader allegation about the boundaries of honest medicine promotion. The Panel considered that the survey would stimulate interest in the use of botulinum toxins as a class for primary headache or migraine although none of the products

currently marketed were licensed for such use. A clinical study into such use had been presented at the 2009 IHS meeting and Allergan was planning a US licence extension for Botox to include migraine. The survey did not give disproportionate weight to any specific botulinum toxin. The Panel considered that in so much as the survey promoted all botulinum toxins it also promoted Botox. If this were not the case then the effect would be for companies to promote classes of medicines as a means of avoiding the restrictions in the Code. The Panel considered that the survey promoted Botox in a manner which was inconsistent with the particulars listed in its summary of product characteristics (SPC). A breach of the Code was ruled, which was upheld on appeal by Allergan. Botox did have a marketing authorization and so in that regard the Panel ruled no breach of the Code.

The Panel considered that the material at issue promoted botulinum toxins in the guise of a survey. In that regard the promotional activity was disguised and the Panel ruled a breach of the Code, which was upheld on appeal by Allergan. The Panel noted its ruling that the survey was promotional material. It thus followed that it was not a market research activity or the like as referred to the Code. No breach of the Code was ruled.

The Panel considered that given the survey was not a market research activity but promotional and solicited an interest in unlicensed indications the attached cheque for £35 was wholly inappropriate. A breach of the Code was ruled. Upon appeal by Allergan the Appeal Board was concerned that the payment of a fee for completing a study that was ruled in breach of the Code was unacceptable. However the Appeal Board considered that the payment of £35 was not in itself an inducement to prescribe Botox. Thus no breach of the Code was ruled.

The Panel considered that, overall, high standards had not been maintained. A breach of the Code was ruled, which was upheld on appeal by Allergan. The Panel further considered that the content and distribution of the marketing study were such as to bring discredit upon, or reduce confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled. Upon appeal by Allergan the Appeal Board did not consider the circumstances were such as to bring discredit upon, or reduce confidence in, the pharmaceutical industry. No breach of Clause 2 was ruled.

The Panel was very concerned about all the arrangements for the survey and noted that over 800 clinicians had each been sent £35. In the Panel's view the cheque would encourage them to read and complete the marketing study which promoted a class of products for an unlicensed indication. The Panel reported Allergan to the Code of Practice Appeal Board in accordance with Paragraph 8.2 of the Constitution and Procedure. Given its rulings above, however, the Appeal Board decided to take no further action.

A consultant neurologist complained about a survey headed 'Neurology Pharmaceutical Survey' sent by a market research agency which consisted of two pages of 22 questions and sub-questions. Nine questions, ie all but one, on page 2 related to the use of botulinum toxin injections. Six of the questions specifically referred to the use of botulinum toxin injections for the treatment of primary headache or migraine.

The accompanying letter from the agency described the survey as a marketing study on the management of primary headache and migraine conditions. It was being carried out on behalf of a pharmaceutical company which had a specific interest in individual clinicians' treatment practice in this therapy area. The letter further stated that as this was a marketing study as opposed to a market research study participants would be identifiable to the company commissioning the research. A cheque for £35 was also included.

Allergan marketed Botox (botulinum toxin). Botox was not licensed for the treatment of primary headache or migraine.

COMPLAINT

The complainant provided a copy of the material at issue, together with part of a poster of the more successful trial presented at the recent International Headache Society (IHS) meeting in Philadelphia (Dodick *et al* 2009). The complainant found it hard to believe this that 'marketing study' was not a means of assembling large numbers of willing users of the medicine before the National Institute for Health and Clinical Excellence (NICE) had established whether the modest (though mathematically significant) improvement over the effect of placebo was cost-effective.
The complainant queried whether Allergan (through its agent) had strayed over the boundaries of honest promotion.

The identity of the commissioning pharmaceutical company was not clear from the documentation. The agency confirmed that it was Allergan Limited.

When writing to Allergan the Authority asked it to respond in relation to Clauses 2, 3.1, 3.2, 9.1, 12.1, 12.2 and 18.1 of the Code.

RESPONSE

Allergan submitted that the Neurology Pharmaceutical Survey was not a promotional activity. These types of surveys were routinely undertaken in the UK and Europe by many pharmaceutical companies and other healthcare organisations. They were designed to gain market intelligence to enable companies to communicate effectively with health professionals with the aim of minimising irrelevant approaches by pharmaceutical personnel. Allergan provided a statement from the agency which gave additional background information on this matter.

The complainant alleged there was some link between data presented at the recent IHS meeting in Philadelphia and the survey. The poster provided by the complainant was not enclosed with the survey. No clinical data was enclosed with the survey and there was no reference or link to clinical results of any kind in either the letter or the survey.

Allergan commissioned the Neurology Pharmaceutical Survey to seek information and opinions from senior health professionals actively involved in the management of primary headache and migraine conditions. Allergan would use the information to develop a deeper understanding of the market and assist with the communication and development of its products and services in this area. It would enable Allergan, in the future, to communicate more effectively with health professionals and ensure these communications were effectively targeted. Whilst some of the information provided might assist in the way products or services were marketed, this did not make the survey promotional.

The survey was conducted in accordance with the British Market Research Society (MRS) regulations, 'Using Research Techniques for Non-Research Purposes'. To comply with these regulations the survey was termed a marketing study rather than a market research study. The distinction between market research and marketing studies was made as a result of data protection considerations.

A market research study aimed to gather market intelligence from a selected group of individuals. Typically an agency contacted individual respondents directly to ask various questions. The answers were not reported back in named form to the sponsor, rather the data was aggregated. Market research was by its nature therefore confidential. The market research community commonly accepted that where a survey was not confidential, ie the sponsor wished to see identified results, then this should not be termed market research. Therefore, the letter to potential participants stated that the survey was 'a marketing study as opposed to a market research study'. The sole reason for this was that participating health professionals would be identifiable to Allergan. It was important from a data protection perspective that the potential participants knew this before they participated in the survey.

The survey and letter were sent to 805 senior neurologists in the UK (14 of whom were professors).

Further contact with recipients depended on their response to the data protection notice at the bottom of the survey. If they opted in and agreed to potential contact to undertake further surveys of this type (ie marketing studies) in the future, then Allergan could conduct further surveys, should it choose to, although none were planned.

Allergan did not believe the survey itself was promotional. The survey was not disguised promotion, it was a legitimate way to gain market intelligence regarding current practice around the treatment and understanding of primary headache and chronic migraine conditions. Therefore, the survey was not in breach of either Clause 12.1 or 12.2.

The questions aimed to obtain detailed market intelligence regarding current practice around the treatment and understanding of primary headache and chronic migraine conditions. There was limited mention of brand names in the survey, only when the question specifically required it (questions 17 and 18 only). Where product was mentioned it was balanced fairly across all brands currently available and did not focus on a specific one vs its competitors. In addition, participants would not know which company commissioned the survey. Allergan denied breaches of Clauses 3.1 and 3.2.

Regarding payment, cheques for £35, addressed to individual doctors, were enclosed with the survey. The reason for enclosing the cheque was explained to the potential participant in the accompanying letter. This approach was widely used for market research or market study surveys to overcome the main problem of some participants not receiving their honorarium, or not receiving it quickly enough. Potential respondents were asked to dispose of the cheque if they were not interested in participating.

The amount paid (£35) was calculated in line with the European Pharmaceutical Market Research Association (EphMRA) Pharmaceutical Market Research Code of Conduct (Clause 3.1) which stated that:

> 'Where an interview is conducted with a 'professional' respondent such as a doctor, or with a member of staff of an organisation such as a hospital, it may be necessary and appropriate to recompense that person or organisation for the amount of their working time taken up by the interview. Such incentives or rewards to respondents should be kept to a minimum level proportionate to the amount of their time involved, and should not be more than the normal hourly fee charged by that person for their professional consultancy or advice.'

Allergan did not consider the payment of £35 was an inducement. Firstly, the survey was not linked to a particular product; there was limited mention of any brand names and where a brand was mentioned, it was balanced fairly across all those currently available and did not focus on a specific one vs its competitors. In addition, participants would not know which company commissioned the survey. £35 was an appropriate recompense for the time required to undertake the survey; it was in line with the EphMRA Code of Conduct. The letter accompanying the survey asked the recipient to dispose of the cheque and questionnaire if they did not wish to participate. Therefore, the survey was

not in breach of Clause 18.1.

Allergan was confident that this activity was not in breach of the Code and, in particular, was not in breach of either Clause 9.1 or Clause 2.

The survey was examined by two senior employees of Allergan, as required by the supplementary information to Clause 14.3 – Examination of Other Material. The survey was considered to comply with the specific requirements of the Code. This item was examined, rather than certified.

In summary, Allergan re-iterated that the scientific data included by the complainant was not enclosed with the survey and was not linked to the survey. The survey was not promotional in nature; it was conducted in accordance with British MRS Regulations. In order to comply with these regulations the survey was termed a marketing study rather than a market research study due to data protection considerations. The agency had run this type of survey for three years with a number of pharmaceutical companies.

In response to a request for further information Allergan stated that there was no NICE guidance on the use of botulinum toxin generally, or Botox specifically, in the management of primary headache or migraine. Further, this topic was not on the current list of NICE clinical guidelines in development.

Allergan provided a printout of the online NHS database for new medicines. The entry for botulinum A toxin (Botox) showed that Allergan was planning a US licence extension to include migraine. Details of any such plans in the UK were confidential.

PANEL RULING

The Panel noted Allergan's submission that the purpose of the Neurology Pharmaceutical Survey was to seek information and opinion from senior health professionals actively involved in the management of primary headache and migraine conditions. The information gained would ensure that Allergan's communications were effectively targeted. Allergan did not argue that the survey was market research outside the scope of the Code but described it as a marketing survey as the participants would be identified to the company. Allergan had examined the survey in relation to the requirements of the Code as non promotional material under the supplementary information to Clause 14.3.

The Panel considered that market intelligence gathering was a legitimate business activity. Such activity had to comply with the Code. Clause 12.2 of the Code required that market research must not constitute disguised promotion and must be conducted with a scientific or educational purpose. The supplementary information to Clause 12.2, Market Research, stated that market research was the collection and analysis of information and must be unbiased and non-promotional. The use to which the statistics or information was put might be promotional. The two phases must be kept distinct. Attention was drawn to guidelines – The Legal and Ethical Framework for Healthcare Market Research – produced by the British Healthcare Business Intelligence Association (BHBIA) in consultation with the ABPI. It was further stated that market research material should be examined to ensure that it did not contravene the Code. The Panel noted that Paragraph 4 of The Legal and Ethical Framework for Healthcare Market Research stated that the principle of the confidentiality was the most crucial distinction between market research and most other forms of marketing activity. The Panel noted that it was consideration of these data protection issues which had led to the survey being described by Allergan as a marketing study. The Code did not make such a distinction. Paragraph 4 of The Legal and Ethical Framework for Healthcare Market Research also stated that, as an activity market research was quite distinct from, *inter alia*, database building.

The Panel examined the survey. The Panel noted that most of the questions on page 2 of the survey referred to the use of botulinum toxin injections. Six of the questions referred to the use of such injections for the treatment of primary headache or migraine. One question asked which was the respondent's preferred brand and named each botulinum toxin injection brand available in the UK. Another question similarly named all the brands. None of the botulinum toxin injections currently marketed were licensed for the treatment of primary headache or migraine. Question 19a asked 'Are you currently aware of the use of botulinum toxins for any type of primary headache or migraine?'. Question 22 asked clinicians to choose which one of four statements best described their usage intentions of botulinum toxins for headaches/migraine assuming that such a use was officially approved. The third statement read 'I am not interested in trying botulinum toxins for headache/migraine patients, neither injecting them or referring them, unless they become a very common and successful treatment for headache/migraine'. The Panel considered that the nature of the questions and the survey's broad distribution to over 800 clinicians was such that it went beyond merely seeking information and opinion from senior clinicians actively involved in the management of primary headache and migraine conditions as submitted by Allergan. The questions were such that they were designed to stimulate interest in the use of botulinum injections for an unlicensed indication. In the Panel's view the survey was a marketing tool which was subject to the Code.

The Panel noted the complainant's primary concern regarding the lack of NICE guidance about the use of botulinum toxins to treat primary headache or migraine but noted that providing the relevant marketing authorization had been granted

medicines could be promoted before NICE guidance on their use had been issued. Similarly, the promotion of medicines did not have to be in accordance with any such guidance. In this regard the Panel did not consider that Allergan had failed to maintain high standards as alleged. No breach of Clause 9.1 was ruled.

The Panel noted that the complainant had also made a broader allegation about the boundaries of honest promotion.

The Panel considered that the survey would stimulate interest in the use of botulinum toxins as a class for primary headache or migraine although none of the products currently marketed were licensed for such use. A clinical study into such use had been presented at the 2009 IHS meeting and Allergan was planning a US licence extension for Botox to include migraine. The survey did not give disproportionate weight to any specific botulinum toxin. The Panel considered that in so much as the survey promoted all botulinum toxins it also promoted Botox. If this were not the case then the effect would be for companies to promote classes of medicines as a means of avoiding the restrictions in the Code. The Panel considered that the survey promoted Botox in a manner which was inconsistent with the particulars listed in its summary of product characteristics (SPC). A breach of Clause 3.2 was ruled. Botox did have a marketing authorization and so in that regard the Panel ruled no breach of Clause 3.1.

The Panel considered that the material at issue promoted botulinum toxins in the guise of a survey. In that regard the promotional activity was disguised and the Panel ruled a breach of Clause 12.1. The Panel noted its ruling that the survey was promotional material. It thus followed that it was not a market research activity or the like as referred to in Clause 12.2. No breach of that clause was ruled.

Clause 18.1 of the Code stated that no gift, benefit in kind or pecuniary advantage should be offered or given to members of the health professions as an inducement to prescribe, supply, administer, recommend, buy or sell any medicine, subject to the provisions of Clause 18.2. The Panel considered that given the survey was not a market research activity but promotional and solicited an interest in unlicensed indications the attached cheque for £35 was wholly inappropriate. A breach of Clause 18.1 was ruled.

The Panel considered that, overall, high standards had not been maintained. A breach of Clause 9.1 was ruled. The Panel further considered that the content and distribution of the marketing study were such as to bring discredit upon, or reduce confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

The Panel was very concerned about all the arrangements for the survey and noted that over 800 clinicians had each been sent £35. In the Panel's view the cheque would encourage them to read and complete the marketing study which promoted a class of products for an unlicensed indication. The Panel decided to report Allergan to the Code of Practice Appeal Board in accordance with Paragraph 8.2 of the Constitution and Procedure.

APPEAL BY ALLERGAN

Allergan submitted that the survey was not promotional in either its intent or execution. The crux of this case was the Panel's ruling that the survey was promotional. All the other rulings of breaches derived from this ruling and thus fell with it. Allergan considered that, on the evidence, the survey should be viewed as a legitimate non-promotional business activity.

Allergan submitted that the survey was developed with agency and complied with The Legal and Ethical Framework for Healthcare Market Research produced by the BHBIA in consultation with the ABPI. The aim of the survey was to gain market intelligence on the level of interest in Botox in anticipation of a licence variation currently under review by the Medicines and Healthcare Products Regulatory Agency (MHRA) for a new indication of chronic migraine. Earlier surveys had demonstrated widespread off-label use by British neurologists. The aim of the survey was to collect market information necessary to assist Allergan in its preparations and planning for the launch of Botox for a new indication. It was intended that the data collected would be used as input in modelling and planning for the optimal and affordable size of the sales force required to support the market launch of Botox subject to marketing authorization. Botox would essentially constitute a new unique therapy in this new indication, for which there were currently no or few treatment options. Hence, as the target market was not currently well characterised, the need for collecting first hand market information was even more critical in order to make wise investment and hiring decisions.

Allergan submitted that a drug utilisation study, which it conducted at the request of regulatory bodies to support an EU risk management plan, had established that there was currently extensive off-label use of botulinum toxins. Allergan's intention, therefore, was to design a survey to identify those neurologists who were already interested in the use of botulinum toxins in headache/migraine and who would, therefore, be likely to welcome information on the new indication for Botox, once this had been granted. The purpose of the survey was not to promote within the survey or encourage use in migraine but to enable Allergan to provide the profession with appropriate and targeted information on the new indication, but only once the change to the marketing authorization had been approved by the regulatory authorities.

Allergan noted that Clause 12.2 of the Code expressly provided that, while market research, ie

the collection and analysis of information, must be unbiased and non-promotional, the use to which the information was put might be promotional. It followed, therefore, that Allergan could not be in breach of the Code by its future intention to use the survey results to promote a prescription only medicine in accordance with the SPC only once this had been amended to include the new indication. Moreover, the Panel had stated in its ruling that market intelligence gathering was a legitimate business activity.

Allergan provided a copy of the signed and agreed project proposal with the agency which clearly described the intended use of the data following the launch of the new indication.

Allergan re-iterated that the scientific data included by the complainant was not enclosed with the survey and was not referenced in, or linked in any way to it. The Panel referred to 'a clinical study at the 2009 IHS meeting'. This data was not referenced or cited in the survey.

Allergan noted that 'marketing study' was used for a specific reason in the context of the survey. A more detailed explanation was given below but, in summary, market research had to be confidential. Where the participant was identifiable (with their consent), as in the case of the survey, then it strictly could not be termed market research. The typical terminology used was 'marketing study'. However, this term should not suggest that the survey was promotional. The survey was conducted in accordance with the British MRS regulations, 'Using Research Techniques for Non-Research Purposes'. To comply with these regulations the survey was termed a marketing study rather than a market research study. The distinction between market research and marketing studies reflected important data protection considerations. A market research study sought to gather market intelligence from a selected group of individuals and typically involved the appointment of an agency by a sponsor company. The agency would contact individual respondents directly in asking various questions. The answers were not reported back in named form to the sponsor, rather the data was aggregated or in the form of a report. Market research was by its nature confidential.

Allergan submitted that the methodology used in this survey (ie that it was nominative) meant that it was not, strictly speaking, market research but might be referred to as a 'marketing study' or 'database building'. Allergan referred to Paragraph 4.3 of the BHBIA framework document (February 2008) and paragraph 4c of the updated version (November 2009). This made it clear that database building was a legitimate activity so long as the appropriate data protection rules were observed ie that the participants were fully informed of the use to which their data would be put. This condition was completely fulfilled by the information set out at the bottom of page 2 under the legend in bold 'IMPORTANT DATA PROTECTION NOTICE'. Allergan accepted that that the Code did not expressly refer to the distinction between these two activities but it did refer to the BHBIA framework, which was developed in consultation with the ABPI. It must follow, therefore, that both the ABPI and the PMCPA endorsed the analysis contained in the Framework and this was what guided Allergan and the agency in designing the study.

Allergan submitted that this was why the letter to potential participants stated that the survey was 'a marketing study as opposed to a market research study'. The sole reason for this was that participating health professionals would be identifiable to Allergan. It was important from a data protection perspective that the potential participant knew this before participating in the survey.

Allergan submitted that two senior employees examined the survey, as required by the Code (supplementary information to Clause 14.3 – Examination of Other Material) and considered that it complied with the Code and was non-promotional.

Allergan submitted that the survey was not promotional. The aim of the questions was to obtain detailed market intelligence regarding current practice around the treatment and understanding of primary headache and migraine conditions. There was limited mention of product brands in the survey, and then only when the question specifically required it. Where product was mentioned it was balanced fairly across all brands mentioned and did not focus on a specific product vs its competitors. Allergan noted that participants were not aware of the company commissioning the survey. Clause 1.2 of the Code defined promotion as '... any activity undertaken by a pharmaceutical company or with its authority which promotes the prescription, supply, sale or administration of its medicines'. Nothing in the survey promoted Botox. No claims were made for Botox and no comparisons were made with other products. Botox was not singled out for any special mention. Brand names were only used in two questions where the brand names of all botulinum toxins available in the UK were used. The real focus of the questions was the use of botulinum toxins as a class but the survey was not designed to stimulate interest in the use of botulinum toxins. It was designed to measure interest. The survey was targeted at neurologists, specialists in the management of headache and migraine and the use of botulinum toxins and produced a snapshot of their current practice and future intentions.

Allergan submitted that more specifically, regarding section 3 (page 2) of the survey, question 16 established current use of botulinum toxins across a range of indications, both on and off-label. Questions 17 and 18 related to the use of toxins in any aspect of a neurologist's work, and local product availability. Question 19 established current usage, if any, for headache or migraine – that botulinum toxins were used in this way by some

neurologists was established in a recent drug utilisation study commissioned at the request of the regulatory authorities. Questions 20 and 21 established, where applicable, referral patterns for patients treated with botulinum toxin, and how this might change in the future. Question 22 noted that use for migraine/headache was not currently approved, it then went on to establish future intentions. More specific details regarding the rationale behind the questions in section 3 of the survey were detailed in a supporting letter provided to Allergan by the agency along with examples of similar questions from other studies completed in the UK. In all cases Allergan considered that these were legitimate, non-promotional questions which contained no material which could properly be described as encouraging the prescription of botulinum toxins as a class or Botox in particular. The survey was a legitimate business activity designed to gain data for potential future promotional use.

Allergan submitted that the arrangements for paying the survey participants were in line with the BHBIA Framework and accepted practice in market research. Cheques for £35, made out to individual doctors, were enclosed with the survey; the reason for this was explained to the potential participant in the accompanying letter. This approach was widely used for market research or market study surveys to overcome the main problem of some participants not getting their honorarium or not getting it quickly enough. Along with the explanation for the enclosure of the cheque, potential respondents were asked to dispose of the cheque if they were not interested in participating. Allergan reiterated that the amount paid was calculated in line with the EphMRA – Pharmaceutical Market Research Code of Conduct (Clause 3.1).

Further contact with the recipients depended on their response to the data protection notice at the bottom of the survey. If they opted in and agreed to potential contact to undertake further surveys of this type (ie marketing studies) in the future then Allergan had the option to conduct further surveys, should it choose to, although none were planned at this time.

Allergan submitted that the nature of the survey, with the option for potential future contact, was the reason why the survey was sent to 805 senior neurologists. Unlike market research where a small sample might be sufficient, here the aim was to develop a target list of individuals who were interested in the relevant disease area, had experience of using botulinum toxins or would consider referring patients to another specialist for this treatment if it became available.

The survey was mailed to 805 consultants to avoid any inadvertent bias in the sample as a result of selecting a certain target audience. Further, the greater the response, the higher the statistical robustness of any subsequent analysis for statistical modeling purposes. However, given that a response rate of less than 100% was anticipated (20-40% was usual for this type of survey), it was standard practice to send the survey to the broader consultant universe in order to reach statistical significance when the universe was small. The study focused on regional discrepancies in prescribing behavior as well as individual physician needs and interests. It was essential to have as many respondents as possible (ideally 250 to 300) in order to perform the non-biased targeting and segmentation analysis at this level of granularity.

Allergan hoped that the supporting declaration from the agency provided further reassurance around both the intent and execution of this survey. The format used for these questions was standard practice and commonly used in market research studies where a company investigated perceptions to product concepts before investing in market launch preparation activities.

Allergan submitted the 'Neurology Pharmaceutical Survey' was conducted in accordance with the Code and most importantly that the survey was non-promotional. A number of these kinds of studies were run in the UK and Europe by a number of pharmaceutical companies and other healthcare organisations. The aim was to obtain detailed market intelligence regarding current practice around the treatment and understanding of primary headache and chronic migraine conditions. There was limited mention of product brands in the survey, only when the question specifically required it (Q17 and Q18 only). Where product was mentioned it was balanced fairly across all brands currently available and did not focus on a specific one vs its competitors. In addition, the participants were not aware of the company commissioning the survey.

Allergan fully understood the Panel's concerns that these questions might be considered promotional. However, in the context of a marketing survey, with a target audience of senior neurologists, Allergan submitted that this was not the case for the reasons outlined above. There was never any intent for this to be a promotional activity, the survey was solely designed as a tool to assist potential future targeting of communications. Allergan denied a breach of Clause 3.2.

As stated above, Allergan submitted that the survey itself was not promotional. The nature of the survey was made clear to the recipient of the letter. As explained above, to comply with MRS regulations, the survey must be called a marketing study. The distinction between market research and marketing studies was made as a result of data protection considerations. The survey was not disguised promotion, it was a legitimate way to gain market intelligence about treatment and understanding of primary headache and chronic migraine conditions. Allergan denied a breach of Clause 12.1

Allergan submitted that the survey was not promotional and therefore the payment of £35 was

not an inducement; it was appropriate recompense for the time required to undertake the survey. The amount paid was calculated in line with the EphMRA Pharmaceutical Market Research Code of Conduct (as outlined above). The covering letter asked the recipient to dispose of the cheque and questionnaire if they did not wish to participate. Allergan denied a breach of Clause 18.1.

Allergan was very concerned to be ruled in breach of Clauses 2 and 9.1; the company took its commitment to the Code very seriously. The survey was never designed as a promotional activity, disguised or otherwise. Allergan submitted that as it had fully taken account of the BHBIA framework referred to in Clause 12.2 of the Code and taken this as the appropriate standard, it should not be possible to conclude that high standards had not been maintained. Taking into account MRS regulations this was a legitimate non promotional market intelligence gathering survey to aid future effective targeting of communications with neurologists. The industry could not be brought into disrepute by Allergan's adherence to the very guidelines to which attention was drawn in the supplementary information to Clause 12 of the Code as well as to other sets of guidelines drawn up by bodies with a special responsibility for setting standards in market research.

Allergan submitted that the survey was, in itself, non-promotional in intent and execution. Allergan denied any breach of the Code and particularly any breach of either Clauses 9.1 or 2.

COMMENTS FROM THE COMPLAINANT

The complainant was confident that the argument that Allergan's method of promoting the prescription of botulinum toxin for headache fell outside the Code would be made to the Appeal Board. The complainant remained unconvinced that NICE would ever see that the likely costs of this treatment were supported by sufficiently robust clinical evidence of superiority over placebo in a group of very suggestible patients. Allergan might submit that it had done a 'marketing study', but it was transparently obvious that this was being done to assemble a list of willing users of the medicine, in order that sales were well established before the costs were fully appreciated.

ALLERGAN'S COMMENTS ON THE REPORT FROM THE PANEL

Allergan did not submit any written comments on the report from the Panel but its representatives at the appeal hearing noted that in Allergan's view the survey at issue was a standard, legitimate activity. The company had tried very hard to comply with the guidelines and it did not consider that the survey was promotional.

APPEAL BOARD RULING

The Appeal Board noted Allergan's submission that there was currently extensive off-label use of botulinum toxins. Allergan was hoping to be granted a licence extension for the use of Botox in the treatment of chronic migraine. Allergan submitted that the purpose of the Neurology Pharmaceutical Survey was to asses the level of interest amongst neurologists in using botulinum toxins in headache/migraine. Once Allergan's licence extension had been granted it planned to contact interested responders with information on Botox injections for the treatment of chronic migraine. Allergan would also use the data from the survey to determine the resources it would need to support the launch of the proposed new indication. The Appeal Board considered that market intelligence gathering was a legitimate business activity. Such activity had to comply with the Code.

The Appeal Board noted that most of the questions on page 2 of the survey referred to the use of botulinum toxin injections either as a class or by brand. Six of the questions referred to the use of such injections for the treatment of primary headache or migraine. In that regard the Appeal Board noted that the proposed new indication for Botox was specifically chronic migraine, not primary headache or migraine. The Appeal Board considered that the questions were too specific with regard to the treatment at issue and also that they differed in that regard from some of the more open sample questions provided by the agency. In the Appeal Board's view neurologists reading the survey would get the impression that a botulinum toxin injection would soon become a licensed treatment for headache/migraine. The Appeal Board considered that surveys such as the one at issue might well stimulate interest in a new treatment for a particular condition; this was not necessarily unacceptable. However the Appeal Board did not consider that reasonable steps had been taken with the survey in question to prevent the identification of the medicine at issue. The nature of the questions and the broad distribution of the survey were such that it went beyond seeking opinion and would stimulate interest in the use of botulinum toxin for an unlicensed indication. The Appeal Board considered that in so much as the survey promoted all botulinum toxins it also promoted Botox. If this were not the case then the effect would be for companies to promote classes of medicines as a means of avoiding the restrictions in the Code. The Appeal Board considered that the survey promoted Botox in a manner which was inconsistent with the particulars listed in its SPC. The Appeal Board upheld the Panel's ruling of a breach of Clause 3.2. The appeal on this point was not successful.

The Appeal Board considered that the material at issue promoted botulinum toxins in the guise of a survey. In that regard the promotional activity was disguised and the Appeal Board upheld the Panel's ruling of a breach of Clause 12.1. The appeal on this point was not successful.

There were concerns that the payment of a fee for

completing a study that was ruled in breach of Clause 3.2 was unacceptable. However the Appeal Board considered that the payment of £35 to complete the survey was not in itself an inducement to prescribe Botox as prohibited by Clause 18.1. Thus no breach of Clause 18.1 was ruled. The appeal on this point was successful.

The Appeal Board considered that, overall, high standards had not been maintained. The Appeal Board upheld the Panel's ruling of a breach of Clause 9.1; the appeal on this point was not successful. The Appeal Board did not consider the circumstances were such as to bring discredit upon, or reduce confidence in, the pharmaceutical industry. No breach of Clause 2 was ruled. The appeal on this point was successful.

Given its rulings above the Appeal Board decided to take no further action in relation to the Panel's report, made to it in accordance with Paragraph 8.2 of the Constitution and Procedure.

Complaint received **7 October 2009**

Case completed **25 January 2010**