

# CODE OF PRACTICE REVIEW

The Prescription Medicines Code of Practice Authority (PMCPA) was established by The Association of the British Pharmaceutical Industry (ABPI) to operate the ABPI Code of Practice for the Pharmaceutical Industry independently of the ABPI. The PMCPA is a division of the ABPI which is a company limited by guarantee registered in England & Wales no 09826787, registered office 7th Floor, Southside, 105 Victoria Street, London SW1E 6QT.

## ANNUAL REPORT FOR 2015

The Annual Report of the Prescription Medicines Code of Practice Authority for 2015 will be published on our website ([www.pmcpcpa.org.uk](http://www.pmcpcpa.org.uk)) shortly.

There were 54 complaints in 2015 compared with 51 in 2014. There were 80 complaints in 2013.

The 54 complaints in 2015 gave rise to 66 cases (35 cases ruled in breach of the Code). The number of cases usually differs from the number of complaints, the reason being that some complaints involve more than one respondent company and some complaints do not become cases at all because they are withdrawn.

Of the 198 rulings made by the Code of Practice Panel in 2015, 179 (90%) were accepted by the parties, 13 (7%) were unsuccessfully appealed and 6 (3%) were successfully appealed. This compares with the 5% of rulings which were successfully appealed in 2014. The average time to deal with all cases in 2015 was 9.8 weeks (11.7 weeks in 2014). There was also a decrease in the time taken for cases settled at the Panel level, 8.5 weeks in 2015 (10 weeks in 2014) and cases which were appealed, 19.2 weeks in 2015 (23.3 weeks in 2014).

Each quarter the Authority advertises brief details of cases completed in the previous three months where companies were ruled in breach of Clause 2 of the Code, were required to issue a corrective statement or were the subject of a public reprimand. These advertisements which are published on the PMCPA website and placed in the BMJ, The Pharmaceutical journal and the Nursing Standard act as a sanction and highlight what constitutes a serious breach of the Code.

## REPRESENTATIVES EXAMINATION – IMPORTANT BOOKING ADVICE

It is sometimes the case that representatives request an extension to the time in which to either sit or pass an appropriate examination because they have left it too late to book an examination and get a place within the required time (1 year in which to sit an examination and 2 years in which to pass it). Candidates, or those booking places on their behalf, must ensure that they think well ahead and do not leave booking the first examination until the last minute and that if re-sits are needed they book them as quickly as possible within the second year so that candidates can be sure of passing the examination by the end of that year.

## PUBLIC REPRIMANDS AND SUSPENSION FOR ASTELLAS

Astellas Pharma Europe and Astellas UK have been publicly reprimanded twice by the Code of Practice Appeal Board. Once for breaches of the Code in relation to providing false information in response to a previous case and for reporting the outcome of the previous case in a dismissive manner. Secondly for providing inaccurate information to the Authority.

In Case AUTH/2780/7/15, the Code of Practice Panel ruled breaches of the Code with regard to the provision of false information in response to a previous case (Case AUTH/2747/1/15) and for the dismissive manner in which a senior employee reported the outcome of that case to Astellas staff. The Panel reported Astellas UK and Astellas Europe to the Appeal Board. The Appeal Board required a corrective statement to be issued; both companies were also publicly reprimanded and required to undergo audits of their procedures in relation to the Code.

Following the audits the Appeal Board decided that both companies should be reaudited in September 2016. In addition Astellas Europe subsequently admitted it had provided inaccurate information. This was considered by the Code of Practice Panel which again reported both companies to the Appeal Board. The Appeal Board decided to require a third corrective statement, to publicly reprimand both companies for a second time and to report them to the ABPI Board.

The ABPI Board was extremely concerned at the multiple organisational and cultural failings. There was institutional failure. Very senior staff at Astellas Europe had lied and there was deception on a grand scale which was appalling and shocking. The totally unacceptable behaviour of senior staff was potentially harmful to the integrity of self-regulation.

The ABPI Board suspended Astellas UK from membership of the ABPI for 12 months commencing on 24 June. It also decided that it wanted sight of the reports of the September 2016 reaudits of the companies so that it could review the position, including the length of the suspension, before the end of 2016. The reaudits must show demonstrable improvements at both companies particularly in relation to corporate culture. Astellas Europe and Astellas UK will continue to be required to comply with the Code and accept the jurisdiction of the PMCPA during the period of suspension.

Full details of Case AUTH/2780/7/15 and Case AUTH/2747/1/15, including the corrective statements, can be found on the PMCPA website.

## CODE OF PRACTICE TRAINING

Training seminars on the Code of Practice, run by the Prescription Medicines Code of Practice Authority and open to all comers, are held on a regular basis in central London.

These full day seminars offer lectures on the Code and the procedures under which complaints are considered, discussion of case studies in syndicate groups and the opportunity to put questions to the Code of Practice Authority.

The next Code of Practice seminar dates on which places remain available are:

Thursday 6 October 2016  
Monday 5 December 2016

Short training sessions on the Code or full day seminars can be arranged for individual companies, including advertising and public relations agencies and member and non member companies of the ABPI. Training sessions can be tailored to the requirements of the individual company.

*For further information regarding any of the above, please contact Nora Alexander for details (020 7747 1443 or [nalexander@pmcpa.org.uk](mailto:nalexander@pmcpa.org.uk)).*

## HOW TO CONTACT THE AUTHORITY

Our address is:  
Prescription Medicines Code of Practice Authority  
7th Floor, Southside, 105 Victoria Street, London SW1E 6QT  
[www.pmcpa.org.uk](http://www.pmcpa.org.uk)

Telephone: 020 7747 8880  
Facsimile: 020 7747 8881

Copies of the Code of Practice for the Pharmaceutical Industry and of this Review can be obtained from Lisa Matthews (020 7747 8885 or [lmattews@pmcpa.org.uk](mailto:lmattews@pmcpa.org.uk)).

Direct lines can be used to contact members of the Authority.

Heather Simmonds: 020 7747 1438  
Etta Logan: 020 7747 1405  
Jane Landles: 020 7747 1415  
Tannyth Cox: 020 7747 8883

The above are available to give informal advice on the application of the Code of Practice.

The Authority rather than the ABPI is the contact point for information on the application of the Code.

# BAYER v GUERBET

## Offer of equipment

Bayer plc complained about its competitors, including Guerbet Laboratories, offering radiological contrast injection equipment on long term loan or as a gift to customers who agreed to purchase the company's contrast agent.

Bayer noted that a document produced by a purchasing organisation stated that three suppliers of radiological contrast media, including Guerbet, were offering the loan of injectors as part of a framework agreement based on defined-spend value through the respective suppliers' contrast.

Bayer alleged that a gift had been supplied, offered or promised to health professionals as an inducement to prescribe, supply, administer, recommend, buy or sell medicine. Bayer conceded that the Code did not prevent the offer of package deals whereby the purchase of a particular medicine was linked to the provision of certain associated benefits such as apparatus for administration, but stated that it considered a gift of that magnitude meant that the Code's additional requirement that the transaction as a whole must be fair and reasonable could not be satisfied. Bayer further alleged that such activities were likely to bring discredit upon, or reduce confidence in, the pharmaceutical industry in breach of Clause 2.

The detailed response from Guerbet is given below.

The Panel noted Guerbet's submission that its injectors were not offered on either long term loan or as a gift. Guerbet described the arrangement as a loan based on defined-spend value. The injectors remained the property of Guerbet and NHS customers could return the injector and stop buying contrast media from Guerbet at any point and Guerbet could refuse to supply the injector if it was not being used properly. The defined-spend value was based on the workload of the department. The Panel noted that a contract for the provision of a second soft bag injector (SBI) to a hospital in the form of a letter provided by Guerbet described the arrangement as the provision [of a second SBI injector], free of charge and on loan. Guerbet agreed not to increase the price of its contrast media for 5 years and the hospital agreed to commit to buying the range of contrast media required for the equipment for 5 years. The length of the agreement was 5 years from the date of the original agreement to provide the first injector. The Panel noted that each package deal would be negotiated individually with each NHS organisation.

The Panel noted that whilst Guerbet was the only company to provide contrast media pre-filled in a soft bag, other contrast media could be used with its injectors. Indeed such usage was common as there were supply issues with Guerbet's pre-filled bags. The Panel noted that the injector remained

the property of Guerbet and an example of such loans for 3 and 5 years had been provided. The Panel queried whether a 5 year loan could be described as a short term loan and whether it was in fact a gift as described in the Code. The Panel noted that whilst it was unusual for customers not to meet their defined-spend, the continued loan of the injector appeared to be dependent on achieving it. In such circumstances the Panel did not consider that the arrangements could be described as fair and reasonable and a *bona fide* package deal as set out in the Code.

The Panel noted, however, that as submitted by Guerbet there was a complicating factor in that it had previously been decided that the relevant clause in the Code applied to individuals rather than organisations etc. The Panel noted its decision above in relation to the package deal but also noted that there was no evidence of any benefit to an individual. The Panel was thus obliged to rule no breach of the Code. The Panel, however, was concerned that the arrangements did not constitute a *bona fide* package deal; it appeared that the injectors remained with customers only for as long as they continued to buy Guerbet's medicines to at least a pre-defined value each year. The Panel considered that the loan of injectors conditional upon a minimum annual spend with regard to Guerbet's medicines was unacceptable. In that regard the arrangements brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

Bayer plc complained about the activities of its competitors in the radiological contrast field including Guerbet Laboratories Ltd.

### COMPLAINT

The activity in question was the offer of contrast injection equipment on long term loan or as a gift to customers who agreed to purchase the company's contrast agent. Bayer stated that some of its NHS customers confirmed that these deals took place and others questioned the legitimacy of the activities which caused concern for the reputation of the industry.

By way of background Bayer explained that images obtained from radiographic procedures could be considerably enhanced by the use of contrast agents. Use of the agents during a series of scans precisely coordinated to the various phases of the contrast agent could improve the diagnostic capabilities of the procedure. In particular, the approach had been successfully applied to the injection of iodine-based contrast agents during computed tomography (CT) imaging and gadolinium-based contrast agents in magnetic resonance imaging (MRI). Exact coordination of the injection and contrast agent

to the scanner cycle was a key part of the process. The use of a contrast injector linked to the scanner controls, enabling the rapid, exactly-timed delivery of contrast agents coordinated with the acquisition procedure had improved diagnosis and reduced costly repeat investigations. Many, but not all, of the UK companies involved in the manufacture and distribution of contrast agents also distributed contrast injectors. They were sophisticated items of equipment with an NHS price between £20,000 and £35,000, were not linked to a specific contrast agent and in some instances were third-party sourced.

Bayer stated that it had long been aware, but lacked proof, that several of its competitors had offered contrast injectors either as gifts or long term loans, to hospitals agreeing to sign a contract for supply of that company's contrast agents. Bayer became aware of a document, Implementation Brief for Supply of X-Ray Contrast Media, produced by a purchasing organisation that provided services to NHS and private hospitals in the UK. The implementation brief stated that three suppliers of radiological contrast media, one of which was Guerbet, were offering the loan of injectors as part of the framework agreement based on defined-spend value through the respective suppliers' contract.

Bayer had written to Guerbet stating that in its opinion such activity potentially breached Clause 18.1 in that a gift had been supplied, offered or promised to members of the health professions as an inducement to prescribe, supply, administer, recommend, buy or sell medicine. In its letter, Bayer conceded that the Code did not prevent the offer of package deals whereby the purchase of a particular medicine was linked to the provision of certain associated benefits such as apparatus for administration, but stated that it considered a gift of that magnitude meant that the Code's additional requirement that the transaction as a whole must be fair and reasonable could not be satisfied.

According to Bayer, Guerbet replied stating that it considered that an injector was apparatus for administration, the loan or gift of which was fair and reasonable and therefore exempted from the restrictions of Clause 18.1. Guerbet stated that as no individual health professional had benefitted from the offer meant that such a gift was not an inducement to prescribe. Guerbet did not deny that such gifts had been provided by its sales staff. Copies of inter-company dialogue were provided.

Bayer stated that some NHS customers had confirmed that inducements were being offered and an anonymised email from one such customer was enclosed which stated 'Guerbet give us the injectors as long as we use their contrast', implying that more than one injector might be on offer to customers agreeing to use Guerbet contrast agents in preference to others.

In Bayer's experience, contrast media injectors sold for around £20,000 to £35,000, depending on the model and the technology being used. The features offered varied widely but even basic models from the suppliers named by the purchasing organisation would not sell for less than £20,000. Additionally,

there were installation and servicing costs which would normally be charged to the customer. Bayer reiterated that the offer of injectors in the above price range as part of a package deal was neither fair nor reasonable.

In recent years Bayer had become increasingly concerned about the activities of its competitors in the field and was aware that they had been in activities proscribed by the Code, but had been frustrated by the lack of documentary evidence to support an approach to Guerbet or the Authority. Bayer stated that in this instance the purchasing organisation had fortunately provided it with publicly available evidence. That the offer of inducement had been made on behalf of Guerbet by a third party did not, in Bayer's opinion, provide an adequate defence against the charge.

Bayer had little doubt that the provision of contrast injectors valued between £20,000 and £35,000 by Guerbet to health authority departments as part of a package deal for contrast agents was not a fair or reasonable arrangement and therefore was in breach of Clause 18.1. Bayer alleged that such activities were likely to bring discredit upon, or reduce confidence in the pharmaceutical industry in breach of Clause 2.

## RESPONSE

Guerbet stated that whilst Bayer had clearly explained the purpose of contrast media and the benefit of using an injector to administer it, it failed to disclose that it had a strong interest in selling injectors, in fact, Bayer was the market leader in injectors (trading in the name of Medrad) and it benefitted greatly from sales of medical disposables which were needed for the use of its injectors. Bayer also failed to disclose that it had withdrawn its contrast media Ultravist (iopromide) from the UK market a few years ago, probably due to a profit issue as the product was still available in other parts of the world where prices were generally better. Therefore, it was clear that Bayer was not able to offer the same services as other suppliers and was facing stiff challenges to the sale of its injectors.

The letter from Bayer to Guerbet Laboratories in October 2015 included the assumptions that: Guerbet was aware of the document provided by the purchasing organisation; all injectors were priced around £20,000 or more; and Guerbet was giving injectors away as gifts.

Guerbet submitted that Bayer had no knowledge about the financial charges incurred and what customers paid for the use of Guerbet injectors; it had no knowledge about the cost of Guerbet's injectors and the ownership of the injectors. Guerbet did not see why it needed to disclose its business arrangements to Bayer just as it did not expect Bayer to disclose its business dealings to Guerbet.

In response to a request from the case preparation manager for a full response, Guerbet submitted that it had no further comment to add, however it would review its arrangement with the existing customer base to determine if it had breached the Code and

rectify those cases if necessary. Guerbet suggested that the Panel reach out to customers of Guerbet whom it thought could have been misled to enter into such an arrangement in order to get a different perspective on the matter.

In response to a request for further information from the Panel, Guerbet submitted that Bayer had accused it of offering the long term loan or gift of contrast injection equipment. Guerbet clarified that the injectors remained the property of Guerbet and were therefore not a gift, neither were they on long term loan. NHS customers were free to return the injector and stop buying contrast media from Guerbet at any point and Guerbet could refuse to supply the injector if it was not being used properly.

Guerbet noted that Bayer implied the cost of contrast injectors ranged between £20,000 and £35,000. The NHS supply chain published price list was a national framework price list which all NHS trusts in the country were able to use. The prices were significantly lower compared to what Bayer claimed it was worth.

Guerbet stated that Bayer repeatedly implied that via the purchasing organisation, Guerbet had offered injectors as a gift or on long term loan to induce the sales of contrast media; there was no explicit nor implied message within the purchasing organisation implementation brief that this was so. Firstly, the injector was offered on loan based on defined-spend value and therefore it was not a gift. Secondly, the framework agreement was being reviewed and renewed every 2-3 years following an open tender exercise; NHS trusts were not obliged to stay with Guerbet's product and could choose any supplier listed on the Framework Agreement and Bayer's accusation was unfounded.

Bayer claimed that some NHS customers had confirmed that inducements were being offered and provided an email exchange between a Guerbet customer and Bayer's representative as evidence. Guerbet stated that the email was dated after Bayer had sent the original complaint to Guerbet and queried if Bayer had actively solicited the email in order to support its claim. The email clearly stated that the NHS trust's concern was that it was not able to purchase two CT injectors, presumably from Bayer, due to financial constraints. Although, the email used the word 'give', Guerbet assumed that it was a figure of speech and possible misunderstanding on the part of the author. The injector belonged to Guerbet and continued to do so. Guerbet was prepared to clarify the use of the word 'give' with the author if Bayer provided the name of the person concerned, however, Guerbet queried whether it was a tactic used by the author to fend off the overly zealous Bayer representative.

To further demonstrate that the provision of its injector was not a gift or long term loan, Guerbet shared with the PMCPA prices which NHS customers had to pay for the use of one of its contrast media compared to products for a similar purpose from competitors. Guerbet insisted that this was confidential information that was not disclosed to

Bayer or any other company. When iobitridol in a soft bag was administered using Guerbet's soft bag injector, it offered customers the convenience of not having to transfer the contrast solution into an empty syringe or container which meant saving time for preparation, reduced chances of contamination and there was less waste material to dispose of following administration among other benefits. Guerbet submitted that NHS customers were not buying its contrast media because they were induced by the offer of a free-to-use injector but because they were looking at the total cost of contrast media administration and the time saving and aseptic practice that the system (contrast media + injectors) offered. Guerbet submitted that contrary to Bayer's accusation, its practice was well within the permitted scope of Clause 18.1.

Guerbet submitted that the purchasing organisation supported over 400 public and private sector organisations throughout the UK, partnering with them to deliver innovative and best value procurement solutions. Guerbet was a manufacturer and supplier of contrast media and medical devices, it participated in the tender exercise called for by the purchasing organisation on behalf of its customers. Following this, the products and services offered by Guerbet were deemed to be competitive and as bringing value to the NHS trusts. Therefore Guerbet was accepted as one of the framework suppliers together with three other contrast media manufacturers, with the exception of Bayer, which had been delisted.

The purchasing organisation did not purchase from Guerbet and Guerbet did not supply it. Whilst the purchasing organisation acted on behalf of its customers, NHS trusts, to negotiate and secure the best deal available in the market, Guerbet sought to expand business by offering the best possible products and services in a competitive manner.

Guerbet reiterated that the purchasing organisation did not consult it before issuing the Legal Services Framework Brief, the first time it was seen was with Bayer's complaint dated 16 October 2015. Guerbet submitted that it was an internal document, contrary to Bayer's claim that it was publicly available. Guerbet's customers were NHS trusts and the arrangements for the supply of contrast media and injectors were between Guerbet and the respective trust, the purchasing organisation had acted on behalf of the participating trust to put together a pricing framework agreement but the required spend value for each account was subject to negotiation between Guerbet and the respective trust. Guerbet submitted that the supply of injectors in conjunction with sales of contrast media could be categorised under the supplementary information for Clause 18.1 Package Deals.

Guerbet further stressed the legitimacy of such a deal by explaining that the NHS trusts were provided with options, in this case there were three other companies who offered similar packages, each with its own unique features. For example the nature of the contrast media (viscosity, hydrophilicity, osmolality, concentration etc); pack sizes (50ml,

75ml, 100ml, 150ml, 200ml etc); presentation type (pre-filled syringe, soft bag, glass bottle, plastic bottle); clinician preference.

Depending on the type of presentation, some added advantages could be derived from the use of a specific injector. For example, the efficiency of using Guerbet contrast media which were supplied in soft bags, was greatly enhanced if they were used with a soft bag injector. However, the NHS trust would have to pay a higher price for the contrast media for the added convenience and improved aseptic handling of the contrast solution.

Guerbet also noted that the provision of an injector did not personally benefit any individual NHS customer, except to enable them to deliver the service they were expected to deliver under the constraint of not having sufficient funding to acquire new equipment, increased workload and no additional manpower.

Therefore, Guerbet disagreed with Bayer's allegation that provision of its soft bag injector was an inducement to purchase its contrast media; it was a necessity if the customer wanted to fully capitalize the advantages of having contrast media in a soft bag and Guerbet denied a breach of Clause 18.1.

In response to a further request from the Panel for more information, Guerbet explained that the defined-spend value was calculated based on the workload of the department either independently or collectively if there was more than one site. The department was generally expected to perform approximately 3,000 contrast enhanced scans per site per year. As prices of contrast media were pre-determined and confirmed by the framework agreement, the expected revenue from each injector installed could be estimated.

Guerbet provided a contract agreement it had with a named hospital as an example and submitted that it was uncommon for hospitals to experience a sudden significant reduction in workload. Therefore if pre-installation assessment was done correctly with both parties being transparent and honest about existing workload and expectations, the chances of not meeting defined-spend was unusual. In the event that an NHS trust bought significantly less contrast media from Guerbet it could only mean that it had found a cheaper alternative. Such an example was provided wherein a customer asked Guerbet to remove its injector from the department as it was no longer needed.

Guerbet submitted that NHS employees took good care of equipment which was entrusted to their use so it did not see injectors being abused or misused such that it warranted removal of an injector which could jeopardise continuous operation of the department.

Guerbet submitted that it was the only company that provided contrast media pre-filled in a soft bag; it was a patented technology. However, other companies' contrast media could be used with its injector if it was transferred into empty bags which

were commercially available. The use of contrast media from other pharmaceutical companies was common over the past 18 months as Guerbet had supply issues with its pre-filled bags.

The injector remained the property of Guerbet, however, if a hospital wished to purchase it, it was open to discussions. Guerbet had had no such request thus far.

## PANEL RULING

The Panel noted that the relevant Clauses were identical in both the 2015 and 2016 versions of the Code. The Panel thus considered this matter under the 2016 version of the Code.

The Panel noted Bayer's allegation that the provision of contrast injectors valued between £20,000 and £35,000 as part of a package deal for contrast agents was not a fair or reasonable arrangement and alleged, *inter alia*, a breach of Clause 18.1. The Panel noted Guerbet's submission that it had not seen the purchasing organisation report provided by Bayer prior to the complaint. In the Panel's view Bayer's allegation was as stated above. The purchasing organisation report was provided as general evidence that package deals were being offered. The Panel noted Guerbet's submission that it negotiated each package deal directly with the relevant NHS body.

The Panel noted that Clause 18.1 prohibited the provision, offer or promise of a gift, pecuniary advantage or benefit to health professionals or other relevant decision makers as an inducement to prescribe, supply, administer, recommend, buy or sell any medicine. Its supplementary information Long term or Permanent Loan stated that the requirements of Clause 18.1 could not be avoided by the provision of items on long term or permanent loan. Such items would be regarded as gifts and subject to the requirements of that clause. The supplementary information Package Deals stated that Clause 18.1 did not prevent the offer of package deals which were commercial arrangements whereby the purchase of a particular medicine was linked to the provision of certain benefits as part of the purchase price. Examples given included apparatus for administration, the provision of training on its administration or the services of a nurse to administer it. The transaction as a whole must be fair and reasonable and the associated benefits must be relevant to the medicine involved.

The Panel noted Guerbet's submission that its injectors were not offered on either long term loan or as a gift. Guerbet described the arrangement as a loan based on defined-spend value. The injectors remained the property of Guerbet and NHS customers could return the injector and stop buying contrast media from Guerbet at any point and Guerbet could refuse to supply the injector if it was not being used properly. The defined-spend value was based on the workload of the department. The Panel noted that a 2012 contract for the provision of a second SBI injector to a hospital in the form of a letter provided by Guerbet described the arrangement as the provision [of a second

SBI injector], free of charge and on loan. Guerbet agreed not to increase the price of its contrast media for 5 years and the hospital agreed to commit to buying the range of contrast media required for the equipment for 5 years. The length of the agreement was 5 years from March 2011, the date of the original agreement to provide the first injector. The Panel noted that each package deal would be negotiated individually with each NHS organisation.

The Panel noted that whilst Guerbet was the only company to provide contrast media pre-filled in a soft bag, other contrast media could be used with its injectors. Indeed such usage was common as there were supply issues with Guerbet's pre-filled bags. The Panel noted that the injector remained the property of Guerbet and an example of such loans for 3 and 5 years had been provided. The Panel queried whether a 5 year loan could be described as a short term loan and whether it was in fact a gift as described in the supplementary information to Clause 18.1. The Panel noted that whilst it was unusual for customers not to meet their defined-spend, the continued loan of the injector appeared to be dependent on achieving it. In such circumstances the Panel did not consider that the arrangements could be described as fair and reasonable and a *bona fide* package deal as set out in the supplementary information to Clause 18.1.

The Panel noted, however, that as submitted by Guerbet there was a complicating factor in that it had previously been decided that Clause 18.1 applied to individuals rather than organisations etc. The Panel noted its decision above in relation to the package deal but also noted that there was no evidence of any benefit to an individual. The Panel was thus obliged to rule no breach of Clause 18.1. The Panel, however, was concerned that the arrangements did not constitute a *bona fide* package deal; it appeared that the injectors remained with customers only for as long as they continued to buy Guerbet's medicines to at least a pre-defined value each year. The copy of an agreement provided by Guerbet showed the defined-spend for two injectors. The Panel considered that the loan of injectors conditional upon a minimum annual spend with regard to Guerbet's medicines was unacceptable. In that regard the arrangements brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

**Complaint received**                      **1 December 2015**

**Case completed**                              **4 May 2016**

# BAYER v MALLINCKRODT

## Offer of equipment

Bayer plc complained about its competitors, including Mallinckrodt UK Commercial, offering radiological contrast injection equipment on long term loan or as a gift to customers who agreed to purchase the company's contrast agent.

Bayer noted that a document produced by a purchasing organisation stated that three suppliers of radiological contrast media, including Mallinckrodt, were offering the loan of injectors as part of a framework agreement based on defined-spend value through the respective suppliers' contrast.

Bayer alleged that a gift had been supplied, offered or promised to health professionals as an inducement to prescribe, supply, administer, recommend, buy or sell medicine. Bayer conceded that the Code did not prevent the offer of package deals whereby the purchase of a particular medicine was linked to the provision of certain associated benefits such as apparatus for administration, but stated that it considered a gift of that magnitude meant that the Code's additional requirement that the transaction as a whole must be fair and reasonable could not be satisfied. Bayer further alleged that such activities were likely to bring discredit upon, or reduce confidence in, the pharmaceutical industry in breach of Clause 2.

The detailed response from Mallinckrodt is given below.

The Panel noted Bayer's allegation that the provision of contrast injectors valued between £20k and £35k as part of a package deal for contrast agents was not a fair or reasonable arrangement in breach of the Code.

The Panel noted Mallinckrodt's submission that its injectors were not offered on long term or permanent loan.

The Panel noted Mallinckrodt's explanation that package deals (mainly for 2-3 years) were developed based on customer usage requirements to ensure that the provision of an injector complied with the Code. Provided the commitment to volume of Mallinckrodt product was achieved, customers could choose alternative contrast media suppliers and retain the injector. Package deals were based on the value of the equipment being a given percentage of the total value of consumables/contrast media which Mallinckrodt submitted was in accordance with NHS terms and conditions. The ownership of the injector transferred to the customer on delivery as part of the total package deal and was inclusive of the purchase price of the pre-filled syringes. Mallinckrodt submitted that this was fair and

reasonable because the equipment was necessary for performing clinical tasks as outlined in the Code.

The Panel noted that according to the template contract, in return for the payment of the equipment price, the service fee and the purchase of an agreed volume of consumables at agreed prices, Mallinckrodt agreed to supply the injector and services to the customer. The customer acknowledged that the level of discount was offered on the basis of the total value of the package deal. The Panel noted that the template was inconsistent in some regards; it referred to title passing to the customer on payment in full of the equipment price although Mallinckrodt had confirmed that ownership passed on delivery. The Panel noted Mallinckrodt's submission that there was no contractual or other mechanism to recover the investment if insufficient volume was purchased and that currently the company did not wish to impose a financial penalty for failing to use sufficient product and not achieving the threshold. The Panel noted that Section 9 set out a termination clause by which either party could give notice for breach of a material term. The Panel noted that in effect under the contract the customer paid for the injector at an agreed level of discount which was related to the total value of the package deal.

The Panel noted Mallinckrodt's submission that it had only one imaging injector with a price anywhere near the £20k quoted by Bayer. This injector had never been placed on a package deal since end users had decided not to use the Mallinckrodt contrast media in question.

The Panel noted that the relevant supplementary information to the Code referred to the provision of apparatus for administration. The Panel noted that the injector could be used not only with Mallinckrodt's contrast media but also with others. Ownership apparently passed to the customer upon delivery although the Panel noted its comments on the contract above. The injector would not be removed if agreed volumes were not achieved and it appeared that the total cost paid by the customer included an element which reflected the discounted cost of the injector. In the Panel's view the overall agreement did not appear to be unfair or unreasonable and thus it considered that the arrangements constituted a *bona fide* package deal.

The Panel noted that, as submitted by Mallinckrodt, there was a complicating factor in that it had previously been decided that the relevant Clause in the Code applied to individuals rather than organisations etc. The Panel noted its decision above that the arrangements were a *bona fide* package deal and further that there was no benefit to an individual. In any event Mallinckrodt had not



**provided an injector which would sell for £20k to £35k as alleged. The Panel ruled no breach of the Code. Further, the Panel ruled no breach of Clause 2.**

Bayer plc complained about the activities of its competitors in the radiological contrast field including Mallinckrodt UK Commercial Ltd.

## COMPLAINT

The activity in question was the offer of contrast injection equipment on long term loan or as a gift to customers who agreed to purchase the company's contrast agent. Bayer stated that some of its NHS customers confirmed that these deals took place and others questioned the legitimacy of the activities which caused concern for the reputation of the industry.

By way of background Bayer explained that images obtained from radiographic procedures could be considerably enhanced by the use of contrast agents. Use of the agents during a series of scans precisely coordinated to the various phases of the contrast agent could improve the diagnostic capabilities of the procedure. In particular, the approach had been successfully applied to the injection of iodine-based contrast agents during computed tomography (CT) imaging and gadolinium-based contrast agents in magnetic resonance imaging (MRI). Exact coordination of the injection and contrast agent to the scanner cycle was a key part of the process. The use of a contrast injector linked to the scanner controls, enabling the rapid, exactly-timed delivery of contrast agents coordinated with the acquisition procedure had improved diagnosis and reduced costly repeat investigations. Many, but not all, of the UK companies involved in the manufacture and distribution of contrast agents also distributed contrast injectors. They were sophisticated items of equipment with an NHS price between £20,000 and £35,000, were not linked to a specific contrast agent and in some instances were third-party sourced.

Bayer stated that it had long been aware, but lacked proof, that several of its competitors had offered contrast injectors either as gifts or long term loans, to hospitals agreeing to sign a contract for supply of that company's contrast agents. Bayer became aware of a document, Implementation Brief for Supply of X-Ray Contrast Media, produced by a purchasing organisation that provided services to NHS and private hospitals in the UK. The implementation brief stated that three suppliers of radiological contrast media, one of which was Mallinckrodt, were offering the loan of injectors as part of the framework agreement based on defined-spend value through the respective suppliers' contract.

Bayer had written to Mallinckrodt stating that in its opinion such activity potentially breached Clause 18.1 in that a gift had been supplied, offered or promised to members of the health professions as an inducement to prescribe, supply, administer, recommend, buy or sell medicine. In its letter, Bayer conceded that the Code did not prevent the

offer of package deals whereby the purchase of a particular medicine was linked to the provision of certain associated benefits such as apparatus for administration, but stated that it considered a gift of that magnitude meant that the Code's additional requirement that the transaction as a whole must be fair and reasonable could not be satisfied.

According to Bayer, Mallinckrodt replied stating that it considered that an injector was apparatus for administration, the loan or gift of which was fair and reasonable and therefore exempted from the restrictions of Clause 18.1. Mallinckrodt did not deny that such gifts had been provided by its sales staff.

In Bayer's experience, contrast media injectors sold for around £20,000 to £35,000, depending on the model and the technology being used. The features offered varied widely but even basic models from the suppliers named by the purchasing organisation would not sell for less than £20,000. Additionally, there were installation and servicing costs which would normally be charged to the customer. Bayer reiterated that the offer of injectors in the above price range as part of a package deal was neither fair nor reasonable.

In recent years Bayer had become increasingly concerned about the activities of its competitors in the field and was aware that they had been in activities proscribed by the Code, but had been frustrated by the lack of documentary evidence to support an approach to Mallinckrodt or the Authority. Bayer stated that in this instance the purchasing organisation had fortunately provided it with publicly available evidence. That the offer of inducement had been made on behalf of Mallinckrodt by a third party did not, in Bayer's opinion, provide an adequate defence against the charge.

Bayer had little doubt that the provision of contrast injectors valued between £20,000 and £35,000 by Mallinckrodt to health authority departments as part of a package deal for contrast agents was not a fair or reasonable arrangement and therefore was in breach of Clause 18.1. Bayer alleged that such activities were likely to bring discredit upon, or reduce confidence in the pharmaceutical industry in breach of Clause 2.

## RESPONSE

Mallinckrodt submitted that it manufactured and supplied contrast media and injectors for diagnostic purposes. In November 2015, Mallinckrodt CMDS (just injectors and contrast media) separated from Mallinckrodt Pharmaceuticals and transferred to Guerbet Laboratories under a share transfer. Currently, it continued to trade legally as Mallinckrodt UK Commercial Ltd and would continue to do so for several months. Mallinckrodt accepted that once it legally became Guerbet, it would fall under the obligations to follow the Code unless it was deemed unnecessary to do so for reasons such as administrative burden.

Mallinckrodt submitted that its response below was not an agreement to sign up to the Code; as a non-

member it was not required to provide a formal response but as it had core values of quality and integrity, it had operated within the guidelines of the Code to the best of its ability since October 2007 recognising that it was best practice.

Mallinckrodt noted that it could not influence the rhetoric used by customers. Despite its awareness of the issue at hand, the purchasing organisation had recently re-tendered, requesting details for injectors on loan/lease or purchase. Mallinckrodt provided a copy of its most recent response to the purchasing organisation and submitted that a request for a loan injector was either incorrect use of language or an unsolicited request to find the most cost effective way for end users to use their product of choice.

### **Market evolution and dynamics**

Mallinckrodt submitted that it had been a key player in developing contrast media molecules and the use of contrast media since the launch of Conray (iothalamate meglumine), an ionic contrast medium, in 1962 followed by Optiray (ioversol), a non-ionic, low osmolar contrast medium, in 1989. With the acquisition of Liebel Flarshiem in 1996 it became the first company to offer both the injector and contrast medium. Mallinckrodt launched the first pre-filled syringe containing Optiray in 1996 and this had since been offered as a choice for departments preferring a pre-filled syringe option. Bayer had not succeeded in launching a pre-filled Ultravist (iopromide) syringe. It was widely recognised that pre-filled syringes offered advantages for user and patient, however this could be a more expensive option and as cost constraints had become priority for the NHS in recent years, Optiray had lost, not gained market share as one would expect from tactics which were allegedly designed to induce prescribing. Evidence was provided (usage data provided by European Contrast Media Group) to show that market share had mostly been lost to another named company.

Bayer became the second company to offer both injectors and contrast media in or around 2006. There were distinct advantages in doing so such as an acute awareness of pharmacovigilance issues surrounding injecting a pharmaceutical and the compliance guidelines governing these. It was clear from the activities of companies (mainly distributors, and at this time, excluding Bayer) which offered injectors without the pharmaceutical, that compliance was far greater when a pharmaceutical was involved.

Although Mallinckrodt had not seen official notification, it was widely understood that Bayer had recently withdrawn Ultravist in the UK and customers had sought alternative contrast medium. Since injectors had a life of 7 to 10 years, there would be significant accounts in the UK which would have continued to use the 'Medrad' injector from Bayer with alternative contrast media. Bayer would continue to receive revenue from the sale of disposals for those which were generally proprietary. Again, it was not a scenario in which an injector could be allegedly used to 'bribe or induce' a customer into using Mallinckrodt contrast

media, since the pre-filled syringes did not fit and there were cheaper alternatives to Optiray in glass bottles, which was not price competitive in the UK. Mallinckrodt referred to a diagram of an injector with a pre-filled syringe and an empty syringe in situ to assist in understanding the machinery and how it could be used with alternative contrast media.

### **Clinical choice and presentation preference**

Mallinckrodt submitted that Bayer failed to note that there were various presentations to administer contrast media (eg vials with empty syringes, soft bags, pre-filled syringes) which tended to be specific to certain injectors. Mallinckrodt submitted that injector placements based on the sale of related consumables and disposables were far more commonplace although it reserved to make an allegation against any specific company. The type of presentation tended to be a clinical choice based on technique, efficiency and infection control safety standards rather than the functionality of an injector. If a customer used a pre-filled syringe, it was a clinical decision for which they had limited options regarding the injector. Therefore the placement of an injector, whether loaned (which Mallinckrodt did not do), rented (which it also did not do but it was seeking legal advice on the feasibility of this option), package deal (which Mallinckrodt could offer based on a compliance calculation as a percentage of the total deal) or sale was secondary to the choice of presentation. A customer might choose a pre-filled syringe over a vial and empty syringe to save time or due to local hospital directives in line with advice from the National Patient Safety Agency that injectable medicines were pre-filled wherever possible. A customer might also choose soft bags to reduce the numbers of smashed glass vials received or to reduce storage space. Vials were still most commonly chosen due to cost and the flexibility to use any contrast media within an empty syringe. Mallinckrodt therefore contested that it would be difficult to persuade customers to purchase an expensive contrast media in a presentation which did not fulfil their requirements based on the alleged loan of an injector.

Mallinckrodt submitted that as outlined above, the Optivantage injector from Mallinckrodt was not limited solely to the use of pre-filled syringes. Customers could, and did, use empty syringes with contrast media from other suppliers. It did not make commercial sense to allegedly loan equipment based on an assumption that revenue would be achieved by the sale of contrast media if competitor contrast media could also be used.

### **Alleged practice**

In its complaint, Bayer stated that it was 'aware that some NHS customers have confirmed that inducements are being offered'. If there was concrete evidence of this, Mallinckrodt urged the PMCPA to encourage Bayer to disclose to it names of hospitals for further investigation. Mallinckrodt would not expect any customer to have previously viewed a 'loan agreement' as an inducement to prescribe or to consider that Mallinckrodt had offered

an injector as a 'gift' rather than as part of a business deal which provided the means for administering their choice or presentation of contrast media. In addition, Mallinckrodt could supply contact details of customers who had had injectors on package deals to investigate whether they considered that Mallinckrodt had offered inducements.

### **Current practice**

Package deals were developed based on customer usage requirements to ensure that the provision of an injector complied with Clause 18.1. Deals were not long term, they were mainly for 2-3 years. Provided the commitment to volume of Mallinckrodt product was achieved, customers could choose alternative contrast media suppliers whilst retaining the injector. Package deals were based on the value of the equipment being a given percentage of the total value of consumables/contrast media which was in accordance with NHS terms and conditions. The ownership of the injector was transferred to the customer on delivery as part of the total package deal and was inclusive of the purchase price of the pre-filled syringes. Mallinckrodt submitted that this was fair and reasonable as the equipment was necessary for performing clinical tasks as outlined in the supplementary information to Clause 18.1 Package Deals.

Mallinckrodt referred to its compliance calculator and package deal template which were used in executing the process since February 2015. The compliance calculator included installation costs, average selling price of the associated injector and service and maintenance costs in accordance with NHS terms and conditions.

### **Pricing for the NHS**

Mallinckrodt submitted that the package deal stated list price, however, it did not sell injectors at list price. Since January 2012, it had operated on the basis that NHS supply chain pricing was visible to all and would therefore serve as its 'guide price' when quoting. NHS supply chain should be the most cost effective route to purchase a product and therefore its pricing must be in line or slightly above NHS supply chain end user pricing which typically included 5% on cost. This was in line with its average selling price. Mallinckrodt provided evidence that it had started to address the issue with a legal firm.

Tables provided showed that only one MR imaging injector had a price anywhere near the £20,000 quoted by Bayer. That injector had never been placed on a package deal with MRI contrast media since end users had made a clinical decision not to use Optimark (gadoversetamide), the Mallinckrodt MR imaging gadolinium contrast media. If the placement of injectors via any kind of deal was an inducement to prescribe rather than as a necessary component for the administration of the product choice, it would follow that Mallinckrodt would undertake these alleged activities in MR imaging as well.

Mallinckrodt provided a table of the NHS supply chain pricing as of January 2012 and January 2015.

Mallinckrodt submitted that market assumptions were not that injectors were sold for 'upward of £20,000' and it suggested that Bayer declared the average selling price of its injectors to the PMCPA to validate its comments and assist in benchmarking standards.

### **Conclusion**

Mallinckrodt submitted that it had followed documented internal processes which recognised the Code as best practice and had already taken steps to rectify where it had fallen short of this as demonstrated by the evidence provided.

\* \* \* \* \*

The Panel decided that given Guerbet Laboratories Ltd's acquisition of Mallinckrodt on 27 November 2015 and in accordance with its established practice, Mallinckrodt was now covered by Guerbet's status as a non-member company which had agreed to comply with the Code and accept the jurisdiction of the Authority. The Panel would thus consider the complaint in the normal way. Mallinckrodt was invited to comment on this matter.

### **Further comments from Mallinckrodt**

Mallinckrodt submitted that given the complaint was raised on 16 October 2015 in relation to activities prior to that date, it contested the Panel's decision that Mallinckrodt fell under the rules to comply with the Code and its associated jurisdiction during the period leading up to that date.

Mallinckrodt submitted that as outlined above, although it had not signed up as a non-member in the past, it had always sought to comply with the guidelines of the Code. Mallinckrodt noted that it was a separate legal entity in the UK with separate regulatory and marketing authorizations and associated premises.

Mallinckrodt had provided a detailed response regardless of its membership position in order to clarify the complaint process it had instated in the UK to ensure it met the guidelines of the Code.

Mallinckrodt submitted that its response pertained solely to the activities undertaken by it as a separate legal entity to its parent company Guerbet and to practices which occurred before the acquisition.

Mallinckrodt thanked the Panel for highlighting an inconsistency in its contract detail and confirmed that ownership of the injector was transferred to the customer upon delivery.

Mallinckrodt submitted that regrettably, there was no mechanism to recover the investment due to insufficient volume of product purchased by the customer. Volume commitment was typical practice in secondary care pharmaceutical tenders via purchasing consortia who had never offered the

mechanism to penalise customers for not achieving committed volumes. Through Mallinckrodt's knowledge of the radiology environment and close collaboration with customers, it was rare that a customer would over-commit except in exceptional circumstances such as unplanned down-time and this would be taken into consideration.

A contrasted scan was a necessary diagnostic procedure which was led purely by the number of scans required. Mallinckrodt could not therefore work with a customer to increase the number of scans performed to ensure that they achieved 5% threshold. Currently, Mallinckrodt did not want to impose a financial penalty on a customer for failing to use sufficient product.

Volumes for all customers were regularly monitored. A 'class A' sales operations and inventory planning process was based on building its manufacturing plan from customer level.

Mallinckrodt submitted that agreements were typically made for 2-3 years. The life of the injector was 7-10 years. To ensure greater compliance, the calculation was done based on the term of the package deal which was based on customer requirements. Mallinckrodt referred to its new compliance calculator and explained what the coloured cells represented. The time period was specified. Mallinckrodt welcomed suggestions from the PMCPA regarding how this could be improved.

## PANEL RULING

The Panel noted Mallinckrodt's comment that its submission of a response was not an agreement to join the list of companies which, although non-members of the ABPI, agreed to comply with the Code and accept the jurisdiction of the Authority. The Panel noted that Mallinckrodt was a manufacturer and supplier of contrast media and injectors for diagnostic purposes. On 27 November 2015, Mallinckrodt CMDS (just injectors and contrast media) was transferred to Guerbet Laboratories under a share transfer. The Panel noted that Guerbet was a non-member company that had previously agreed to comply with the Code. When Mallinckrodt submitted its initial response to the PMCPA (8 January 2016) the companies had yet to be fully integrated. The Panel noted the company's submission that it had operated within the guidelines of the Code to the best of its ability since 2007. The Panel noted that the company's letterhead bore the prominent company name Guerbet in logo format beneath which in smaller typeface appeared 'Mallinckrodt UK Commercial Ltd, now part of Guerbet'. In the Panel's view given Mallinckrodt's acquisition by and ongoing integration with Guerbet it was covered by Guerbet's non-member status. Mallinckrodt had been so informed before the Panel's consideration of this matter and asked to comment.

The Panel also noted Mallinckrodt's submission that given the inter-company complaint from Bayer was made on 16 October 2015 in relation to activities before that date, it contested the decision by the Panel that the activity in question and the company fell under the Authority's jurisdiction. The Panel

noted that the complaint dated 27 November was received by the Authority on 1 December. The Panel did not agree that the complaint solely related to matters prior to 16 October. In the Panel's view the broad allegation related to the principle of a package deal whereby an injector of a certain value was provided in conjunction with sales of contrast media. The purchasing organisation document was provided as an example. The document dated from September 2012 and the offers therein had according to Mallinckrodt recently been re-tendered. The Panel noted that the provision of package deals was an ongoing activity. The Panel considered that the activities in question at the date of complaint to the Authority came within its jurisdiction.

The Panel noted Bayer's allegation that the provision of contrast injectors valued between £20,000 and £35,000 as part of a package deal for contrast agents was not a fair or reasonable arrangement in breach, *inter alia*, of Clause 18.1.

The Panel noted that Clause 18.1 prohibited the provision, offer or promise of a gift, pecuniary advantage or benefit to health professionals or other relevant decision makers as an inducement to prescribe, supply, administer, recommend, buy or sell any medicine. Its supplementary information Long term or Permanent Loan stated that the requirements of Clause 18.1 could not be avoided by the provision of items on long term or permanent loan. Such items would be regarded as gifts and subject to the requirements of that clause. The supplementary information Package Deals stated that Clause 18.1 did not prevent the offer of package deals which were commercial arrangements whereby the purchase of a particular medicine was linked to the provision of certain benefits as part of the purchase price such as apparatus for administration, the provision of training on its administration or the services of a nurse to administer it. The transaction as a whole must be fair and reasonable and the associated benefits must be relevant to the medicine involved.

The Panel noted Mallinckrodt's submission that its injectors were not offered on long term or permanent loan. The Panel also noted the company's detailed submission about its past practices when it was part of a separate company at the time of the original purchasing organisation tender which referred to financial loan agreements. The Panel's understanding of Mallinckrodt's response was that post July 2013, when it became a separate company, these loan agreements were no longer offered. The Panel considered the complaint in relation to the company's account of its current practice which had been adopted since February 2015 and was thus in use at the date of the complaint and thereafter.

The Panel noted Mallinckrodt's explanation that package deals were developed based on customer usage requirements to ensure that the provision of an injector complied with Clause 18.1. Deals were mainly for 2-3 years. Provided the commitment to volume of Mallinckrodt product was achieved, customers were free to choose alternative contrast media suppliers whilst retaining the injector. Package deals were based on the value of the

equipment being a given percentage of the total value of consumables/contrast media which Mallinckrodt submitted was in accordance with NHS terms and conditions. The ownership of the injector was transferred to the customer on delivery as part of the total package deal and was inclusive of the purchase price of the pre-filled syringes. Mallinckrodt submitted that this was fair and reasonable due to the fact that the equipment was necessary for performing clinical tasks as outlined in the supplementary information to Clause 18.1.

Mallinckrodt referred to its compliance calculator which included installation costs, average selling price of the associated injector and service and maintenance costs which again Mallinckrodt submitted was in accordance with NHS terms and conditions. The Panel noted that the compliance calculator had been revised subsequent to the receipt of the present complaint; the Panel did not consider the revised version as part of this complaint.

The Panel noted that according to the template contract, in return for the payment of the equipment price, the service fee and the purchase of an agreed volume of consumables at agreed prices, Mallinckrodt agreed to supply equipment [the injector] and services to the customer. The customer acknowledged that the level of discount was offered on the basis of the total value of the package deal. The Panel noted that the template was inconsistent in some regards; it referred to title passing to the customer on payment in full of the equipment price although Mallinckrodt had confirmed that ownership passed on delivery. The Panel noted Mallinckrodt's submission that there was no contractual or other mechanism to recover the investment if insufficient volume was purchased and that currently the company did not wish to impose a financial penalty for failing to use sufficient product and not achieving the threshold. The Panel noted that Section 9 set out a termination clause by which either party could give notice for breach of a material term. The Panel noted that in effect under the contract the customer was

paying for the injector at an agreed level of discount which was related to the total value of the package deal.

The Panel noted Mallinckrodt's submission that it had only one product, an MR imaging injector, with a price anywhere near the £20,000 quoted by Bayer. This injector had never been placed on a package deal with MRI contrast media since end users had made a clinical decision not to use the Mallinckrodt contrast media in question.

The Panel noted that the relevant supplementary information to Clause 18.1 referred to the provision of apparatus for administration. The Panel noted that the injector could be used not only with Mallinckrodt's contrast media but also with others. Ownership apparently passed to the customer upon delivery although the Panel noted its comments on the contract above. The injector would not be removed if agreed volumes were not achieved and it appeared that the total cost paid by the customer included an element which reflected the discounted cost of the injector. In the Panel's view the overall agreement did not appear to be unfair or unreasonable and thus it considered that the arrangements constituted a *bona fide* package deal.

The Panel noted that, as submitted by Mallinckrodt, there was a complicating factor in that it had previously been decided that Clause 18.1 applied to individuals rather than organisations etc. The Panel noted its decision above that the arrangements were a *bona fide* package deal and further that there was no benefit to an individual. In any event Mallinckrodt had not provided an injector which would sell for £20,000 to £35,000 as alleged. The Panel ruled no breach of Clause 18.1. Further, the Panel ruled no breach of Clause 2.

**Complaint received**                      **1 December 2015**

**Case completed**                              **4 May 2016**

# ANONYMOUS, NON-CONTACTABLE v NAPP

## Therapy review and advisory board

An anonymous, non contactable complainant was particularly concerned about a therapy review service run by Napp Pharmaceuticals and its use of advisory boards.

The detailed response from Napp is given below.

The complainant provided material which he/she alleged clearly showed the therapy review service, Optimising the Review and Control of your Asthma Patients (ORCA) was aligned to sales and alleged that staff were told that it should not be offered where a switch was not guaranteed.

The Panel noted that the ORCA service began in February 2015. The service, funded by Napp, was carried out by third party nurse advisors. According to Napp's submission ORCA was a therapeutic review service aimed to help establish Napp as a provider of a first class asthma service to patients, to provide an effective review of asthma patients at steps 3 and 4 of the British Thoracic Society (BTS) guidelines, to optimise asthma control by improving patients' knowledge and understanding and to establish effective working relationships with clinical commissioning groups (CCGs) in relation to asthma services.

The Panel noted that representatives and area business managers (ABMs) could briefly introduce the service during a promotional call to practices in areas of high asthma prevalence or where high levels of variation in care existed compared with local CCGs/practices, and in practices which lacked a trained respiratory nurse specialist or which required additional nurse resource to effectively review their asthma population. Subsequently at a non-promotional call ABMs could present the service and complete the practice authorisation form. The Panel queried whether it was necessary for the ABM to introduce the respiratory nurse on the first day of the service but noted that they had to leave immediately following this and must not be involved in any discussions with the nurse or GP regarding the running of the ORCA service. It appeared that representatives could continue to call on the practice as normal during the implementation of the service.

The Panel noted Napp's submission that following the arrival of the nurse advisor and confirmation of the practice treatment protocol and requirements for service, delivery of the service comprised four phases. Firstly, asthma patients were selected for therapeutic review and baseline reports for each patient were provided to the practice. During phase 2, a patient review for requested groups was conducted in line with the BTS/ Scottish Intercollegiate Guidelines Network (SIGN) guidelines. The practice treatment protocol detailed the clinic treatment protocol including the non-

pharmacological protocol and the pharmacological treatment protocol. The nurse would document the practice's chosen medicine within each step of the BTS/SIGN guideline; there might be multiple options, as advised by the lead GP on behalf of the practice. Following completion of the practice treatment protocol, the practice confirmed asthma patients to be invited to clinic. During the patient's clinic consultation the nurse advisor would document any decision to change or commence treatment and provide the rationale for such changes which was presented to the lead GP who authorised the action in alignment with the practice treatment protocol. Actions might include no action or medicinal or non-medicinal interventions. For all authorised interventions, the nurse advisor would update the patients' electronic records. The decision to change or start any treatment was made for each individual patient by the clinician and documented with evidence that it was made on rational grounds. Lastly, at the end of the final clinic, the nurse advisor would present and discuss the practice report with the GP to bring the service to a close.

The Panel noted Napp's submission that its support of the therapeutic review was not dependent on the customer prescribing a Napp product and that therapy choice arising from the patient clinical review remained the choice and decision of the GP. The nurse advisor could not and would not recommend a specific medicine, write prescriptions, implement a switch service or recommend or take any action that did not comply with the practice treatment protocol. The briefing documents outlined the service and selection criteria, the roles and responsibilities of the representative, ABM and service nurse and the relevant requirements of the Code. It was made clear that representatives could only provide administrative support in relation to service delivery and that support of the service must not be dependent on the customer prescribing a Napp product. Prescribing of specific products must not be linked to the service either in conversation or in writing with any customer. The training slides included a section on the Code requirements for consideration when carrying out a therapy review.

The Panel noted that Napp was responsible for the nurses. The practice treatment protocol document did not require the practice to identify which of the available medicines it used for each step of the BTS/SIGN guidelines if the practice decided to follow the Guidelines. Such information appeared to be required only if the practice treatment protocol was not as per BTS/SIGN guidelines whereupon the practice treatment protocol included selection of a specific medicine ('drug of choice'). This appeared to be inconsistent with Napp's response that the nurse documented with the practices their chosen medicines at each step of the BTS/SIGN guidelines.

The Panel noted Napp's submission that the material provided by the complainant linking ORCA to individual sales targets was a confidential preliminary version of an internal business case document circulated to five Napp employees during a consultation period. The Panel noted Napp's submission that ORCA was removed from the final version before being sent to those not at the original meeting to avoid any misunderstanding. The Panel was very concerned about the document in effect linking ORCA to the use of Flutiform (fluticasone and formoterol). It considered even showing it to five company people was a concern particularly as at least one was a representative.

The Panel noted Napp's submission that the number of ORCA reviews was not included in the sales targets calculation and were not monitored in relation to measuring success against those targets; no one was being incentivised based on the ORCA service.

The Panel noted the flat rate fee agreed between Napp and the third party service provider and queried the lack of reference to a minimum or maximum number of practices to be covered by this fee.

The Panel noted its general comments above about the service. It appeared that at least the complainant considered that the ORCA service was included in sales targets and had been told it should not be offered to anyone where Napp was not guaranteed a switch. It appeared that the choice of medicine was agreed by the practice. The November 2015 monthly report showed the number of patients who changed medication. The key performance indicator of average clinic attendance in 2015 was not met.

The Panel noted that the practice authorisation form included as a footer to the page showing the service flow that '...ORCA... is a full therapeutic review service and not a switch service. A switch service is one where patients are changed from one medicine to another without clinical review'. In the Panel's view it would have been more appropriate to explain what a therapy review service was.

Whilst some concerns were outlined above the Panel did not consider that the complainant had proved his/her complaint on the balance of probabilities. The Panel did not consider that there was any evidence before it to demonstrate that the service as implemented was included in individual sales targets or was only offered where a switch was guaranteed as alleged. The Panel thus ruled no breaches of the Code including Clause 2.

The complainant further alleged that Napp was using advisory boards and educational meetings as a way of promoting its product.

The complainant stated that a Remsima (infliximab) advisory board held in London after the company won the London tender, was only held to generate sales and break down barriers to prescribing. The meeting Chairman was a doctor who used the advisory board to describe his/her positive

experiences of Remsima and why switching to it was a great idea; this was bragged about in the company newsletter. The complainant was concerned that attendees were being paid to be promoted to.

The Panel noted that it was acceptable for companies to pay health professionals and others for relevant advice. Nonetheless, the arrangements for such meetings had to comply with the Code. To be considered a legitimate advisory board the choice and number of participants should stand up to independent scrutiny; each should be chosen according to their expertise such that they would be able to contribute meaningfully to the purpose and expected outcomes of the advisory board. The number of participants should be limited so as to allow active participation by all. The agenda should allow adequate time for discussion. The number of meetings and the number of participants should be driven by need and not the invitees' willingness to attend. Invitations to participate should state the purpose of the advisory board meeting, the expected advisory role and the amount of work to be undertaken. If an honorarium was offered it should be made clear that it was a payment for such work and advice. Honoraria must be reasonable and reflect the fair market value of the time and effort involved.

The Panel noted Napp held a number of advisory board meetings since agreeing the tender in London.

The company newsletter article, written by a senior medical scientific liaison (MSL) who attended the meeting, was headed 'The clinical perspective on using Remsima in Rheumatoid arthritis [RA]' and referred to Remsima being currently 'commercially competitive' in London. It also mentioned the recent very successful advisory board in London. It referred to the objectives of the advisory board and that the Chairman had hands on experience of using Remsima and had decided to move all his/her RA patients from Remicade to Remsima. The newsletter only referred to the Chairman sharing his/her positive experience of using the biosimilar, no mention was made of the fact that not all of his/her patients had a positive experience as submitted by Napp. The article named all the clinicians attending and stated that the advisory board met all the company's objectives and a clear action plan had been put in place.

The Panel noted that it did not have a copy of the original invitations. Material described as such were in fact letters confirming participant's acceptance of the invitations. These letters made it clear that recipients were expected to participate in the meeting. The letters referred recipients to the meeting agenda and unspecified additional documentation to understand, *inter alia*, whether any preparation was required for the meeting. In the Panel's view, whether pre-reading was required should be made abundantly clear. The Panel noted that the pre-reading consisted of two clinical papers focussing on Remsima in RA and ankylosing spondylitis (AS) and a third paper on biosimilar regulation in the UK.

The meeting which was held in November 2015 ran from 6pm to 7.30pm when a buffet dinner was served. The draft agenda stated that the introduction and review of the agenda took ten minutes and twenty minutes was allocated to the Chairman's presentation and questions on preliminary data in approximately twenty patients with RA switched from originator to biosimilar infliximab. Fifty-five minutes was then allocated for discussing views on the Chairman's presentation. The objective of the discussion, according to the draft agenda, was to explore views of the use of biosimilar infliximab in RA, to identify the key factors that might facilitate or prevent biosimilar usage in the current NHS environment, to discuss views on current National Institute for Health and Care Excellence (NICE) guidance, the use of anti-tumour necrosis factors (TNFs) in RA, the impact biosimilar infliximab might have on the treatment pathway and to gain input on key activities Napp should consider to help support clinicians with the use of biosimilars. The meeting ended with a summary (five minutes).

The Chairman's presentation was entitled 'The clinical perspective on using Remsima in Rheumatoid Arthritis'. According to Napp's submission the 39 slides were presented in 20 minutes. Two of the early slides referred to the availability of prescribing information from Napp staff at the event. This was according to Napp due to an oversight when repurposing some of the slides from a previous promotional meeting. The presentation focussed on the Chairman's changing opinion on biosimilars and the outcomes of changes at his/her hospital where patients had been switched from the originator product to Napp's Remsima. One section referred to the failure to hear any concrete evidence of loss of efficacy or unforeseen toxicity and the similarity given the degree of manufacturing variation over the years for all originator biologics. It was queried whether a switch could improve patient care in the broader sense. Adapted NICE treatment algorithms were presented as well as recommendations from an international task force. The presentation highlighted certain 'problems' including that patients with certain levels of disease (DAS28: 3.2-5.1 'moderate activity') were not eligible for anti-TNF therapy in England and Wales. Other countries recommended use of biologics in patients with a persistent DAS>3.2. The presentation referred to departmental issues and that the cost savings should be reinvested elsewhere in the department for patient benefit. A 50:50 gain share agreement had been agreed in London. The difference per vial was £188 (44% reduction in costs). It gave details of how patients were informed and offered the option of switching back to Remicade. The patient acceptability section stated that most had heard about Remsima and had a positive attitude about cost saving. The presentation stated 'Reinvested in improvements to their care'. Detailed switch data so far were presented in RA, AS/spondylo arthritis and psoriatic arthritis. The anticipated annual revenue for reinvestment in rheumatology was around £50,000.

The Panel noted that there was no presentation on the reasons for not switching to add balance to the discussion. It appeared that the focus of the presentation was to inform the audience of the advantages of changing to Remsima.

The Panel considered that the meeting objectives were very much about how Napp could improve the uptake of Remsima in NHS London. There did not appear to be any discussion or attempt to understand why it was not being used. The Panel queried whether the time for debate was sufficient. It was likely that the detailed presentation would lead to quite a few questions. The Panel queried Napp's submission that the Chairman's presentation was necessary to answer its business question. The Panel wondered why Napp had not just asked the advisors why they were not using Remsima rather than the Chairman presenting reasons for why they should be.

The outcome of the meeting was recorded in a summary report which was divided into four sections. The use of biosimilar infliximab (Remsima) section included 'No major issues were seen in historical patients with [RA] ... switched from Remicade to Remsima by the Chairman', it made no reference to the Chairman's presentation which included examples of where patients had not responded well following a switch to Remsima. This section also mentioned that the use of biosimilars could improve patient care for example 'expanding the market in previously restricted indications, where the route to funding is difficult and time-consuming'.

The commissioning section highlighted the variations in approach and concern about CCGs forcing switches in the near future. There needed to be an incentive to switch because of the extra work involved. There was a low level of awareness about local gain share agreements and if this information was shared clinicians would be more inclined to act themselves. Sharing of success stories would help clinicians to achieve the same success in their areas.

The recording a national charity's viewpoint section referred to the charity's willingness to alter its position on switching patient to biosimilars. Learning about experiences in other countries (Norway) appeared to have been influential in this regard. The charity was discussing with NICE funding for the moderate RA patient group as the worst patients in this group needed biologics.

Key activities for Napp to consider were outlined. The Panel considered that many of the actions identified were not surprising and might well have been anticipated and identified by the company itself and/or other previous advisory boards. There had been three other advisory boards within London in 2015 which all focussed on the lack of uptake in London. One in May focussing on gastroenterology indications which the Chairman attended as an advisor and in October on the payer/pharmacist/commissioner perspective. There was also an advisory board in March 2015 on the value of infliximab and antibody testing in inflammatory



bowel disease. The Panel thus queried whether, in this context, there was a *bona fide* need for the advisory board in question.

The Panel was concerned about the number of other advisory boards held with different audiences which discussed similar themes. Further, the only presentation was very positive on the use of Napp's product. The Panel noted its comments above about the arrangements, and feedback for the meeting. Taking all the factors into account, but in particular noting the unbalanced nature of the presentation, the number of similar recent advisory boards and, in this context, the absence of a *bona fide* question to be addressed, the Panel did not consider that the arrangements were such that the UK health professionals had attended a genuine advisory board meeting. It therefore ruled a breach of the Code which was upheld on appeal.

The Panel considered that, as it had ruled the arrangements did not meet the criteria for advisory boards, UK health professionals had been paid to attend a meeting where a product was promoted. This was contrary to requirements of the Code and a breach was ruled which was upheld on appeal. The Panel considered that the requirement that promotional material and activities must not be disguised had not been met and ruled a breach of the Code which was upheld on appeal.

The Panel considered that, overall, high standards had not been maintained and a breach of the Code was ruled which was upheld on appeal.

The Panel noted that Clause 2 was reserved for use as a sign of particular censure. The health professionals had attended the meeting believing it was a legitimate advisory board meeting, which was not so. The Panel noted that unacceptable payments was listed in the supplementary information to Clause 2 as an example of an activity likely to be in breach of that clause. The Panel considered that the arrangements brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled which was upheld on appeal.

An anonymous, non contactable complainant contacted the Authority concerned about the activities of Napp Pharmaceuticals Limited. The complainant submitted that over the past few years, Napp had gone from fearing and respecting the Code to now holding it in disregard. Whilst there were many breaches occurring, the complainant was particularly concerned about Napp's use of advisory boards.

## 1 Therapy Review Programme

### COMPLAINT

The complainant alleged that Napp was spending more on this 'non-promotional' activity than any genuine promotional drive. Whilst this was meant to be a therapy review, it was included in individual sales targets and staff were clearly told that it should not be offered to anyone where a switch was not

guaranteed. There were serious consequences if the service was offered to the wrong surgery. The complainant provided an excerpt which he/she alleged clearly showed the service, Optimising the Review and Control of your Asthma Patients (ORCA) was aligned to sales.

The attachment referred to a proposed new area structure for the sales force stating that every clinical commissioning group (CCG) was categorised into one of four quadrants according to the prescribing environment and the current business performance of Flutiform (fluticasone propionate and formoterol fumarate dehydrate). Two quadrants mentioned ORCA these being 'Development' and 'Priority'. 'Development' (the environment was positive and there were signs of early growth) stated that representatives work here and there was some healthcare development manager work as well as 'start growing'. 'Priority' (the environment and performance was positive and the need was to accelerate growth further) stated that representatives work here and 'accelerating growth'.

The axis for the quadrants was attractiveness potential for growth (y axis) and '[Flutiform]' performance (x axis). The attractiveness axis was driven by potential for growth, including how positive the prescribing environment was for Flutiform (such as being on the formulary and its position on formulary. The Flutiform performance axis was mainly based on growth (short and long term performance).

When writing to Napp, the Authority asked it to respond in relation to Clauses 2, 9.1 18.1 and 19.1 of the Code.

### RESPONSE

Napp stated that the ORCA therapy review programme was offered as a non-promotional service to the NHS via a third party. This service was conducted by respiratory nurse advisors.

Napp explained that the service began in February 2015. The third party provider had 10 years of experience of delivering such services to the NHS and had worked closely with Napp medical affairs, compliance and legal to deliver an asthma review service to primary care that specifically upheld Clauses 18.1 and 19.1.

Napp submitted that a comprehensive account of the asthma therapy review programme arrangements was provided. This comprised all materials, including those provided to representatives, health professionals, patients, briefing documents, training documents and the contract between Napp and the third party service provider.

Napp noted the complainant's allegation that it was 'spending more on this 'non-promotional' activity than any genuine promotional drive'. The budget and accountability for this non-promotional activity was held within medical and not sales and marketing. The investment in the ORCA service as a percentage of spend on Flutiform promotional activities was

provided as was the number of practices signed up and completed. The number of nurse days was also provided.

The ORCA review service was not included in any individual sales targets ('AE briefing Q3 redacted' and 'Napp incentive scheme sales force briefing Q4') and Napp refuted the allegation that representatives and area business managers (ABMs) were told that the service 'should not be offered to anyone where a switch was not guaranteed'. ORCA was not a switch programme. The briefing documents clearly explained the therapeutic review service and the roles of the representatives in introducing the service and ABM. Napp submitted that these documents showed that careful attention had been given to explain Clause 19.1, differentiating therapeutic review service from switch with a question and answer section for clarity. Representatives could only introduce the service against the specified selection criteria in the service documents.

Napp submitted that the one page excerpt provided by the complainant was from a confidential internal preliminary version of an internal business case document. This formed part of a communication about the Napp re-structure involving the sales force. ORCA was on the preliminary version of the four-quadrant diagram to illustrate, in an earlier internal meeting, that if the sales force was to be redistributed to these areas, where asthma burden was greatest, that this was where representatives could introduce the ORCA service to interested health professionals. It was simply to illustrate that under the proposal this was part of where the sales force would be working and therefore where the service would be introduced. This was not linked to sales and was not communicated as such.

This document was a preliminary version of the minutes circulated to a small representative panel of five employees during a consultation period on the restructuring of Napp. During that meeting a question was raised on the rationale for the proposed change to the primary care sales force deployment in the UK. Napp stated that its salesforce was currently evenly distributed based predominantly on geography and the promotion of a pain product that was no longer actively promoted. The four quadrant image was used to describe the potential business environment, performance of Napp's asthma brand and therefore the distribution of the majority of the sales force into 'priority' and 'development' accounts where the asthma burden was high and thus use of asthma medications was also proportionally high (over 66% of the country). ORCA was never discussed in the presentation, as this was purely used to illustrate the reasons for the sales force redeployment and was simply a proposal for discussion at the time.

Napp stated that the minutes were reviewed by legal and compliance and amended before final distribution on 11 November, such that 'ORCA' was removed from the graph in case of any misunderstanding from those who were not at the meeting, so Napp was puzzled as to how the complainant obtained a copy.

## ORCA Therapeutic Review Service

Napp stated that although it funded the ORCA service, therapy choice arising from the patient clinical review process remained the choice and decision of the GP, and offering of the service was not conditional on the prescribing of any Napp product. In line with Clause 19.1, the ORCA service provided a full therapeutic review and clinical assessment for individual patients leading to a rational management decision by the GP. This allowed the patient to receive optimal treatment or other non-medicinal intervention as decided by the GP. The respiratory nurse advisors did not suggest and would not implement switch services which simply changed a patient from one medicine to another without a full clinical assessment. Napp referred to the (nurse briefing and practice treatment protocol).

Napp provided details of its third party provider and design and delivery of nursing and IT services to practices in the UK on behalf of a variety of NHS and pharmaceutical company customers. The third party provider had invested in the provision of specialist nurse advisors to ensure it provided highly qualified disease management experts across a variety of long term conditions, such as asthma. Napp believed in collaborative working with health professionals for the benefit of patients and chose to work with the third party provider due to its experience in service delivery within the field of respiratory medicine.

Napp chose to fund the ORCA service in order to:

- Help establish a position for Napp as a provider of a first class asthma service to patients
- Provide an effective review of asthma patients at steps 3 and 4 of the British Thoracic Society (BTS) guidelines
- Optimise asthma control by improving patients knowledge and understanding
- To establish effective working relationships with CCGs in relation to asthma services.

The ORCA service was a full therapeutic review service, which reviewed asthma patients from 5 years old, at steps 3 and 4 of the BTS/SIGN (Scottish Intercollegiate Guidelines Network) guidelines. The rationale behind this was that it was believed that patients at steps 3 and 4 of the BTS/SIGN guidelines were more complex to manage. This patient group accounted for 36% of the adult population in the UK. At steps 3 and 4, patients were generally managed in the community by GPs and practice nurses. Usually patients at step 5 would attend (or would have attended) specialist hospital services. Step 3 and 4 patients were the most severe patients managed largely in the community and the therapeutic options to treat this group could be complex, thus requiring specialist support. At step 1 there was a single class, short acting B2 agonist (SABA) and at step 2 a single additional class (inhaled steroid). Step 3 and 4 options included introducing a long acting B2 agonist (LABA), increasing the steroid dose, adding a leukotriene receptor antagonist (LTRA) or theophylline or some combination of these. As these patients tended to have more severe disease and co-morbidities could co-exist, the requirement

to identify, agree and implement a useful treatment strategy was greater. There was little evidence to guide decision making at step 4 which might require specialist skills (BTS/SIGN Asthma guidelines 2014).

The ORCA programme focussed on assisting practices to review this group of patients by:

- The provision of a respiratory nurse specialist
- Asthma baseline audit (for patients with a confirmed diagnosis of asthma)
- Clinical review of step 3 and step 4 patients in line with NHS Quality and Outcomes Framework (QOF) AST003: The percentage of patients with asthma, on the register, who have had an asthma review in the preceding 12 months that included an assessment of asthma control using the three Royal College of Physicians (RCP) questions. ([https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/213226/Summary-of-QOF-indicators.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213226/Summary-of-QOF-indicators.pdf) Summary of QOF indicators)
- Service outcome report.

Without the service provider resource the GP/practice might not be in a position to identify existing asthma patients who might benefit from a clinical review due to budgets. Napp anticipated that the ORCA service would contribute positively to the practice's achievement of meeting QOF indicators and targets without practice resource being stretched.

### **Practice selection**

The practice selection criteria were defined as:

- Practices in high areas of asthma prevalence or where high levels of variation in care existed in comparison to other CCGs/practices within their own locality
- Practices which lacked a trained respiratory nurse specialist
- Practices which required additional nurse resource to effectively review their asthma population.

Napp stated that its support of a therapeutic review was not dependent on the customer prescribing a Napp product. This must be neither the fact in practice nor the impression given either verbally or in any documents connected with the project, internal or external. The prescribing of specific products must not be linked to the service in conversation, or in writing, with any customer. Detailed discussion about the service was not instigated at the same time as a call at which products were promoted. This had been clearly communicated to all Napp and service provider personnel involved in the service offering through sales force and nurse briefing and training.

### **The role of representatives**

Napp stated that its representatives and ABMs could introduce the ORCA service by briefly describing it during a promotional call but they could not instigate a detailed description about it at the same time as a call when products were promoted, it should be done in a non-promotional call. If following the brief description of the ORCA service, the practice wanted

more information the representative/ABM would proceed to organise a non-promotional call that would be conducted by the relevant ABM, where the service bridging piece might be utilised. The service bridging piece outlined the service offering, the service aims, service process and details of the third party provider and its credentials relating to offering the service.

Once a practice confirmed it wished to utilise the ORCA service, the ABM, within a non-promotional call, would then complete the practice authorisation form, a legal document which when completed frameworked the arrangements and understanding between the practice and third party to provide the ORCA service.

Following completion of the practice authorisation form, the ABM would then discuss possible service commencement dates with the practice and telephone the third party service provider to book the first day of service. The ABM could introduce the respiratory nurse to the practice on the nurse's first day at the practice, but must leave immediately following this and must not be involved in any discussions with the nurse or GP regarding the service.

### Field force training:

Before the service started on 17 February 2015, the field force (ABMs and representatives) were comprehensively trained on the ORCA service.

The ABMs attended in-house training on 28 January 2015. During the morning they attended a general compliance workshop run by the senior code compliance advisor which covered amongst other items, medical and educational goods and services (MEGS) and therapeutic review.

This was followed by a specific ORCA therapeutic review training session in the afternoon where the ABMs received presentations from senior Napp staff and a third party provider.

During this training session the ABMs were provided with the approved documentation, including the ABM briefing which they had to read.

Following the initial training session, a teleconference in February 2015 further clarified the roles of the ABMs and representatives. This involved the regional operational managers, ABMs, marketing manager, senior medical advisor, senior compliance advisor, training manager and senior scientific advisor. The objective of the teleconference was to communicate the ORCA process to provide absolute clarity on the involvement of representatives and the way in which they could compliantly introduce the ORCA service to customers appropriately.

The ABMs were then required to successfully complete the ABM validation. A report from these validations was provided. The report documented the full list of ABMs and the dates on which they successfully completed the validation questions. The representatives had to confirm that they had read and understood the briefing material provided

via email. A report documenting the full list of representatives who had read and understood the briefing was provided. The ABMs also went through the ORCA process with their respective representatives using the briefing documents.

In addition, representatives and ABMs were advised via the representative briefing to direct all queries regarding the service to either the senior code compliance advisor or senior scientific advisor which they did if they had any compliance related queries.

### **The role of the third party nurse advisors**

The ORCA service was provided by a third party, and the asthma clinics were run by the third party's qualified nurse advisors who also received mandatory training on:

- Anaphylaxis, basic life support and use of automated external defibrillator
- Conflict resolution
- Infection control
- Consent and Mental Capacity Act
- Record keeping
- Raising concerns
- Safeguarding
- Adverse events via Wellards
- ABPI Code of Practice via Wellards.

The nurse advisors were responsible for delivering the service and their key responsibilities were:

- Initial meeting with the GP to confirm practice protocols
- To run the Miquet software tool to identify and complete a full therapeutic review for asthma patients
- Present an asthma baseline report to the practice
- Facilitate patient review with the practice
- Deliver asthma clinics to identified step 3 and 4 asthma patients within the practice
- Implement authorised intervention if requested by the GP
- Produce end of service outcome report.

The nurse advisor could and would not:

- Recommend a specific pharmaceutical product
- Write prescriptions
- Implement a switch service
- Recommend or take any action that did not comply with the practice treatment protocol.

The nurse advisors involved in the ORCA service had provided written confirmation that they had not received any funding or honorarium from Napp in the past. Before commencement of the service, the nurse advisors were provided with the Nurse Briefing Document along with relevant training from the third party provider managing director, head of nursing and medical director which included contractual responsibility for the Code.

### **Service delivery**

#### Phase 1 – Patient identification

During phase 1 of service delivery the nurse advisor

identified asthma patients using the Miquet Software Tool and conducted a full therapeutic review of every patient and presented baseline reports to the practice.

#### Phase 2 – Patient review

During phase 2 a patient review for requested groups was conducted, in line with BTS/SIGN guidelines. The practice confirmed the practice treatment protocol; section 3 detailed the clinic treatment protocol. This was the formal documentation which detailed the non-pharmacological protocol and the pharmacological treatment protocol. The nurse would document the practice's chosen medicine within the practice treatment protocol document. Medicines were documented within each step of the BTS/SIGN guideline. The medicines listed might be in line with local asthma prescribing guidelines, or might defer from these, and at each BTS/SIGN step there might be multiple options, as advised by the lead GP on behalf of the practice. Patients attending clinic would be counselled in accordance with the practice treatment protocol.

Following completion of the practice treatment protocol, the practice confirmed asthma patients to be invited to clinic. Copies of the patient invitation letters were provided.

#### Phase 3 – Asthma patient review clinic

The nurse advisor conducted asthma patient review clinics and implemented the practice treatment protocol. The practice nurse might attend some or all of the nurse advisor clinics in line with practice requirements.

During the patient consultation the nurse advisor would complete a Clinical Assessment Sheet to document any decision to change or commence treatment and provide the rationale for such changes. The Clinic Assessment Sheet documented details of the review and included the following:

- Patient consent
- History
- Current asthma medication (including BTS step and date of last influenza vaccine)
- Asthma control
- Clinical measurements
- Inhaler technique assessment and any subsequent instructions given by the nurse advisor
- Self-management plan
- Nurse summary
- GP recommendations and requests.

Following the patient review, the Clinical Assessment Sheet for each patient consultation was presented to the lead GP. The GP then authorised the action proposed by the nurse advisor in alignment with the practice treatment protocol. This might include no action as well as medicinal or non-medicinal interventions. For all interventions that were authorised, the nurse advisor would update the patients' electronic records to incorporate any medicines or other changes as requested by the GP. The decision to change or start any treatment must be made for each individual patient by the clinician

and every decision to change an individual patient's treatment must be documented with evidence that it was made on rational grounds and this was the case with the ORCA asthma review service.

Napp and the third party provider believed that it was good clinical practice that no patient interventions or changes to patient treatment were implemented without the patient being present and as part of a face-to-face consultation. Nurse advisors as part of the ORCA service would not implement such requested changes unless the patient had been invited at least twice for review as part of the service and failed to respond. If that was the case and the GP requested treatment interventions for and on behalf of the practice then a detailed process was followed. The process was only implemented, for change to medicine, and if the patient failed to attend the clinic following two separate invitations to do so. If the change to medication involved changing to a different device (eg dry powder inhaler or pressurised metered dose inhaler), this would only occur after the patient had seen the practice nurse. In such cases the patient would receive a letter informing them of this.

#### Phase 4 – Service completion

At the end of the final clinic in the practice, the nurse advisor would present and discuss the practice report with the GP to bring the service to a close.

The practice report documented:

- The practice's baseline data
- ORCA clinic logistics and activity
- Review of the practice objectives (as agreed and set out in the practice treatment protocol)
- Outstanding practice reviews awaiting completion.

#### **ORCA metrics**

Napp stated that it did not monitor any uplift in sales in areas where the ORCA service had been conducted. Neither were representatives bonused on ORCA. The senior scientific advisor (who was non-promotional and sat within the medical department) was the project lead and had regular telephone contact and meetings with the third party provider. The third party provider also provided details of the completed practices to the project lead, which were documented from a transfer of value perspective.

The client report, which Napp received on a monthly basis, detailed anonymised information about the:

- Event breakdown (including practice recruitment numbers and nurse days delivered)
- Bookings made by current month and year to date (YTD)
- Clinic breakdown
- Review outcomes (Add medicine, increase dose, decrease dose, change device, change medicine, medicine stopped, education only, referral to specialist care/GP, spacer added, other, number of patients who received a self-management plan (SMP))

- Practice feedback YTD
- Patient satisfaction questionnaire YTD
- Third party provider practice feedback YTD
- Performance against key performance indicators (KPIs).

In conclusion, Napp strongly disagreed with the allegations made by the anonymous complainant. Napp submitted that it had provided comprehensive evidence in its response. Napp stated that it had robust and compliant processes and systems, training to implement a proper therapeutic review service via its third party supplier and integral to the non-promotional service to the NHS it had paid particular focus on Clauses 18.1 and 19.1. Napp submitted that it had at all times maintained high standards as per Clause 9.1, and this activity had not brought discredit upon, or reduced confidence in the pharmaceutical industry as per Clause 2.

In response to a request for further information, Napp submitted that its sales team did not monitor and/or incentivise any uplift in sales in areas where the ORCA service was conducted. Napp explained that the ORCA therapy review monitoring was solely between the medical team and the third party service provider.

The sales teams, including managers, did not have access to the ORCA client reporting metrics as this was a non-promotional activity. There was deliberately no discussion or link by a manager between a sales person's sales targets for his/her geographic area and the therapy review service. The sales force were deployed geographically. It was simply for ease of understanding internally that the ORCA monthly management report used the same terminology for the geographic areas rather than by CCG. Although it could be inferred that the sales targets and incentive scheme in certain areas matched with the name in the ORCA monthly event management report this was coincidental and they were not linked. The report was discussed within the medical and code compliance department, and the geography allowed Napp to ensure that it was offering the service across the UK and not restricted to very few regions. As stated, when Napp set sales targets, ORCA asthma therapy reviews were not included in the calculation used to determine what growth a territory could deliver (territory effectively being an arbitrarily defined geography based on the practices/CCGs that a sales person worked). The number of ORCA reviews by area were not included at any point in the targets calculation and were not monitored in relation to measuring success against target. Napp did not include any planned or future ORCA reviews in the calculations used to determine the sales targets and were not incentivising anybody on ORCA reviews and no individual sales person's target was affected by ORCA reviews.

Napp submitted that the nurse briefing was developed between Napp and the service provider for the asthma therapy review; there were no other similar briefings on products and interventions provided by the service provider to their nurses. Napp stated that the service provider provided further information below regarding details about

the initial meeting of their nurses with the GP practice as follows and highlighted the sequence of events that happened on the first service day and subsequent clinic days to add further clarity to the points that have been raised in particular around practice protocols and any requested interventions.

### **Initial meeting between service provider nurse and practice**

Following a practice requesting the ORCA service the Napp ABM completed the practice authorisation form with the practice during a non-promotional call as highlighted in the Napp ABM briefing document. In addition, to the completion of that document with the practice, the ABM met the nurse advisor on the first day of service delivery to introduce him/her to the practice and would then leave and not be party to any discussion between the nurse advisor and the GP in relation to service requirements and practice protocols. This was outlined in the nurse briefing document which was given to the Napp ABMs as part of the service training. Therefore the instruction provided to the ABMs and service provider by Napp was that the ABM should not be present in the practice whilst service requirements and practice treatment protocols were being confirmed between the practice and the service provider.

Following the departure of the Napp ABM, the nurse advisor commenced service delivery in line with the main actions contained within the Nurse Briefing Document. The first action was to confirm with the practice their treatment protocols and requirements for service delivery. The practice treatment protocol provided the nurses with the framework for the initial meeting with the practice and lead service GP. The nurse worked through this document, page by page, with the practice in order to ensure the practice understood all elements of the service flow to aid in the smooth running of the service. The practice was also asked what they would like to gain from nurse support and those objectives were captured. Stated objectives varied, but for example might include to issue self-management plans to all patients attending clinic or to prioritise review of patients at steps 3 and 4 of the BTS/SIGN who might be overusing their reliever inhaler. It was also established if the practice followed the BTS/SIGN guidelines or other local guidelines. In addition the practice was asked to confirm its products of choice at each of the BTS/SIGN steps and this was written in the practice treatment protocol either generically or by brand as per the practice requirements. The GP then signed against the protocol and the nurse implemented practice documented requirements through the clinic process. In addition the clinical review logistics were agreed, the clinical assessment sheet was completed for each patient attending clinic. In addition, the nurse advisor outlined that with practice and patient approval. Each patient reviewed would be asked to complete an anonymous patient satisfaction questionnaire and a service completion questionnaire practice treatment protocol. In short the instructions and briefings given to nurse advisors in running this initial meeting could not be more explicit and working through the practice treatment protocol with the

practice ensured a consistent approach to facilitate the initial meeting with the GP and ensured that the service provider had a thorough and documented understanding of practice, disease and prescribing protocols before any patient review commenced.

### Products and interventions provided by the service provider to its nurses

Following the review of patients within the clinic in line with the requested practice treatment protocol, the nurse advisor presented the completed clinical assessment sheet to the GP for review and authorisation as outlined above. Clear guidance on interventions was provided by the service provider to its staff in the nurse briefing document. The nurse advisors also received a briefing which stipulated what they could not do including recommending a specific pharmaceutical product, write prescriptions, implement a switch service or recommend or take any action that did not comply with the practice treatment protocol. This guidance was provided in the nurse briefing document.

Napp submitted that as outlined above the service provider provided clear documented briefings to the nurses in relation to the process that had to be followed regarding the implementation of all service steps including those for medicinal and non-medicinal interventions.

### Further Relevant Information

All nurse advisors working on this service were respiratory nurse specialists. As part of their induction process all nurses were clinically validated by senior nurse managers and were required to discuss in depth case studies surrounding the management of asthma. All nurses were provided with the current BNF and MIMS and received any relevant clinical updates as new products were launched. The nurses also received quarterly clinic updates as well as having their Primary Care Respiratory Society membership funded by the service provider to ensure that the team's knowledge remained current. The nurses also received quarterly clinical updates from key opinion leaders in asthma related topics.

The completion of all service paperwork with the practice was subject to validation on the nurse's initial training course (ITC), following which each nurse advisor received regular 4 weekly field visits conducted by experienced respiratory nurse managers in order to assess both adherence to process and clinical competency in line with Care Quality Commission (CQC) requirements. A documented report for each field visit was maintained on record.

All nurse advisors were required to complete ABPI validation as part of their ITC together with other mandatory training.

The nurse advisors had not received any briefings in relation to Napp respiratory products from Napp or the service provider. As highly qualified specialists they were aware of what products and inhaler

devices were on the market together with their respective licence indications and their overall aim was to improve asthma outcomes for practices and patients in line with practice requested treatment protocols and prescribing policy. The nurses also received and were taken through the service training deck. When nurses joined they were already specialist asthma nurses. The service provider's aim was to ensure that they were trained in service processes and that their knowledge remained current.

## PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable. Anonymous complaints were accepted and like all complaints judged on the evidence provided by the parties. The complainant had the burden of proving his/her complaint on the balance of probabilities.

The Panel noted the complainant's allegation that although the ORCA service was meant to be a therapy review, it was included in individual sales targets and employees were told that it should not be offered to anyone where a switch was not guaranteed.

Clause 19.1 stated that medical and educational goods and services must enhance patient care or benefit the NHS and maintain patient care. The relevant supplementary information provided further guidance about the implementation of such services and the limited role of representatives. Representatives could introduce a service by means of a brief description and/or delivering materials but could not instigate a detailed discussion about the service at the same time as a call at which products were promoted. The supplementary information made reference to representatives providing administrative support in relation to the provision of a service and made it clear that Clauses 18.1 and 19.1 prohibited switch services paid for or facilitated directly or indirectly by a pharmaceutical company whereby a patient's medicine was simply changed to another. A therapeutic review which aimed to ensure that patients received optimal treatment following a clinical assessment was a legitimate activity for a pharmaceutical company to support. The decision to change or commence treatment must be made for each individual patient by the prescriber and every decision to change an individual patient's treatment must be documented with evidence that it was made on rational grounds.

The Panel noted that the ORCA service began in February 2015. It noted the number of practices that had signed up; the number where the service had completed and the numbers ongoing and those not yet commenced. The Panel noted there was a discrepancy in the number of practices and the reason for the discrepancy was unclear. The service funded by Napp was carried out by third party nurse advisors. According to Napp's submission ORCA was a therapeutic review service aimed to help establish a position for Napp as a provider of a first class asthma service to patients, to provide an effective review of asthma patients at steps 3 and 4

of the BTS guidelines, to optimise asthma control by improving patients knowledge and understanding and to establish effective working relationships with CCGs in relation to asthma services.

The Panel noted that representatives and ABMs could briefly introduce the service during a promotional call to practices in areas of high asthma prevalence or where high levels of variation in care existed in comparison to other CCGs/practices within the locality, in practices which lacked a trained respiratory nurse specialist and in practices which required additional nurse resource to effectively review their asthma population. Subsequently at a non-promotional call ABMs could present the service and complete the practice authorisation form. The Panel queried whether it was necessary for the ABM to introduce the respiratory nurse on the first day of the service but noted that they had to leave immediately following this and must not be involved in any discussions with the nurse or GP regarding the running of the ORCA service. It appeared that representatives could continue to call on the practice as normal during the implementation of the service.

The Panel noted Napp's submission that following the arrival of the nurse advisor and confirmation of the practice treatment protocol and requirements for service delivery the service comprised four phases. Firstly, asthma patients were selected for therapeutic review via a data collection search tool and baseline reports for each patient were provided to the practice. During phase 2, a patient review for requested groups was conducted in line with the BTS/SIGN guidelines. The practice treatment protocol which detailed the clinic treatment protocol including the non-pharmacological protocol (checking adherence with existing therapies, checking inhaler technique and eliminating trigger factors) and the pharmacological treatment protocol. The nurse would document the practice's chosen medicine within each step of the BTS/SIGN guideline; there might be multiple options, as advised by the lead GP on behalf of the practice. Following completion of the practice treatment protocol, the practice confirmed asthma patients to be invited to clinic. During the patient's clinic consultation the nurse advisor would complete a clinical assessment sheet to document any decision to change or commence treatment and provide the rationale for such changes which was presented to the lead GP who authorised the action proposed by the nurse advisor in alignment with the practice treatment protocol. Actions might include no action or medicinal or non-medicinal interventions. For all authorised interventions, the nurse advisor would update the patients' electronic records to incorporate any medicines or other changes as requested by the GP. The decision to change or start any treatment was made for each individual patient by the clinician and documented with evidence that it was made on rational grounds. Lastly, at the end of the final clinic, the nurse advisor would present and discuss the practice report with the GP to bring the service to a close.

The Panel noted Napp's submission that its support of the therapeutic review was not dependent on

the customer prescribing a Napp product and that therapy choice arising from the patient clinical review remained the choice and decision of the GP. The nurse advisor could and would not recommend a specific pharmaceutical product, write prescriptions, implement a switch service or recommend or take any action that did not comply with the practice treatment protocol. The briefing documents outlined the service and selection criteria, the roles and responsibilities of the representatives, ABM and service nurse and the relevant requirements of the Code. It was made clear that representatives could only provide administrative support in relation to service delivery and that support of the service must not be dependent on the customer prescribing a Napp product. Prescribing of specific products must not be linked to the service either in conversation or in writing with any customer. The training slides included a section on the Code requirements for consideration when carrying out a therapy review.

The Panel noted that Napp was responsible for the nurses. The practice treatment protocol document did not require the practice to identify which of the available medicines it used for each step of the BTS/SIGN guidelines if the practice decided to follow the guidelines. Such information appeared to be required only if the practice treatment protocol was not as per BTS/SIGN guidelines whereupon the practice treatment protocol included selection of a specific medicine ('drug of choice'). This appeared to be inconsistent with Napp's response that the nurse documented with the practices their chosen medicines at each step of the BTS/SIGN guidelines. Local asthma prescribing guidelines could also be referred to. In the Panel's view medicines might be discussed during completion of the form. Whilst the form made it clear that the nurses could not recommend a specific product it was important that companies could satisfy themselves that the nurses' training was such as to ensure that all such discussions including all direct and indirect references to medicines were non-promotional, fair and accurate and otherwise complied with the Code. This applied irrespective of the fact that the GP reviewed and mandated all clinical decisions as such decisions might be indirectly influenced by the preceding discussion with the nurse. The Panel noted Napp's comments regarding the nurses' initial meeting including discussions about the practice treatment protocol and the nurses' qualifications and ongoing training. The Panel was concerned that Napp had to seek additional information about the initial meeting and ongoing training from the third party service provider on request from the Panel. In the Panel's view Napp should have had this information on certification of the arrangements. The nurse briefing dealt primarily with matters of process rather than discussion of medicines and thus did not adequately cover this point.

The Panel noted Napp's submission that the attachment provided by the complainant linking ORCA to individual sales targets was a confidential preliminary version of an internal business case document circulated to five Napp employees during a consultation period. It referred to ORCA to illustrate the areas where representatives could

introduce the service following the sales force re-structure. The document explained that the deployment of the sales force with the vast majority being deployed in 'Priority' or 'Development' accounts where the asthma burden was high. The other two quadrants were 'Opportunistic' and 'Maintenance'. The updated document did not mention ORCA in the 'Development' or 'Priority' categories. The Panel noted Napp's submission that ORCA was removed from the final version before being sent to those not at the original meeting to avoid any misunderstanding. The Panel was very concerned about the document in effect linking ORCA to the use of Flutiform. It considered even showing it to 5 company people was a concern particularly as at least one was a representative.

The Panel queried Napp's submission that the sales in areas where the ORCA service was carried out was not monitored given that the ORCA monthly event management report recorded ORCA bookings made by region per month and the representative briefing and Napp incentive scheme salesforce briefing targets were determined for each area/territory and for each CCG which filtered down to targets for individual representatives. The regions in the ORCA monthly event management report correlated to those areas in the AE briefing and Napp incentive scheme salesforce briefing. The Panel, however, noted Napp's submission that sales teams, including managers, did not have access to the ORCA client reporting metrics as this was a non-promotional activity. There was deliberately no discussion or link by a manager between a sales person's sales targets for his/her geographic area and the therapy review service. Napp stated that it was simply for ease of understanding internally that the ORCA monthly management report used the same terminology for the geographic areas rather than by CCG. Although it could be inferred that the sales targets and incentive scheme matched with the areas in the ORCA monthly event management report this was according to Napp coincidental and they were not linked.

The Panel further noted Napp's submission that the number of ORCA reviews was not included in the sales targets calculation and were not monitored in relation to measuring success against those targets; no one was being incentivised based on the ORCA service.

The Panel noted the flat rate fee agreed between Napp and the third party service provider and queried the lack of reference to a minimum or maximum number of practices to be covered by this fee.

The Panel noted its general comments above about the service. It appeared that at least the complainant considered that the ORCA service was included in sales targets and had been told it should not be offered to anyone where Napp was not guaranteed a switch. It appeared that the choice of medicine was agreed by the practice. The November 2015 monthly report showed the number of patients who changed medication. The key performance indicator of average clinic attendance in 2015 was not met.



The Panel noted that the practice authorisation form included as a footer to the page showing the service flow that ‘...ORCA... is a full therapeutic review service and not a switch service. A switch service is one where patients are changed from one medicine to another without clinical review’. In the Panel’s view it would have been more appropriate to explain what a therapy review service was.

The Panel was concerned that Napp had only provided the updated contract between itself and the service provider when the Panel queried the agreed fees rather than with its initial response. The Panel noted that when Napp provided complete copies of the nurse briefing document, the practice authorisation form, ABM briefing and the practice treatment protocol they were not accompanied by certificates as were the incomplete documents that were previously sent. The Panel queried whether Napp had certified the incomplete documents.

Whilst some concerns were outlined above the Panel did not consider that the complainant had proved his/her complaint on the balance of probabilities. The Panel did not consider that there was any evidence before it to demonstrate that the service as implemented was included in individual sales targets or was only offered where a switch was guaranteed as alleged. The Panel thus ruled no breach of Clauses 18.1 and 19.1. Subsequently no breach of Clauses 9.1 and 2 were also ruled.

## 2 Advisory board

### COMPLAINT

The complainant alleged that Napp was using advisory boards and educational meetings as a way of promoting its product. According to the complainant, Napp staff were actively encouraged to use educational meetings as a way to ‘get-in’ with health professionals and then promote to them. Napp was also using health professionals to talk to their peers on its behalf knowing that what they were saying and how they were saying it was wrong.

The complainant referred to a Remsima (infliximab) advisory board held in London after the company won the London tender. The complainant alleged that the only reason it was held was to generate sales and break down barriers to prescribing. It was chaired by a doctor who used the advisory board to describe his/her positive experiences of Remsima and why switching to it was a great idea; this was bragged about in the company newsletter. The complainant was concerned that attendees were being paid to be promoted to.

When writing to Napp, the Authority asked it to respond in relation to Clauses 2, 9.1 12.1, 18.1 and 23 of the Code.

### RESPONSE

Napp strongly refuted the complainant’s allegation that it was using advisory boards to ‘generate sales & break down barriers to prescribing’. According to Napp:

- The advisory board in question was convened solely to answer legitimate business questions which Napp did not know the answer to; it was not a disguised promotional meeting.
- A group of seven advisors attended which was the minimum number required to achieve the stated objective.
- 15 minutes of the 90 minute meeting was set aside for introductions/conclusions; 20 minutes for clinical data presentation, and 55 minutes (61%) for advisor feedback.
- The advisory board discussion related solely to the stated objective, and a comprehensive report of the advice received was generated and used to guide Napp’s business decisions.
- Only a single advisory board was conducted on the specific topic.
- Written contracts were undertaken with each advisor, and their compensation reflected fair market value. Napp submitted that the arrangements and use of consultants as advisors had upheld Clauses 12.1 and 23.1.
- The venue was appropriate and conducive to the business purpose of the meeting.
- Payments made to individuals were appropriate and Napp had upheld Clause 18.1.
- All arrangements for this genuine consultancy were appropriate to the advisory board, including remuneration and expenses paid to the advisors. Napp had upheld Clause 23.
- High standards were maintained throughout the creation, organisation, conduct, and reporting of this genuine non-promotional advisory board. Napp had upheld Clauses 9.1 and 2.

### Materials

Napp provided copies of the invitations, agenda and all material provided to attendees about the arrangements for the advisory board including the written agreements as well as all materials and presentations used on the day and a full account of the hospitality. Copies of internal documents which set out the objectives for the meeting and the questions to which Napp needed an answer were provided.

Napp submitted that one presentation was delivered during the advisory board; it was not distributed as pre-reading as the slides needed to be viewed in conjunction with the verbal presentation given by the Chairman. The discussion of data also prompted further questions and discussion from the advisors which would not have been possible with pre-reading. Napp stated that although the approved presentation consisted of 39 slides, the Chairman was made aware of required timings and the 20 minutes stated on the agenda was strictly adhered to. Slides 3 and 4 contained reference to prescribing information due to an oversight when repurposing some of the slides from a previous promotional meeting. The presentation given during the advisory board was not intended to be promotional, was not received as such by the delegates, and prescribing information was not distributed. No other materials were used during the advisory board.

## Hospitality

The hospitality provided included: water, coffee, orange juice and biscuits prior to and during the meeting. A hot buffet was served in another room immediately after the conclusion of the meeting.

The total cost of hospitality was £444. Seven advisors attended the meeting, two Napp staff participated in the meeting (a senior scientific advisor and senior medical science liaison (MSL)), two Napp staff (senior marketing manager and medical advisor) observed the meeting, and a contracted medical writer took notes, making a total of twelve attendees. The total cost of hospitality was therefore £37 per head.

## Basis of consultant selection

Napp submitted that advisory board members were selected on the basis that they were consultant rheumatologists based in greater London with detailed understanding of biological medicines and biosimilars.

Napp considered that advisors selected using these criteria would be best able to meet the pre-defined objectives of the meeting, which were:

- To explore the views of the attendees on the use of biosimilar infliximab in rheumatoid arthritis (RA).
- To identify the key factors which might facilitate or prevent biosimilar usage in RA in the current NHS environment in London.
- To discuss the views of the attendees on the current NICE (National Institute for Health and Care Excellence) guidance on the use of anti-tumour necrosis factors (TNFs) in RA, and the impact infliximab could have on the treatment pathway.
- To gain input on the key activities Napp should consider to support rheumatology clinicians with biosimilars.

These non-promotional criteria were also provided in the internal company newsletter provided by the complainant. This was authored by a senior MSL who took part in the advisory board.

Additionally, a senior representative from a charity was selected to represent the important patient's viewpoint on switching from an originator medicine to a biosimilar. It was appropriate for him/her to attend the advisory board in the capacity of a 'relevant decision maker' when considering the use of biologic and biosimilar medicines in RA. The names of five consultants including their job title, hospital/organisation and the amount they were paid were provided.

The Chairman previously attended an advisory board in May 2015 which was mainly focused on gastroenterology to provide a rheumatology perspective on the use of infliximab. He/she also attended a rheumatology advisory board relating to Remsima in July 2014 and acted as a contracted speaker at a Remsima meeting in October 2015. Napp confirmed that none of the other advisors had

previously advised Napp or attended any other Napp meeting.

## Rationale why a London advisory board was held after Napp had won the London tender

Napp submitted that three brands of infliximab were currently available for prescription in the UK: Remicade (Merck Sharp and Dohme), Inflectra (Hospira), and Remsima (Napp). Remicade was described as the 'originator infliximab' and had been available since approximately 1999, whereas Inflectra and Remsima were biosimilar versions available since February 2015. In February 2015 a local pricing agreement was made between Napp Pharmaceuticals Limited and the London Procurement Partnership to provide Remsima at a favourable price to London hospitals. This commercial agreement excluded Inflectra, but did not exclude Remicade.

Subsequent uptake of Remsima in London was much slower than Napp anticipated, reaching a low market share (details provided) in September 2015 when planning for this advisory board was initiated. This was a surprising given that:

- It had been demonstrated in a head-to-head randomised clinical trial (RCT) in rheumatoid arthritis that Remsima had equivalent efficacy and safety to Remicade.
- The acquisition cost of Remsima was significantly lower than that of Remicade in the London area (approximately 47% reduction in acquisition cost).

Napp wanted to understand the reasons for this low uptake of such a highly cost-effective medicine and that was why the advisory board was convened 'after winning the London tender'.

Remsima was approved for a total of six clinical indications in rheumatology, gastroenterology and dermatology and Napp therefore held a number of separate advisory boards to encompass those as well as from a payer/commissioner perspective.

The advisory board at issue was the only advisory board Napp carried out in 2015 focusing on the use of Remsima in rheumatology (rheumatoid arthritis, ankylosing spondylitis (AS) and psoriatic arthritis (PsA)). Napp convened two other Remsima related advisory boards in 2015 that sought advice on the uptake of Remsima within the London region:

- In May 2015 focussing on the use of Remsima in gastroenterology indications (the inflammatory bowel diseases [IBD] called ulcerative colitis and Crohn's disease) within London. The Chairman attended this advisory board as an advisor. This meeting was held in conjunction with the Korean manufacturer and marketing authorisation holder for Remsima.
- In October 2015 focussing on the payer/pharmacist/commissioner perspective on use of Remsima within London.

The proposal forms for these gastroenterology and payer advisory boards were provided. Prior to that Napp had not conducted any Remsima related

advisory boards since March 2015. The March 2015 advisory board was on 'the value of infliximab anti-drug and antibody (ADA) testing in the management of inflammatory bowel disease'.

### **Briefing material and contracts**

Napp submitted that the Chairman was the only person formally contracted as a 'speaker' based on his/her clinical experience as a rheumatologist, the other six delegates did not give specific presentations and were contracted only as 'advisors'. The presentation given by the Chairman to advisors was necessary to answer Napp's business question. The pre-reading material sent to all advisors consisted of two clinical papers on the use of Remsima in rheumatology indications, and a paper giving an overview of the regulation of biosimilars in the EU. Napp required the advisors to conduct one hour of pre-reading prior to commencement of the advisory board in order to allow adequate time for participation and discussion.

A presentation summarising the key points and a detailed report of the advisory board were provided.

In conclusion Napp strongly disagreed with the allegation that it was using advisory boards as disguised promotion. Napp submitted that it had not breached Clause 12.1 in that regard. Napp provided comprehensive details as requested. The use of consultants at the advisory board was in accordance with all the requirements of Clause 23 and appropriate payments were made in accordance with Clause 18.1. Napp submitted that it had maintained high standards at all times as per Clause 9.1, and had not made unacceptable payments so as to bring discredit upon, or reduce confidence in the pharmaceutical industry as per Clause 2.

In response to a request for further information, Napp submitted that the Chairman was an independent consultant rheumatologist at a London hospital. He/she alone decided to switch his/her patients (RA, AS and psoriatic arthritis (PsA) to biosimilar infliximab (Remsima) in order to benefit his/her clinical service and the care delivered to his/her patients. Napp was pleased to hear that several (though not all) of his/her patients had a positive experience to date, and that was stated in the internal company newsletter. Napp staff were always keen to read about the positive difference that its medicines made to patient's lives, hence why it was included in the internal newsletter. It was not intended in any way to constitute promotion, and Napp was not 'bragging' as alleged by the complainant. The front page of every Napp internal newsletter stated:

'FOR INTERNAL USE ONLY. The articles in this newsletter do not constitute a briefing and should not be discussed with anyone outside of Napp or our independently associated companies. Please ensure you comply with all company briefings and policies at all times and note that talking to friends and family members about any of our products may be seen as promotion.'

Napp submitted that the Chairman was not

promoting Remsima at the advisory board, which would clearly have been in breach of the Code. His/her terms of reference letter, as for all advisors made it very clear that it was not a promotional meeting especially the top of page 2 dealing with compliance 'with the ABPI Code of Practice for the Pharmaceutical Industry in respect of your participation in the Advisory Board, including compliance with the following guidelines...'. His/her briefing and slides addressed all of the pre-determined meeting objectives and having prior experience in the clinical use of Remsima was highly relevant which was highlighted in the meeting summary report key activities for Napp to consider to facilitate biosimilar use, eg:

- Encourage sharing of data and good practice amongst clinicians.
- Share the Chairman's experience and thoughts online to make it easily accessible, and show the benefits of his/her approach.
- RA charity would be willing to consider hosting this.

### **PANEL RULING**

The Panel noted that the complainant was anonymous and non-contactable. Anonymous complaints were accepted and like all complaints judged on the evidence provided by the parties. The complainant had the burden of proving his/her complaint on the balance of probabilities.

The Panel noted that it was acceptable for companies to pay health professionals and others for relevant advice. Nonetheless, the arrangements for such meetings had to comply with the Code, particularly Clause 23. To be considered a legitimate advisory board the choice and number of participants should stand up to independent scrutiny; each should be chosen according to their expertise such that they would be able to contribute meaningfully to the purpose and expected outcomes of the advisory board. The number of participants should be limited so as to allow active participation by all. The agenda should allow adequate time for discussion. The number of meetings and the number of participants should be driven by need and not the invitees' willingness to attend. Invitations to participate should state the purpose of the advisory board meeting, the expected advisory role and the amount of work to be undertaken. If an honorarium was offered it should be made clear that it was a payment for such work and advice. Honoraria must be reasonable and reflect the fair market value of the time and effort involved.

The Panel noted Napp held a number of advisory board meetings since agreeing the tender in London.

The company newsletter article was written by a senior MSL who attended the meeting. The article was headed 'The clinical perspective on using Remsima in Rheumatoid arthritis' and referred to Remsima being currently 'commercially competitive' in London. It also mentioned the recent very successful advisory board in London. It referred to the objectives of the advisory board and that it was chaired by a doctor who also had hands on

experience of using Remsima and had decided to move all his/her RA patients from Remicade to Remsima. The newsletter only referred to the Chairman sharing his/her positive experience of using the biosimilar, no mention was made of the fact that not all of his/her patients had a positive experience as submitted by Napp. The article named all the clinicians attending and stated that the advisory board met all the company's objectives and a clear action plan had been put in place.

The Panel noted that it did not have a copy of the original invitations. Material described as such were in fact letters confirming participant's acceptance of the invitations. These letters made it clear that recipients were expected to participate in the meeting. The letters referred recipients to the meeting agenda and unspecified additional documentation to understand, *inter alia*, whether any preparation was required for the meeting. In the Panel's view, whether pre-reading was required should be made abundantly clear. The Panel noted that the pre-reading consisted of two clinical papers focussing on Remsima in RA and AS and a third paper on biosimilar regulation in the UK.

The meeting which was held in November 2015 ran from 6pm to 7.30pm when a buffet dinner was served. The draft agenda stated that the introduction and review of the agenda took ten minutes and twenty minutes was allocated to the Chairman's presentation and questions on preliminary data in approximately twenty patients with RA switched from originator to biosimilar infliximab. Fifty-five minutes was then allocated for discussing views on the Chairman's presentation. The objective of the discussion, according to the draft agenda, was to explore views of the use of biosimilar infliximab in RA, to identify the key factors that might facilitate or prevent biosimilar usage in the current NHS environment, to discuss views on current NICE guidance, the use of anti-TNFs in RA, the impact biosimilar infliximab might have on the treatment pathway and to gain input on key activities Napp should consider to help support clinicians with the use of biosimilars. The meeting ended with a summary (five minutes).

The Chairman's presentation was entitled 'The clinical perspective on using Remsima in Rheumatoid Arthritis'. According to Napp's submission the 39 slides were presented in 20 minutes. Two of the early slides referred to the availability of prescribing information from Napp staff at the event. This was according to Napp due to an oversight when repurposing some of the slides from a previous promotional meeting. The presentation focussed on the speaker's changing opinion on biosimilars and the outcomes of changes at the Chairman's hospital where patients had been switched from the originator product to Napp's Remsima. One section referred to the failure to hear any concrete evidence of loss of efficacy or unforeseen toxicity and the similarity given the degree of manufacturing variation over the years for all originator biologics. It was queried whether a switch could improve patient care in the broader sense. Adapted NICE treatment algorithms were

presented as well as recommendations from an international task force. The presentation highlighted certain 'problems' including that for certain disease levels (DAS28: 3.2-5.1 'moderate activity') patients in England and Wales were not eligible for anti-TNF therapies. Other countries recommended use of biologics in patients with a persistent DAS>3.2. Data was presented in relation to patients 'stuck in DAS 28 3.2-5.1 range and DMARDS continue?' showing changes from year 1 to years 2 and 3. Data on eventual joint failure and surgery rates was also included and long term outcome. The presentation referred to departmental issues and that the cost savings should be reinvested elsewhere in the department for patient benefit. A 50:50 gain share agreement had been agreed in London. The difference per vial was £188 (44% reduction in costs). It gave details of how patients were informed and offered the option of switching back to Remicade. The patient acceptability section stated that most had heard about Remsima and had a positive attitude about cost saving. The presentation stated 'Reinvested in improvements to their care'. Detailed switch data so far were presented in RA, AS/SpA (spondylo arthritis) and PsA. A copy of the hospital leaflet for patients was shown. The anticipated annual revenue for reinvestment in rheumatology was around £50,000.

The Panel noted that there was no presentation on the reasons for not switching to add balance to the discussion. It appeared that the focus of the presentation was to inform the audience of the advantages of changing to Remsima.

The Panel considered that the meeting objectives were very much about how Napp could improve the uptake of Remsima in NHS London. There did not appear to be any discussion or attempt to understand why it was not being used. The Panel queried whether the time for debate was sufficient. It was likely that the detailed presentation would lead to quite a few questions. The Panel queried Napp's submission that the presentation given by the Chairman was necessary to answer its business question. The Panel wondered why Napp had not just asked the advisors why they were not using Remsima rather than the Chairman presenting reasons for why they should be.

The outcome of the meeting was recorded in a summary report which was divided into four sections. The use of biosimilar infliximab (Remsima) section included 'No major issues were seen in historical patients with [RA] ... switched from Remicade to Remsima by [the Chairman]', it made no reference to the Chairman's presentation which included examples of where patients had not responded well following a switch to Remsima. This section also mentioned that the use of biosimilars could improve patient care for example 'expanding the market in previously restricted indications, where the route to funding is difficult and time-consuming'.

The commissioning section highlighted the variations in approach and concern about CCGs forcing switches in the near future. There needed to be an incentive to switch because of the extra work

involved. There was a low level of awareness about local gain share agreements and if this information was shared clinicians would be more inclined to act themselves. Sharing of success stories would help clinicians to achieve the same success in their areas.

The RA charity's viewpoint section referred to its willingness to alter its position on switching patients to biosimilars. Learning about experiences in other countries (Norway) appeared to have been influential in this regard. The charity was discussing with NICE funding for the moderate RA patient group as the worst patients in this group needed biologics.

Key activities for Napp to consider included recording reliable data and encouragement of sharing of data and good practice. Easing the workload involved in switching including, for example, providing non branded patient information. Reinforcing the message that even different batches of originator infliximab were not identical, to build confidence in the properties of biosimilars. The provision of extra resources including nurse workshops were seen as important in increasing confidence.

The Panel considered that many of the actions identified were not surprising and might well have been anticipated and identified by the company itself and/or other previous advisory boards. There had been three other advisory boards within London in 2015 which all focussed on the lack of uptake in London. One in May focussing on gastroenterology indications which the Chairman attended as an advisor and in October on the payer/pharmacist/commissioner perspective. There was also an advisory board in March 2015 on the value of infliximab and antibody testing in IBD. The Panel thus queried whether, in this context, there was a *bona fide* need for the advisory board in question.

The Panel was concerned about the number of other advisory boards held with different audiences which discussed similar themes. Further, the only presentation was very positive on the use of Napp's product. The Panel noted its comments above about the arrangements, and feedback for the meeting. Taking all the factors into account, but in particular noting the unbalanced nature of the presentation, the number of similar recent advisory boards and, in this context, the absence of a *bona fide* question to be addressed, the Panel did not consider that the arrangements were such that the UK health professionals had attended a genuine advisory board meeting. It therefore ruled a breach of Clause 23.1. This ruling was appealed by Napp.

The Panel considered that, as it had ruled the arrangements did not meet the criteria for advisory boards, UK health professionals had been paid to attend a meeting where a product was promoted. This was contrary to requirements of Clause 18.1 and a breach of that Clause was ruled. This ruling was appealed by Napp. The Panel considered that the requirement that promotional material and activities must not be disguised had not been met and ruled a breach of Clause 12.1. This ruling was appealed by Napp.

The Panel considered that, overall, high standards had not been maintained and a breach of Clause 9.1 was ruled. This ruling was appealed by Napp.

The Panel noted that Clause 2 was reserved for use as a sign of particular censure. The health professionals had attended the meeting believing it was a legitimate advisory board meeting, which was not so. The Panel noted that unacceptable payments was listed in the supplementary information to Clause 2 as an example of an activity likely to be in breach of that clause. The Panel considered that the arrangements brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled. This ruling was appealed by Napp.

## APPEAL BY NAPP

### Process for inviting the advisors and pre-reading

Napp disagreed with the Panel statement that 'The [invitation] letters referred recipients to the meeting agenda and unspecified additional documentation to understand, *inter alia*, whether any preparation was required for the meeting' (emphasis added). Napp further disagreed with the Panel's view that whether pre-reading was required should be made abundantly clear.

Napp explained that each advisor was first approached face-to-face. Following an explanation outlining Napp's advisory board rationale, agenda, and amount of work required, each verbally agreed to attend and were asked to hold the advisory board date in their diaries. Each of the seven participants was sent a hard copy letter confirming this conversation (previously provided) and listing the four meeting objectives for which Napp was seeking advice. The letter also stated 'Please find attached a more detailed agenda for the meeting together with additional reading ahead of the meeting' (emphasis added).

Napp submitted that enclosed within a package was the confirmation letter, the agenda, the terms of reference agreement for signature and the additional pre-reading: printed copies of three scientific papers. Therefore it was abundantly clear to the advisors about the required pre-reading. All signed agreements were returned before the advisory board took place.

Napp submitted that in addition the Panel incorrectly noted that '... the pre-reading consisted of two clinical papers focusing on Remsima in RA and ankylosing spondylitis and a third paper on biosimilar regulation in the UK'. The background pre-reading actually consisted of three peer reviewed published papers and these would not be a focus of the advisory board. Two of the papers (Park *et al* 2013 and Yoo *et al* 2013) were not on Remsima *per se*, they were about the two pivotal clinical trials of biosimilar infliximab CT-P13 (which became marketed as the brands Remsima and Inflectra) in RA and AS. These papers included details of both clinical efficacy and adverse events, including immunogenicity. The safety data was in the studies.

This information provided a balanced view of biosimilar infliximab as pre-reading to the advisors, contrary to that suggested by the Panel.

The final paper by Finnish Medicines Agency regulatory experts (Kurki and Ekman 2015) was an expert review of the biosimilar regulation in the EU, and not in the UK, as stated by the Panel. The pre-reading was to help the advisors with background information and help them to provide clear advice on their views and any outstanding questions they might have on biosimilars. This was evident from their subsequent advice and discussion that was presented later.

### **The balanced nature of the advisory board presentation**

Napp submitted that the Panel's interpretation of the Chairman's advisory board presentation placed particular emphasis on his/her '... positive experience of using biosimilar infliximab ...' and that the internal company newsletter '... only referred to the Chairman sharing his/her positive experience of using the biosimilar, no mention was made of the fact that not all of his/her patients had a positive experience' as submitted by Napp' (emphasis added). The Panel summarised the content of the 39 slides presented by the Chairman and concluded that '... there was no presentation on the reasons for not switching to add balance to the discussion'. Furthermore that '... it appeared that the focus of the presentation was to inform the audience of the advantages of changing to Remsima'. Finally the Panel concluded that '... taking all the factors into account, but in particular noting the unbalanced nature of the presentation...' the Panel did not consider that the arrangements were such that the UK health professionals had attended a genuine advisory board meeting' and ruled a breach of Clause 23.1' (emphasis added).

Napp submitted that its reasons for appealing Clause 23.1 required a detailed explanation of the timings and content of the Chairman's presentation, especially to address the balance between positive experience and any reasons or precautions for not switching, as well as by the attending consultant rheumatologist advisors. The Chairman's presentation was structured around the objectives of the advisory board, sharing his/her experiences and helping to draw out advice from the expert attendees. The advisory board was recorded with the consent of the participants, and was submitted in confidence as part of the appeal.

Napp submitted that the text below listed the reasons and concerns explained by the Chairman for not switching to biosimilar infliximab. A more detailed summary, including the timings of the Chairman's presentation was also provided. The key points made during the presentation (in bold) demonstrated balance, and especially the discussion of the one patient (slide 33) who did not continue Remsima – though not because he/she had any negative (adverse) reaction or side effect, hence why this was not included in the internal company newsletter or report.

Detailed reasons for not using biosimilar infliximab and precautionary recommendations presented by the Chairman were provided.

### **Advisory board advice and time for discussion**

Napp submitted that the four advisory board meeting objectives were clear from the outset and stated in the invitation letters, the agenda and finally the opening slide and concluding slide of the Chairman's presentation.

- To explore attendees' views on the use of biosimilar infliximab in RA.
- To identify the key factors which might facilitate or prevent biosimilar use in the current NHS environment in London.
- To discuss the attendees' views on the current NICE guidance on the use of anti-TNFs in RA, and the impact which biosimilar infliximab could have on the treatment pathway.
- To gain input on the key activities which Napp should consider to help support rheumatology clinicians with biosimilars.

Napp submitted that the objectives were to ultimately understand how it could increase uptake of Remsima in appropriate rheumatology patients within the licenced rheumatology (RA, AS and PsA) indications. The Panel stated that 'There did not appear to be any discussion or attempt to understand why it was not being used. The Panel queried whether the time for debate was sufficient' (emphasis added).

Napp disagreed with the Panel as from the agenda 55 minutes were allocated for advice, discussion and debate. At the actual advisory board there was advice and discussion for 70 minutes of the total 98 minute meeting – 71% of the allocated time.

To address in detail the Panel's statement that '... there did not appear to be any discussion or attempt to understand why it was not being used' Napp provided a summary of the points of advice and discussion against each of the 4 advisory board objectives over the 70 minutes. The detailed timings of this section were also provided.

Napp submitted that it was clear that the advisors were asked to explain why they were and also were not using biosimilar infliximab. This provided a balance and was encompassed in the all of the objectives for the advisory board. Contrary to the Panel's ruling, Napp had shown that the advisors did not spend fifty-five minutes 'discussing views on the Chairman's presentation'.

Napp submitted that the outcomes of the meeting were recorded in a summary report and Napp had explained clearly that there were in effect no patients treated by the Chairman who had not clinically responded well following a switch to Remsima – hence why this was not discussed.

The Panel considered that '... many of the actions identified were not surprising and might well have been anticipated and identified by the company itself and/or other advisory boards'. Napp submitted

that this was a broad statement which could be ascribed to almost any pharmaceutical company advisory board. The Panel was unclear as to which specific actions were 'not surprising' for Napp to address, and it noted that it had no heritage in these therapy areas. Furthermore, whilst Napp 'might well' anticipate certain actions, their importance or otherwise was credibly verified or refuted via advice from clinical or non-clinical experts in the relevant therapeutic areas and/or within the NHS. There were several strategic reasons for this rheumatology focused advisory board:

- Rheumatology had not been strategically an area of focus for Napp since the launch of biosimilar infliximab in February 2015. Thus Napp did not have detailed insights into this specific health professional group, such as why the majority of rheumatologists were not using Remsima.
- For those few rheumatologists that had begun to gain experience of biosimilar infliximab, eg the Chairman, Napp wanted to gain an in-depth of understanding of which patients they used the product in and how the process was implemented.
- Napp wanted to understand what gain share meant to rheumatologists ie their opinions of how they would re-invest the savings. For example in a gastroenterology advisory board Napp had learned that this was mainly used to provide additional nurse/pharmacist resource, but with rheumatology it transpired that this was not possible due to the more limited cost savings, and that instead it helped release money to avoid the need for individual funding requests (IFRs) based upon exceptionality.
- Napp gained a deeper insight into the frustrations of the rheumatologists over NICE treatment pathways that they considered less than optimal for those with moderately severe RA. The rheumatologists' key focus was to treat patients earlier in their disease course.
- Napp wished to guide its strategy for this specific therapy area – did it focus biosimilar use earlier in the RA treatment pathway to achieve a DAS of 2.6 -3.2? NICE recommended biologic treatment at DAS scores above 5.2 for cost reasons? Biosimilars could be used earlier in treatment within their licensed indications as seen in Europe, eg the European League Against Rheumatism (EULAR) guidelines. The advice that Napp obtained at this advisory board indicated that it should not yet take this approach as this was an ongoing debate between BSR and NICE following a failed BSR/NRAS appeal. Instead Napp would focus on switching patients on cost-effective rationale. Subsequently Napp rolled out a new switch campaign in January 2016.
- Finally, from this rheumatology advisory board, a clear example was the advice on the need to provide specialist nurse educational programmes around 'What is a biosimilar?' which Napp planned to deliver regionally in 2016.

### Number of advisory boards

With regard to other advisory boards Napp submitted that it had explained its rationale for this advisory board meeting in its response above. Napp could understand the Panel's comment if it

had convened three London-specific rheumatology advisory boards in 2015. This was the only one. The three advisory boards did not address the same topics, and they sought to gain advice and compare these from different stakeholder perspectives eg advice on gain share topic from the perspectives of prescribing clinicians, CCG commissioners, pharmacists and hospital trust payers.

Napp submitted that infliximab was approved in six clinical indications in rheumatology, gastroenterology and dermatology. As could be seen from the advice and discussion at this meeting there were many different views and opinions on the clinical use and procurement of biosimilar infliximab, including gain-share agreements. Gain share was an evolving area within the NHS for what was the world's first monoclonal antibody biosimilar with few if any precedents, and no clear national guidance. The NHS adoption of biosimilars and biosimilar infliximab was therefore not a routine well developed pathway. There was lack of clarity and only mutual dialogue was available to formulate what had to be localised policies. In fact NHS England encouraged such two way discussions to define pathways and practice towards adoption. Overall, Napp submitted that the role of advisory boards at this stage of introduction were important and reflected the localisation and need for flexibility around funding mechanisms/gain share.

Napp submitted that the three other advisory boards in London in 2015 were in gastroenterology, a meeting to gain advice on funding considerations from a payer/pharmacist/commissioner perspective, and an infliximab anti-drug antibody (ADA) testing advisory board. Although they each had in common biosimilar infliximab lack of uptake these were not the only reasons for convening the advisory boards. The use of infliximab in the clinical treatment pathway (along with several other biologic medicines) of the NICE guidelines for RA had minimal overlap with the use of infliximab in the inflammatory bowel diseases (IBD) Crohn's and ulcerative colitis. Whilst infliximab might slow disease progression in RA, in IBD it might prevent the need for bowel resection surgery and subsequent stoma care. The gastroenterology advisory board also was dominated by advice to gain real world data in IBD, as the existing pivotal data was in the rheumatology conditions of RA and AS.

Napp submitted that it was clear from the payer advisory board (October 2015) that the payers, pharmacists and commissioners shared different approaches to funding streams. This advisory board was composed of nine senior advisors who were heads of medicines management, chief pharmacists and procurement leads. Levers and barriers to prescribing were discussed. It was clear from the discussion that across London there were strikingly different biologics commissioning experiences. Biosimilar infliximab introduction was being used as a learning curve prior to the arrival of further biosimilar products in the next five years. Napp considered that it was a *bona fide* reason to hold such advisory boards with relevant stakeholders to verify the facts within a fragmented NHS healthcare system from different perspectives. For example,

several of the advisors said that commissioners and pharmacists were reluctant to 'push' clinicians, they were not used to challenging hospital consultants to change their use of medicines or to challenge their prescribing choices. This advisory board was therefore focused on different questions to the one held in November 2015.

Napp submitted that the objective of the infliximab ADA testing national advisory board (March 2015) was to discuss the clinical evidence on the value of the medicine and antibody testing, in order to highlight in which clinical settings the testing would be most informative and valuable in aiding treatment decisions. The advice and discussion was relevant to all infliximab medicines (Remicade, Inflectra and Remsima). There was currently no consensus on the methods of ADA testing, their standardisation and interpretation were yet to be agreed. This advisory board recommended medicine trough level and ADA testing at week 14 for all patients; for loss of response; and at 12-month review. It was thought that the balance of current evidence did not recommend testing for adherence; after medicine holiday; or for routine dose optimisation in remission. Data from an ongoing UK Crohn's disease study would also help and might guide selection of further recommendations on the application of ADA testing offered by Napp.

In summary, Napp submitted that taking all the presented factors into account, this was a genuine advisory board meeting. Napp had shown that the 'very positive' presentation by the Chairman was actually an accurate presentation of the facts and was presented in a balanced manner. The aim of the presentation was aligned to the objectives of the advisory board and there was no reason to present any discussion of '... examples of where patients had not responded well following a switch to Remsima' as there were none thus far. The Panel had placed significant emphasis on an unbalanced nature of the presentation as a reason for its ruling of a breach of Clause 23.1 and Napp had shown that the slides were balanced. In addition, although Napp had held three other advisory boards in 2015 they had different objectives and involved different stakeholders. They were only similar in so far that they were about infliximab and two of them explored reasons for lack of uptake from different perspectives. *Bona fide* questions which Napp needed to be answered were addressed and all arrangements were consistent with and not in breach of Clause 23.1. Napp also considered that the arrangements met the criteria for advisory boards and that there was no disguised promotion of its medicine to health professionals as it sought genuine advice as presented, and therefore it was not in breach of Clause 12.1. The health professionals were paid according to the services they provided to Napp which was for genuine advice, and thus not in breach of Clause 18.1. Napp considered that it had maintained high standards by following the requirements of advisory boards and had not breached Clause 9.1. Finally, because Napp submitted that this was a genuine advisory board meeting, the payments were acceptable to health professionals for genuine consultancy and thus not in breach of Clause 2 (supplementary information).

## APPEAL BOARD RULING

The Appeal Board noted the advisory board meeting at issue lasted only 1 hour 30 minutes but had four substantial objectives which were:

- 1 To explore attendees' views on the use of biosimilar infliximab in RA.
- 2 To identify the key factors which might facilitate or prevent biosimilar use in the current NHS environment in London.
- 3 To discuss the attendees' views on the current NICE guidance on the use of anti-TNFs in RA, and the impact which biosimilar infliximab could have on the treatment pathway.
- 4 To gain input on the key activities which Napp should consider to help support rheumatology clinicians with biosimilars.

The Appeal Board queried whether these objectives could be met in such a short space of time. The Appeal Board also noted that according to the transcript it had taken around 25 minutes to present 35 of the 39 slides and that when introducing the advisory board a Napp attendee referred to the Chairman's presentation being 'up to about an hour'. This was different to Napp's submission that the presentation took 20 minutes.

The Appeal Board also noted that Napp had organised its advisory board to try to understand why there was still a low uptake of Remsima in RA after it had won the London tender. The acquisition cost of Remsima was lower than the originator product. The Appeal Board noted that Napp had already undertaken a number of other advisory boards concerning the lack of uptake of infliximab some of which were on indications other than RA.

The Appeal Board noted that the Chairman of the advisory board, and the only person who gave a formal presentation, emphasised the cost savings to be made by switching to Remsima. In implementing a change at the hospital in which he worked, the key issue, after agreeing that the evidence base for biosimilar infliximab was convincing, he said that cost savings should be reinvested for patient benefit. Specific costings were given to show how the 50:50 gain share arrangement worked, generating new funds for the hospital. Slide 36 stated that at the hospital concerned the anticipated annual revenue generated by switching to Remsima in rheumatology would be about £50,000. Not all the attendees knew about the gain share arrangements in NHS London. In the Appeal Board's view, Napp had clearly chosen a Chairman who was very enthusiastic about the cost savings that could, through gain share agreements, be reinvested. The transcript of the meeting showed that such financial budgetary considerations were discussed for at least half an hour. The summary of the meeting provided by Napp, stated that the Chairman advised the delegates to act now whilst the incentive was available for gain share ie whilst there remained a marked price difference between Remsima and the originator product. In the Appeal Board's view, the emphasis given to, and the time spent providing information about, and discussing the monetary implications of, prescribing Remsima meant that the advisory board did not focus on the



clinical perspective of using the medicine in RA as suggested by the title of the meeting nor seeking advice as set out in the meeting objectives.

The Appeal Board did not consider that the arrangements were such that the UK health professionals had attended a genuine advisory board meeting. In the Appeal Board's view the Chairman's presentation and resultant discussion effectively promoted Remsima. The Appeal Board therefore upheld the Panel's ruling of a breach of Clause 23.1. The appeal on that point was not successful.

The Appeal Board considered that, as it had ruled the arrangements did not meet the criteria for advisory boards, UK health professionals had been paid to attend a promotional meeting. The Panel's ruling of a breach of Clause 18.1 was upheld. The appeal on that point was not successful.

The Appeal Board considered that the requirement that promotional material and activities must not be disguised had not been met and it upheld the Panel's ruling of a breach of Clause 12.1. The appeal on that point was not successful.

The Appeal Board considered that, overall, high standards had not been maintained and it upheld the Panel's ruling of a breach of Clause 9.1. The appeal on that point was not successful.

The Appeal Board noted that Clause 2 was reserved for use as a sign of particular censure. The health professionals had been paid to attend the meeting believing it was a legitimate advisory board meeting, which was not so. The Appeal Board noted that unacceptable payments was listed in the supplementary information to Clause 2 as an example of an activity likely to be in breach of that clause. The Appeal Board thus considered that the arrangements brought discredit upon and reduced confidence in the pharmaceutical industry and it upheld the Panel's ruling of a breach of Clause 2. The appeal on that point was not successful.

**Complaint received**                      **7 December 2015**

**Case completed**                              **18 May 2016**

# ANONYMOUS, NON-CONTACTABLE v DAIICHI-SANKYO

## Exhibition stand design and hospitality

An anonymous, non-contactable complainant alleged that the majority of exhibition stands at a European congress held in London in 2015 were extravagant and in poor taste considering today's economic climate. Three examples were given including that Daiichi-Sankyo's stand looked like a Harley Street beauty therapy shop. The complainant stated that there was a real party atmosphere rather than a true scientific congress atmosphere which would be expected in such stands.

The detailed response from Daiichi-Sankyo is given below.

The Panel noted Daiichi-Sankyo's submission that there were no giveaways on the stand, such as USB sticks, pens, or pads. The only take away items were promotional leavepieces and invitations to the promotional satellite symposia organised by Daiichi-Sankyo. The Panel noted that photos taken in a photo booth in the corporate section of the promotional stand were emailed to visitors. In the Panel's view the photographs constituted a gift and even though no hard copies of pictures were printed or distributed at the stand, they were still created on the stand and should thus be considered as being given away from it. The Panel noted Daiichi-Sankyo's submission that the template for the picture was corporate branded with no product branding. However, the photo booth was on a promotional stand albeit in a corporate section and therefore the emailed photos were sent to visitors in connection with the promotion of medicines contrary to the requirements of the Code and a breach was ruled which was upheld on appeal. High standards had not been maintained in this regard. A breach of the Code was ruled which was overturned on appeal.

The Panel noted that the complainant had made a general allegation that the majority of the stands at the congress were extravagant and that Daiichi-Sankyo's stand looked like a Harley Street beauty therapy shop. The complainant, who had the burden of proving his/her complaint on the balance of probabilities, had not provided any material to support these allegations. As the complainant was non-contactable, it was not possible to obtain more information from him/her. A judgement had to be made on the available evidence. Daiichi-Sankyo had provided a photograph of the stand and its general appearance did not appear to be unreasonable. In the Panel's view the complainant had not shown that the exhibition stand was unacceptable as alleged. No breach of the Code was ruled.

An anonymous, non-contactable complainant, who described him/herself as a UK health professional, submitted a complaint about the European Society of Cardiology (ESC) Congress held in London 29 August – 2 September 2015.

### COMPLAINT

The complainant stated that the majority of the stands at the congress were extremely extravagant and in poor taste considering today's economic climate. It showed that pharmaceutical companies had far too much money to splash around. Three examples were given including that Daiichi-Sankyo's stand looked like a Harley Street beauty therapy shop. According to the complainant, there was a real party atmosphere rather than a true scientific congress atmosphere which would be expected in such stands.

When writing to Daiichi-Sankyo the Authority asked it to respond in relation to Clauses 9.1, 9.7 and 18 of the 2015 Code.

### RESPONSE

Daiichi-Sankyo stated that ESC was the world's largest cardiology conference; it attracted over 32,000 attendees from over 140 countries in 2015.

The stand itself, and all materials on it were certified by Daiichi-Sankyo UK as per the Code and the company's standard operating procedures (SOPs).

Daiichi-Sankyo submitted that the stand was designed to accommodate the significant numbers of customers who it anticipated would be interested in a product approved only several weeks previously. For many European physicians, this was their first opportunity to receive product information directly from the manufacturer.

Daiichi-Sankyo provided a plan of the exhibition space to give context as to its relative size compared with other company stands and noted that some companies had multiple stand areas. In terms of square footage, Daiichi-Sankyo's stand was not the largest in the exhibition.

The stand consisted of multiple, clearly delineated areas which were separated by walls.

Areas were dedicated to:

- Promotion of Lixiana (edoxaban) – in brand colours (pink and white walls, white floors)
- Speaker area – also in Lixiana brand colours
- Medical information – in corporate livery (white walls/white floors/ Daiichi-Sankyo logo colours)
- Disease awareness – in separate colours (red/ white floors)
- Corporate communication – in corporate livery.

A 3D likeness of the stand and photographs of the actual stand in situ were provided.

Daiichi-Sankyo submitted that there were no giveaways on the stand, such as USB sticks, pens, or pads. The only take away items were promotional leavestieces and invitations to the promotional satellite symposia organised by Daiichi-Sankyo. These items were provided.

Nine audiovisual screens on the stand displayed certified promotional materials. The content of these screens were provided.

There was a holographic display that outlined the development history of the edoxaban molecule. It was not possible to recreate the 3D display but a copy of the video was provided.

A coffee desk was also available for visitors to the stand.

The corporate section included a photo booth which allowed visitors to take a picture of themselves with their own messages using simple magnetic words on a board behind them. The picture was emailed to the visitor automatically to the email address they supplied. The template for the picture was corporate branded with no product branding. Thus, no hard copies of pictures were printed or distributed at the stand. There were no other displays, quizzes, or games.

Daiichi-Sankyo stated that it was difficult to understand why a physician would come to the conclusion stated in the complaint. Nobody in the team who was involved in the design, build or approval was familiar with the premises described by the complainant, let alone took inspiration from them. Daiichi-Sankyo could only venture that it might have been the clean, uncluttered design. This design was certainly not intended to cause offence.

Regarding the allegation of extravagance, Daiichi-Sankyo submitted that the materials on the stand were of a scientific nature, commensurate with the professional educational setting of the ESC Congress, and there were no physical giveaways.

Daiichi-Sankyo noted that whilst its stand was referred to by the complainant, he/she pointed out a general issue with all the stands at the congress. Therefore, Daiichi-Sankyo submitted that some context needed to be provided regarding activities or materials on competitors' stands which might need to be taken up with other companies. For example, the Daiichi-Sankyo stand did not include augmented reality displays accompanied by iPads, or golfing/gaming simulations which were available at other stands.

Overall, Daiichi-Sankyo firmly believed that the design of its stand was clean and uncluttered, appropriate for a congress such as the ESC, providing materials with appropriate scientific content and no frivolous giveaways.

It was unfortunate that an individual should write to the PMCPA on this subject, in contrast to the positive verbal feedback received by various members of the team who manned the stand.

In response to a request for further information, Daiichi-Sankyo submitted that it had a corporate section on the stand with a photo booth. The booth was in line with the corporate social initiative 'Make your heart feel good' by Daiichi-Sankyo Europe which supported a chosen European charity 'Little Hearts' by raising funds for orphaned children, and also helped to reinforce the importance of healthy 'Big Hearts' by increasing awareness of hypertension and other cardiovascular diseases. Daiichi-Sankyo provided a representation of the photo wall and an example of the digital photoframe. Daiichi-Sankyo asked the question 'What Makes Your Heart Feel Good?' and then visitors to the booth would answer by using magnetic words and icons from a list available, which were approved to be in line with the initiative and did not convey a party atmosphere. Their picture was taken and emailed to them. Daiichi-Sankyo submitted that there were no other props or giveaways.

Daiichi-Sankyo submitted that coffee available on the stand was provided by the congress venue's official caterer; it was provided as a package including the coffee machine, two trained baristas, coffee cups, coffee beans and tea bags. The range was similar to that available to health professionals at coffee shops throughout the conference venue except that only medium sized cups were available on the stand. The cost of the package would be similar to what the other exhibitors would have access to. Daiichi-Sankyo did not have the number of servings distributed so the overall cost per serving was not available. The actual cost of a cup and the hot water/coffee/tea bag would be a matter of pennies. Nevertheless, the perceived value would be no more than what a health professional would be able to buy for themselves at the congress venue. No other drinks were served on the stand and Daiichi-Sankyo considered that the provision of coffee did not contribute to the perceived party atmosphere and was appropriate in the context of the scientific congress.

## PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable. As stated in the introduction to the Constitution and Procedure, anonymous complaints were accepted and like all complaints, judged on the evidence provided by the parties. Complainants had the burden of proving their complaint on the balance of probabilities. The Panel noted that it was not possible to ask the complainant for further information.

Clause 18.1 stated that no gift, pecuniary advantage or benefit might be supplied, offered or promised to members of the health professions or to other relevant decision makers in connection with the promotion of medicines or as an inducement to prescribe, supply, administer, recommend, buy or sell any medicine, subject to the provisions of Clauses 18.2 (patient support items) and 18.3 (inexpensive pens/pencils and notebooks).

The Panel noted Daiichi-Sankyo's submission that there were no giveaways on the stand, such as

USB sticks, pens, or pads. The only take away items were promotional leavepieces and invitations to the promotional satellite symposia organised by Daiichi-Sankyo. The Panel noted that photos taken in a photo booth in the corporate section of the promotional stand were emailed to visitors automatically, to the email address they provided. In the Panel's view the photographs constituted a gift and even though no hard copies of pictures were printed or distributed at the stand, they were still created on the stand and should thus be considered as being given away from it. The Panel noted Daiichi-Sankyo's submission that the template for the picture was corporate branded with no product branding. However, the photo booth was on a promotional stand albeit in a corporate section and therefore the emailed photos were sent to visitors in connection with the promotion of medicines contrary to the requirements of Clause 18.1 and a breach of that clause was ruled. High standards had not been maintained in this regard. A breach of Clause 9.1 was ruled. These rulings were appealed by Daiichi-Sankyo.

The Panel noted that the complainant had made a general allegation that the majority of the stands at the congress were extravagant and showed that companies had far too much money to splash around. Clause 9.7 stated that extremes of format, size or cost of material must be avoided. The Panel noted the complainant's allegation that Daiichi-Sankyo's stand looked like a Harley Street beauty therapy shop. The complainant, who had the burden of proving his/her complaint on the balance of probabilities, had not provided any material to support his/her allegations in this regard; it was not clear from the complaint what aspect of the Daiichi-Sankyo stand was 'extremely extravagant and in poor taste considering today's economic climate' or why it looked like a beauty therapy shop. As the complainant was non-contactable, it was not possible to obtain more information from him/her. A judgement had to be made on the available evidence. Daiichi-Sankyo had provided a photograph of the stand and its general appearance did not appear to be unreasonable. In the Panel's view the complainant had not shown that the exhibition stand was unacceptable as alleged. No breach of Clause 9.7 was ruled.

#### **APPEAL BY DAIICHI-SANKYO**

Daiichi-Sankyo noted that the original allegation, *inter alia*, was that it had an extravagant stand which contributed to a party atmosphere at the 2015 ESC Congress.

Daiichi-Sankyo submitted that its stand was designed to be in keeping with the scientific nature of the meeting, had appropriately distinct promotional areas, and corporate branded, non promotional areas for medical information and corporate communications about the company's charitable activities. These areas were not only physically distinct with walls and barriers between them but were also staffed differently with clear briefings as to roles and responsibilities ie promotional staff were restricted to the promotional areas.

The medical information area was manned by the medical scientific liaison team from the various affiliates and the corporate area by the European corporate communications team. The corporate communication area was dedicated to, and aimed to raise awareness of, Daiichi-Sankyo's long running campaign, 'Make your heart feel good' and was aimed at raising awareness for it. The campaign also tried to raise money towards Daiichi-Sankyo's 'Little Hearts' program to support children at an orphanage in Ukraine.

Daiichi-Sankyo submitted that this campaign was not linked to a product in any way and was branded in corporate colours. An automated photo booth was set up in the corporate section to allow visitors to photograph themselves against a white background upon which words could be magnetically attached. The picture was placed on a template which was branded in corporate colours and had the name of Daiichi-Sankyo's charitable campaign. The picture was emailed to the address the visitor supplied. The email addresses were not collected and used for any other purpose.

The Panel decided that this email constituted a gift from a promotional stand and ruled a breach of Clause 18.1 and subsequently a breach of Clause 9.1. Daiichi-Sankyo disagreed with this interpretation of the Code.

Daiichi-Sankyo submitted that a non-promotional email in connection with raising awareness of charitable activities did not constitute a gift. The picture itself was done by an automated machine and was placed on a template. The picture could not be recycled for any other purpose, had no monetary value and was not linked to the promotion of Daiichi-Sankyo products.

Daiichi-Sankyo submitted that the fact that the picture was sent from the stand also did not automatically mean that it was linked to a product. Daiichi-Sankyo was very careful to delineate the areas not just physically but also when it came to who was staffing the corporate area. No promotional staff was allowed in that space. This was briefed on teleconferences to all attendees before the meeting, at a face-to-face and a briefing meeting before the meeting. If this interpretation was applied, this would make all communication derived from the stand including medical information requests promotional. The disheartening aspect of this was that had this email actually been promotional and in brand colours with promotional messaging on it and accompanied by prescribing information, it would have been considered a promotional aid in accordance with the supplementary information to Clause 18.1. Daiichi-Sankyo submitted that it was ruled in breach for carrying out a genuine charitable endeavour in line with its corporate social responsibility. Daiichi-Sankyo noted that the complainant stated there was an air of extravagance and a party atmosphere at the ESC Congress. Daiichi-Sankyo disagreed that the emails contributed to this impression and it submitted that it had complied with the letter and the spirit of the Code.

## APPEAL BOARD RULING

The Appeal Board noted that the plan of Daiichi-Sankyo's stand showed that the photo booth was in an area labelled 'Photo attract area' which implied that its purpose was to attract delegates to the stand. If delegates approached the stand from the exhibition hall entrance (main traffic flow), they would enter the photo attract area via the branded/promotional areas of the stand. There was some secondary traffic flow shown on the plan such that the photo booth could be accessed via an area labelled 'Patient profile area with pre-launch patient content'.

The Appeal Board noted the explanation from Daiichi-Sankyo at the appeal that the patient profile area focussed on disease awareness with non-promotional staff detailing patients' stories and the difficulties they faced. The Appeal Board noted that a patient case study display within this area featured patients that might be appropriate for treatment with Lixiana. The Appeal Board noted that although the photo booth camera had been positioned such that the resultant photograph would not include any promotional material in the background, attendees in this area could see into the area of the stand that contained promotional messages for Lixiana and the delegate being photographed could see such material.

The Appeal Board noted that the photo template provided by Daiichi-Sankyo did not refer to the company's charitable campaign 'Little Hearts' as submitted. In the bottom left-hand corner of the template was the question 'What Makes Your Heart Feel Good' and in the bottom right was the Daiichi-Sankyo logo. The photo wall similarly did not refer to the charity. In the Appeal Board's view, the resultant photograph was more likely to remind the delegate of Daiichi-Sankyo than of its charitable initiative.

The Appeal Board noted from Daiichi-Sankyo at the appeal that in the planning stage, it decided to switch off the photo booth's capacity to print so that the photographs were emailed to delegates. Further the company had decided that a digital photograph was not a gift as it had no value. The Appeal Board considered that digital photographs were commonplace and easy to produce and had little or no monetary value. Nonetheless, the emailed photograph was something the recipient would not have had unless he/she visited Daiichi-Sankyo's photo booth and so in that regard the Appeal Board considered that it constituted a gift. Clause 18.1 stated that 'No gift, pecuniary advantage or benefit may be supplied, offered, or promised to health professions or other relevant decision makers in connection with the promotion of medicines or as an inducement to prescribe, supply, administer, recommend, buy or sell any medicine subject to the provision of Clauses 18.2 and 18.3'. Clause 18.2 and 18.3 set out the limited items that could be provided to health professionals etc. Personal photographs were not so listed.

Noting its comments above, the Appeal Board considered that the gift of the emailed photograph occurred in a promotional setting and thus it upheld the Panel's ruling of a breach of Clause 18.1. The appeal on that point was unsuccessful.

The Appeal Board did not consider in the circumstances that high standards had not been maintained and it ruled no breach of Clause 9.1. The appeal on that point was successful.

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|---------------------------|-------------------------|
| <b>Complaint received</b> | <b>21 December 2015</b> |
| <b>Case completed</b>     | <b>13 May 2016</b>      |

# ANONYMOUS, NON-CONTACTABLE v PFIZER

## Exhibition stand design and hospitality

An anonymous, non contactable complainant, who described him/herself as a UK health professional, alleged that the majority of exhibition stands at a European congress held in London in 2015 were extremely extravagant and in poor taste considering today's economic climate. Three examples were given including that Pfizer gave out a named proprietary flavoured iced drink. The complainant stated that there was a real party atmosphere rather than a true scientific congress atmosphere which he/she expected in such stands.

The detailed response from Pfizer is given below.

The PMCPA's guidance on items at conferences and exhibition stands stated that the Code allowed the provision of hospitality at scientific meetings including from an exhibition stand; hospitality provided from an exhibition stand must be subsistence only and not such as to induce a delegate to visit the stand eg no more than non-alcoholic beverages, such as tea, coffee and water, and very limited quantities of sweets, biscuits or fruit. In the Authority's view hot dogs, ice-cream, waffles, etc should not be provided at exhibition stands.

The Panel noted the refreshments provided by Pfizer included coffee, tea, hot chocolate, chai latte, flavoured iced drinks and iced coffee as well as some chocolates. Although the range of beverages on offer was on the limits of acceptability, overall the Panel did not consider that the hospitality offered was contrary to the requirements of the Code and no breach was ruled.

The Panel noted that the complainant had made a general allegation that the majority of the stands at the congress were extravagant. The complainant, who had the burden of proving his/her complaint on the balance of probabilities, had not provided any material to support his/her allegations in this regard; it was not clear from the complaint what aspect of the stands were 'extremely extravagant and in poor taste considering today's economic climate'. As the complainant was non-contactable, it was not possible to obtain more information from him/her. A judgement had to be made on the available evidence. In the Panel's view the complainant had not shown that the Pfizer exhibition stands were unacceptable as alleged. No breach of the Code was ruled.

The Panel noted its rulings above and considered that Pfizer had not failed to maintain high standards and thus ruled no breach of the Code.

An anonymous, non contactable complainant who described him/herself as a UK health professional complained about exhibition stands at the European

Society of Cardiology (ESC) Congress held in London 29 August – 2 September 2015.

### COMPLAINT

The complainant stated that the majority of the stands at the congress were extremely extravagant and in poor taste considering today's economic climate. It showed that pharmaceutical companies had far too much money to splash around. Three examples were given including that Pfizer had given out a named proprietary flavoured iced drink. There was a real party atmosphere rather than a true scientific congress atmosphere which the complainant expected in such stands.

When writing to Pfizer the Authority asked it to respond in relation to Clauses 9.1, 9.7 and 22.1 of the 2015 Code.

### RESPONSE

Pfizer submitted that it had three stands at the congress which related to different parts of the portfolio. Two of the stands were organised by Pfizer alone and the third stand was for Eliquis (apixaban) and was organised by Pfizer on behalf of the Bristol-Myers Squibb (BMS) Pfizer Alliance which jointly marketed the product. Pfizer provided details of the costs paid to the organisers for the three stands.

The two stands organised by Pfizer alone distributed only bottled water, with no other refreshments provided. No give-aways were provided on either of these stands. Pfizer submitted that there was no entertainment or music on either of the stands and nothing that could be considered to be a 'party atmosphere'.

The third exhibition stand related to the promotion of Eliquis thus the response regarding this stand was on behalf of the BMS-Pfizer Alliance. The layout and a photograph of the Eliquis stand depicting the refreshment counter were provided. The stand included suspended overhead banners, chairs and tables, electronic tabletops and electronic screens, including one where presentations were given by several eminent key opinion leaders in the field of anticoagulation. A central refreshment booth served coffee, tea, hot chocolate, chai latte, flavoured iced drinks and iced coffee as well as some small chocolates. Water bottles were also available at several locations on the stand. Pfizer submitted that the refreshments available were appropriate and in line with the Code and the PMCPA guidance. The Alliance did not serve the proprietary drink named by the complainant. Pfizer considered it appropriate to offer delegates a cold drink option as not everyone wished to drink tea or coffee. Pfizer stated that the availability of the flavoured iced drinks was not a

major feature of the stand and hence was not an inducement for a delegate to visit the stand, any more than the availability of tea and coffee.

Approximately 34,000 delegates attended the ESC congress and the exhibition stands were open for 3.5 days. Pfizer provided details of the number and costs of the refreshments distributed on the stand.

All materials and activities related to clinical and scientific data and information on Eliquis and anticoagulation. The Alliance staff on the stand were all highly trained and experienced professionals, briefed in detail about the requirements of the Code and how to fulfil their role of informing delegates about Eliquis data. They were of course asked to be pleasant and courteous to all stand visitors at all times, but this could not be construed as encouragement to create a 'party atmosphere'. As with the two Pfizer stands, there were no giveaways or takeaway items of any sort and no 'entertainment' or music.

External speakers presenting on the stand were also carefully selected for their expertise and experience, and briefed in detail about their obligations under the Code. The ambience on the stand was therefore professional and always respected the status of delegates and the subsistence provided was appropriate. Whilst the exhibition stand was busy throughout the congress with seating areas generally well occupied, Pfizer submitted that the atmosphere was not party-like.

In summary, the anonymous complainant made some general claims about extravagance and party atmospheres at exhibition stands. Pfizer and The Alliance strongly submitted that the arrangements, content, materials and ambience of its stands were of the highest standard and in keeping with both the spirit and letter of the Code. Furthermore, the provision of flavoured iced drinks at the stand was appropriate, was not extravagant and was not an inducement to attend the stand. Pfizer and The Alliance denied breaches of Clause 9.1, 9.7 or 22.1.

## **PANEL RULING**

The Panel noted that the complainant was anonymous and non-contactable. As stated in the introduction to the Constitution and Procedure, anonymous complaints were accepted and like all complaints, judged on the evidence provided by the parties. Complainants had the burden of proving their complaint on the balance of probabilities. The Panel noted that it was not possible to ask the complainant for further information.

Clause 22.1 stated that hospitality must be strictly limited to the main purpose of the event and must be secondary to the purpose of the meeting ie subsistence only. The level of subsistence offered must be appropriate and not out of proportion to the occasion. Clause 22.1 applied to scientific meetings, promotional meetings, scientific

congresses and other such meetings and training. The supplementary information to Clause 22.1 also stated that a useful criterion in determining whether the arrangements for any meeting were acceptable was to apply the question 'would you and your company be willing to have these arrangements generally known?'. The impression that was created by the arrangements for any meeting must always be kept in mind.

The PMCPA's guidance on items at conferences and exhibition stands stated that the Code allowed the provision of hospitality at scientific meetings and the like and there was no reason why it should not be offered from an exhibition stand. Companies would have to be certain that the hospitality overall complied with the Code and that any hospitality provided from an exhibition stand was subsistence only and not at a level as to induce a delegate to visit the stand. In the Authority's view companies should provide no more than non-alcoholic beverages, such as tea, coffee and water, and very limited quantities of sweets, biscuits or fruit. The Authority advised that it did not consider that hot dogs, ice-cream, waffles, etc should be provided at exhibition stands.

The Panel noted the refreshments provided by Pfizer included coffee, tea, hot chocolate, chai latte, flavoured iced drinks and iced coffee as well as some chocolates. The Panel further noted the costings and the number distributed. Although the range of beverages on offer was on the limits of acceptability, overall the Panel did not consider that the hospitality offered was contrary to the requirements of Clause 22.1 and no breach was ruled.

The Panel noted that the complainant had made a general allegation that the majority of the stands at the congress were extravagant and showed that companies had far too much money to splash around. Clause 9.7 stated that extremes of format, size or cost of material must be avoided. The complainant, who had the burden of proving his/her complaint on the balance of probabilities, had not provided any material to support his/her allegations in this regard; it was not clear from the complaint what aspect of the stands were 'extremely extravagant and in poor taste considering today's economic climate. As the complainant was non-contactable, it was not possible to obtain more information from him/her. A judgement had to be made on the available evidence. In the Panel's view the complainant had not shown that the Pfizer exhibition stands were unacceptable as alleged. No breach of Clause 9.7 was ruled.

The Panel noted its rulings above and considered that Pfizer had not failed to maintain high standards and thus ruled no breach of Clause 9.1.

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| <b>Complaint received</b> | <b>21 December 2015</b> |
| <b>Case completed</b>     | <b>8 February 2016</b>  |

# ABBVIE v PIRAMAL

## Sevoflurane Material

AbbVie complained about a leaflet detailing a drop test of Sevoflurane Piramal screw top glass bottles produced by Piramal Healthcare UK.

AbbVie alleged that the leaflet was in breach of the Code as the cost of sevoflurane and the date on which the leaflet was drawn up was not stated and there was no statement about the need to report adverse events. AbbVie further alleged that Piramal had not maintained high standards and by not including the adverse event reporting statement which prejudiced patient safety had brought the industry into disrepute in breach of Clause 2.

The detailed response from Piramal is given below.

The Panel noted Piramal's submission that the leaflet was not promotional because it focussed on the packaging of sevoflurane and did not seek to promote the therapeutic value, safety or efficacy of the medicine. The Panel considered, however, that a licensed medicine was the sum of its parts, and packaging (in this case the robustness of the glass bottles) might be a reason why a health professional or other relevant decision maker would choose one medicine over another. Reference was made to sevoflurane Piramal's 5 year shelf life. The Panel noted in that regard the application of the Code; it was not limited to information or claims of a medical or scientific nature. In the Panel's view, a claim about any aspect of a medicine would be caught by the definition of promotion. The Panel thus considered that the leaflet promoted sevoflurane.

The Panel noted that the Code required promotional material to include the cost (excluding VAT) of a medicine. The Panel noted that the SPC and patient information leaflet appeared to have been reproduced in the leaflet; the cost of sevoflurane was not included. The Panel therefore ruled a breach of the Code.

This obligatory statement about adverse event reporting did not appear in the leaflet at issue and the Panel therefore ruled a breach of the Code. Similarly, the Panel ruled a breach of the Code as the leaflet did not include the date on which it was drawn up or last revised.

The Panel considered that high standards had not been maintained and a breach of the Code was ruled.

The Panel noted its rulings above and although it was concerned that the adverse event reporting statement had not been included in the leaflet, it considered that an additional ruling of a breach of Clause 2 would be disproportionate; a ruling of a breach of Clause 2 was used as a sign of particular

**censure and reserved for such use and no breach of that clause was ruled.**

AbbVie Ltd complained about the promotion of sevoflurane by Piramal Healthcare UK Ltd. The piece at issue was a leaflet detailing a drop test of Sevoflurane Piramal screw top glass bottles (ref MKT-SEV-025). The drop test was conducted to investigate the incidence of breakage on four different floor types commonly found in hospitals. Information for health professionals and patient information was on pages 5 and 6 of the leaflet.

Sevoflurane was indicated for induction and maintenance of general anaesthesia in adult and paediatric patients for inpatient and outpatient surgery. AbbVie also marketed sevoflurane.

### COMPLAINT

AbbVie noted that Piramal's primary defence was that the material was non-promotional and therefore did not fall within the scope of the Code. In AbbVie's view, the material was promotional and contained significant issues and omissions that potentially compromised patient safety.

Definition of promotion and application to the materials

AbbVie noted that Clause 1.2 defined promotion as any activity by a pharmaceutical company which promoted the 'purchase, recommendation, sale, supply or use of its medicines'. Piramal's actual or presumed intention, taking into account the totality of the information and circumstances, plus the likely perception of the average physician was relevant. In AbbVie's view, the leaflet was intended to influence the sale, supply or use of Piramal's sevoflurane; the material was not primarily designed to provide medical or financial information and so displayed an actual or presumed promotional intent. Further, AbbVie considered that anything which promoted the 'use' of the product (eg handling, bottle safety and integrity of packaging as in the leaflet at issue) amounted to promotion and fell within the scope of the definition in Clause 1.2. AbbVie alleged breaches as follows:

- The cost of sevoflurane was not stated in breach of Clause 4.2.
- The date on which the leaflet was drawn up was not stated in breach of Clause 4.9.
- There was no statement about the need to report adverse events in breach of Clause 4.10.

AbbVie further alleged that Piramal had not maintained high standards in breach of Clause 9.1.



AbbVie further alleged that Piramal had brought the industry into disrepute by not providing the appropriate safety information in that the adverse event reporting statement was not included. In AbbVie's view this prejudiced patient safety in breach of Clause 2.

### **Inter-company dialogue**

AbbVie explained that during inter-company dialogue Piramal had that the leaflet was not promotional. However, in AbbVie's view it was clearly promotional; it highlighted the glass packaging of sevoflurane which could not be separated from the product itself. In AbbVie's view, the purpose of the item was to increase the purchase, recommendation, sale, supply or use of sevoflurane. Further, the leaflet used promotional language, eg 'Glass represents Quality and Trust' and 'Glass – by choice'.

AbbVie stated that the leaflet also looked and felt promotional; it was glossy and colourful marketing-style communication. Non-promotional material must not contain product claims.

AbbVie noted that Piramal had stated during inter-company dialogue that the Code allowed for the summary of product characteristics (SPC) to be provided in lieu of the specific particulars listed in the 'obligatory information for inclusion in promotional materials' section above. Clause 4.2 made it clear that the legal classification and cost must also be included and those particulars were not in the SPC. As noted above, the cost was not stated in the leaflet.

Piramal failed to acknowledge that the leaflet was promotional and stated that it was being revised, however it had not stated explicitly that it was no longer used in the UK. Piramal provided no written undertaking that the claims to which this complaint related would not be repeated and AbbVie considered that inter-company dialogue had been unsuccessful.

In summary, AbbVie alleged breaches of Clauses 2, 4.2, 4.9, 4.10 and 9.1 of the Code and a breach of the MHRA Blue Guide.

### **RESPONSE**

Piramal submitted that there was no basis for the allegations and responded to each of the points raised by AbbVie.

Piramal provided the background surrounding the preparation and use of the item; Piramal submitted that the item should be considered in context in order to assess the validity of AbbVie's allegations. Secondly, Piramal included its observation with respect to the allegedly promotional nature of the item in the context of Clause 1.2 and applicable law. Lastly, it addressed each of AbbVie's allegations.

Piramal submitted that it was particularly mindful of its over-arching obligation to ensure regulatory compliance of all external communications. Each external communication was subject to rigorous

review according to established processes and procedures. Piramal submitted that its established review policy took full account of the requirements set out in law and in voluntary industry codes of practice. Piramal submitted that it was fully committed to compliance and good governance. Compliance with the promotional and advertising rules for medicines was no exception.

Piramal was disappointed to learn of AbbVie's characterisation to the effect that its materials fell short of the acceptable industry standard. Piramal considered AbbVie's allegations and characterisation to be wholly unfounded.

### **Background information**

Piramal submitted that Sojourn Sevoflurane 100% Inhalation Vapour Liquid (UK PL 29595/0002) was authorised in the UK and twenty seven other EU member states through the decentralised procedure; the UK was the reference member state.

Pursuant to the requirements set out in Article 11 of Directive 2001/83 and the Commission's Guidance on SPC, Piramal, as the marketing authorization holder, must provide information in Section 6.5 on the nature and contents of the primary packaging container of the medicine. Section 6.5 of the SPC read as follows:

'Type III, 250 ml amber coloured glass bottles with two component screw cap made up of the outer black phenolic cover and inner translucent low density polyethylene cone. The pack is provided with an LDPE yellow-coloured collar.'

The UK Public Assessment Report gave the following description on the assessment of the container-closure system:

'The finished product is supplied in Type III, 250 ml amber-coloured, glass bottles, with two component screw caps made up of outer black phenolic covers and inner translucent low-density polyethylene (LDPE) cones. The pack is provided with an LDPE yellow-coloured collar.'

Satisfactory specifications and Certificates of Analysis for all packaging material have been provided for all packaging used. All primary packaging complies with the requirements of Directive 2002/72/EC. In addition, the glass bottles are compliant with the Type III requirements of European Pharmacopoeia monograph 3.2.1 "Glass containers for pharmaceutical use".

In the UK, there were three sevoflurane containing products marketed by AbbVie, Baxter and Piramal as treatment options or alternatives for the induction and maintenance of general anaesthesia in adults and children.

Piramal submitted that the leaflet was used at a European conference in Berlin in May 2015 as a detail aid, and was developed by the marketing team in April 2015 for that purpose. It was used as an informative memory aid for Piramal's sales

personnel and was not intended for publication or distribution in both the UK and EU markets. The information contained in the item reflected an independently conducted research study about glass breakage.

The material provided factual information about the drop test which Piramal had undertaken. The test was conducted in accordance with the standards recommended by the International Safe Transit Association (ISTA) which was accredited by the American National Standards Institute. Testing was performed by a laboratory which was certified by ISTA and accredited by the American Association for Laboratory Accreditation. The test was designed to demonstrate susceptibility (or otherwise robustness) of the primary package constructed from Type III glass to breakage on common hospital floor coverings ie carpet, rubber, linoleum and vinyl composite tile.

The published material provided the test method, the test results and the conclusion.

Nothing in the material purported to convey information about the clinical safety, efficacy or therapeutic use of sevoflurane, nor was a comparator product referred to either expressly or by implication.

New data had since become available and Piramal decided to withdraw the item. A new version would be developed to take account of the new data to ensure that the information reflected the current and up-to-date scientific development. Piramal stated that it informed AbbVie about its decision in November 2015.

Although the material had been subject to Piramal's internal review process, it had never been published or distributed or otherwise used externally in the UK market, nor had Piramal consented to its use by any third party, including its agents, contractors etc.

Piramal submitted that it was therefore surprised and concerned to learn from AbbVie that the material had come into the possession of individuals in the UK outside of Piramal as it had never intended to release the leaflet for external use. Piramal noted that AbbVie had not responded to its repeated requests for information on how it came into possession of the leaflet. Copies of correspondence with AbbVie were provided.

Piramal submitted that AbbVie's allegations therefore concerned material which had either been or was currently being withdrawn globally for reasons that were unrelated to the complaint, and which had never been circulated outside Piramal in the UK with its consent and which was the subject of a possible legal action arising from the unauthorised disclosure of the materials to a third party.

### **The allegedly promotional nature of the materials**

Piramal submitted that AbbVie had consistently objected to the leaflet being used because in its view it was in breach of various clauses of the Code and the relevant guidance published by the MHRA.

#### **(i) Packaging promotion**

Piramal submitted that the leaflet did not promote sevoflurane; it had been prepared to factually describe the quality of the primary packaging material used. It could not be viewed as promotional by conveying the effect of promoting or inducing the prescription, supply, sale or consumption of Piramal's sevoflurane.

The position of the Code was consistent with that set out in Title VIII of Directive 2001/83 with regard to what was considered to be advertising. Advertising of medicines included any form of door-to-door information, canvassing activity or inducement designed to promote the prescription, supply, sale or consumption of medicines. As the Court of Justice of the EU articulated in its decision in the Merck Sharp & Dohme Case (C-316/09), the key basis for distinguishing non-promotional information from advertising was the purpose of the communication. As soon as the communication was intended to promote the prescription, supply, sale or consumption of medicines, it would qualify as advertising.

Piramal submitted that the leaflet provided factual information about the primary packaging used for containing the liquid sevoflurane, consistent with Section 6.5 of the SPC.

The item focussed on the provision of additional factual information about the packaging material used to safely contain and preserve the quality and integrity of sevoflurane. If provision of information on primary packaging was properly characterised as promotion, Piramal accepted that the material was promotional in nature in respect of the primary packaging. However, it did not promote a medicine as envisaged by the Code and in the manner that had been interpreted by the courts in accordance with applicable legislation, as discussed below.

In a broader context, according to the established case-law of the European Court (Novo Nordisk Case C-249/09), claims in advertisements for health professionals who had a higher level of scientific knowledge than the public, did not have to be 'included in or be derivable from' information in the SPC. They could also contain additional information provided that the claims:

- a) confirmed or clarified and were compatible with the details in the SPC and did not distort the latter;
- b) were not misleading and encouraged the rational use of the medicine by presenting it objectively and without exaggerating its properties (see below) and
- c) were accurate, up-to-date, verifiable and sufficiently complete to enable the health professional to form his/her own opinion of the therapeutic value of the medicine.

Even if the leaflet was considered as promotional or advertising as suggested by AbbVie, Piramal denied that it breached the Code and the UK Advertising Regulations that sought to implement the requirements in Directive 2001/83/EC. In that case, the leaflet complied with the particulars listed in the

approved SPC. Moreover, nothing in the material encouraged the irrational use of a medicine by not presenting the nature of the primary packaging objectively or otherwise exaggerating the properties of the packaging material, nor could the content of the material be considered misleading.

For the above reasons, as a general matter, Piramal submitted that it could not identify a proper factual basis to suggest that the material was in breach of the Code or the UK Advertising Regulations.

(ii) 'Promotion' under Clause 1.2 of the Code and applicable law

Consistent with the position set out in EU law, the term 'promotion' was defined in Clause 1.2 as:

'any activity undertaken by a pharmaceutical company or with its authority which promotes the administration, consumption, prescription, purchase, recommendation, sale, supply or use of its medicines'

Having regard to the general EU law position, Piramal now provided reasons as to why the leaflet was not considered to be promotion of a medicine within the context of the Code.

Piramal submitted that as a preliminary point, and without prejudice to the specific points made herein the leaflet could not, on any interpretation, be considered promotional within the meaning of Clause 1.2, as it was not made available to UK health professionals by Piramal or with its authority. As explained, it had never been distributed in the UK. Piramal submitted that even if it had been so distributed in the UK as alleged by AbbVie (and Piramal respectfully disagreed), there was no proper basis to suggest that it breached the requirements set out in the Code or the UK Advertising Regulations.

Clause 1.2 explicitly stated that 'promotion' did not include:

'factual, accurate, informative announcements and reference material concerning licensed medicines and relating, for example, to pack changes, adverse reaction warnings, trade catalogues and price lists, provided they include no product claims'

Whilst the term 'product claims' was not defined in the Code, the MHRA Blue Guide provided that a 'product claim' was:

'anything or any activity which was intended to encourage prescription or supply by healthcare professionals and use of medicines by the general public, generally by means of highlighting qualities of *the medicine*' (emphasis added).

Given the Code could not be applied or otherwise interpreted outside of the statutory framework, the 'product claim' referred to in Clause 1.2 ought to be considered as a 'product claim' for a medicine. In

that case, the material did not seek to promote the therapeutic value, safety or efficacy of a medicine. Instead, it highlighted the qualities of packaging rather than sevoflurane as a therapeutic agent.

The claims (to which AbbVie had consistently objected) related to the nature and the quality of glass packaging, not a medicine. The item accordingly came within the exclusion contemplated by Clause 1.2.

Piramal agreed with AbbVie to the extent that the 'totality of the information' contained in the leaflet must be considered to inform an assessment of whether it had a promotional intent. Piramal also reiterated and emphasised its submission above that its intention underlying the production of the leaflet was to detail the quality of a particular form of packaging, rather than to make claims about the therapeutic value of a medicine.

Piramal rejected AbbVie's allegations that, by not including certain information which was required in connection with the promotion of a medicine, Piramal had breached Clauses 4.2, 4.9 and 4.10.

Piramal reiterated that in its view the leaflet could not be construed as promotion of sevoflurane. Piramal submitted that since the leaflet did not constitute promotional material of the kind that the Code sought to address, it was not obliged to include the information specified in Clause 4.

Piramal submitted that it was mindful of AbbVie's observations that some, but not all, of the information specified in Clauses 4.2, 4.9 and 4.10 had been included in the material. However, the voluntary inclusion of information stipulated under Clause 4 did not render the item promotional within the meaning of the Code and trigger the need to comply with the requirement of the Code to include all such information, given that the leaflet focussed on the packaging and not the medicine.

Piramal noted AbbVie's allegation that it had failed to maintain high standards as required under Clause 9.1.

Piramal stated that notwithstanding its view that it had not breached the Code and that the leaflet at issue did not constitute promotion within the meaning of the Code, it further noted that the supplementary information to Clause 9 indicated that the clause was intended to ensure that aspects such as sexual imagery or emoticons did not form part of medicine advertising, which attracted a higher standard than that of general commodity advertising. Piramal queried the validity of AbbVie's assessment on the applicability of Clause 9 to this case.

Piramal refuted that it had brought the industry into disrepute, contrary to Clause 2. Piramal submitted that AbbVie's allegation was plainly vexatious and wholly unfounded.

Piramal noted that a breach of Clause 2 was consistently reserved for behaviour and activities that were particularly egregious of the Code's

requirements and therefore attracted particular censure. In light of the totality of facts and circumstances in this case, Piramal submitted that a finding of a breach of Clause 2 was not warranted, nor would such a finding, in its view, be proportionate.

Piramal submitted that it fully appreciated and respected its obligations under the Code and applicable legislation with respect to promotion of sevoflurane. However, the leaflet did not constitute an advertisement of a medicine within the meaning of the Code and applicable legislation. The material provided specific information about the nature and quality of the primary packaging material based on a particular type of glass. The allegations made by AbbVie were therefore unfounded and should be dismissed.

Piramal submitted that for the reasons given above, the item was acceptable for the purpose of providing factual information about the glass used as primary packaging. Piramal had identified no proper basis to suggest that the material (even if it was distributed for use in the UK) breached the Code and the UK Advertising Regulations.

In keeping with its legal, regulatory and ethical obligations, Piramal noted that, in spite of telling AbbVie about its decision to withdraw the material, AbbVie submitted the complaint thereby expending the PMCPA's resources on investigating a case that would have no practical consequences and where the allegations were unfounded.

For the reasons given above, Piramal's submitted that AbbVie's complaint was baseless. Accordingly, Piramal requested that the Panel consider holding AbbVie fully accountable under Paragraph 7.2 of the Constitution and Procedure to pay an administrative charge for each matter alleged, but ruled by the Panel not to be in breach of the Code.

In response to a request for further information, Piramal referred to inter-company correspondence in which it informed AbbVie that the leaflet was being updated and as soon as the revision was complete, the revised version would replace the current piece in the near future.

Piramal stated that the leaflet was first used at a European conference in Berlin in May 2015 and had also been used in the UK. The leaflet has been withdrawn from use and external distribution in November 2015.

In response to a request for further information, Piramal apologized that its previous responses might not have fully addressed the Panel's request and appeared to be conflicting or unclear; it might have been in part due to its misunderstanding of the extent to which the Panel was concerned with use of the materials in question outside of the UK. Piramal clarified that the leaflet was developed for multi-country use and not specifically for use in the UK. Piramal further clarified that its only two products on the UK market were both inhaled anaesthetics used exclusively in secondary care and as a consequence its UK organization was very small and so was

its team that interacted directly with UK health professionals or organizations. With such a small team, Piramal was very confident that instructions about use or non-use of materials were complied with and declarations from both team members supporting their use of the materials in question were provided.

Piramal submitted that the leaflet was last used in the UK in November 2015. Declaration of Piramal's UK country manager and regional manager received on 10 March 2016 regarding the use of the leaflet in the UK and an email from Piramal's marketing manager to the UK country manager, dated 11 December 2015, instructing him that none of the materials should be used, were provided.

Piramal hoped that the explanation clarified the position regarding use and withdrawal of the material in the UK, and submitted that every effort was made to ensure that the leaflet was removed from use in the UK to the extent it was able to once concerns relating to its use were raised by AbbVie.

Piramal submitted that it would evaluate whether the leaflet should be revised and subsequently used in the UK; the revised material would be in full compliance with UK law governing advertising of medicinal products and the Code and be consistent with the Panel's rulings.

## **PANEL RULING**

The Panel noted that both in its initial response and in response to a request for further information, Piramal had stated that the leaflet at issue was used in the UK. It was thus subject to the Code. Declarations from members of staff showed that the material was last used in November 2015. Although the leaflet had been withdrawn in November 2015, during the course of inter-company dialogue that fact had not been made clear to AbbVie. From inter-company dialogue it appeared that the leaflet was being revised and that the revised version would replace the current version in due course. Indeed Piramal stated that the leaflet had been withdrawn to update its content in response to the Authority. The Panel thus considered that when AbbVie complained to the PMCPA in December 2015, it had reason to believe that the leaflet was still in use and that inter-company dialogue had been unsuccessful.

The Panel noted Piramal's submission that the leaflet was not promotional because it focussed on the packaging of sevoflurane and did not seek to promote the therapeutic value, safety or efficacy of the medicine. The Panel considered, however, that a licensed medicine was the sum of its parts, and packaging (in this case the robustness of the glass bottles) might be a reason why a health professional or other relevant decision maker would choose one medicine over another. Reference was made to Piramal's sevoflurane 5 year shelf life. The Panel noted in that regard the application of Clause 7, Information, Claims and Comparisons, was not limited to information or claims of a medical or scientific nature. In the Panel's view, a claim about any aspect of a medicine would be caught by the definition of promotion. The Panel thus considered

that the leaflet, which was developed for use at a European conference in Berlin but had also been used with customers and internally in the UK, promoted sevoflurane.

The Panel noted that AbbVie had alleged breaches of the MHRA Blue Guide. The Panel could only make rulings on the Code.

The Panel noted that Clause 4.2 required promotional material to include, as part of the prescribing information, the cost (excluding VAT) of a medicine. The Panel noted that the SPC and patient information leaflet appeared to have been reproduced on pages 5 and 6 of the leaflet; the cost of sevoflurane was not included. The Panel noted that a breach of Clause 4.2 had been alleged. Clause 4.2 listed the components of prescribing information and it was a requirement of Clause 4.1 that such be provided. As the cost of sevoflurane had not been stated the Panel ruled a breach of Clause 4.1.

Clause 4.9 stated that all promotional material must include the prominent statement 'Adverse events should be reported. Reporting forms and information can be found at [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard). Adverse events should also be reported

to [relevant pharmaceutical company]'. This statement did not appear in the leaflet at issue and the Panel therefore ruled a breach of Clause 4.9.

Similarly the Panel ruled a breach of Clause 4.10 as the leaflet did not include the date on which it was drawn up or last revised as required by that clause.

The Panel noted its rulings above and considered that high standards had not been maintained and a breach of Clause 9.1 was ruled.

The Panel noted its ruling of a breach of Clause 4.9 above and although it was concerned that the adverse event reporting statement had not been included in the leaflet, it considered that an additional ruling of a breach of Clause 2 would be disproportionate. A ruling of a breach of Clause 2 was used as a sign of particular censure and reserved for such use. No breach of that clause was ruled.

**Complaint received**                      **22 December 2015**

**Case completed**                              **6 May 2016**

# MEDIA/DIRECTOR v HOSPIRA

## Arrangements for an overseas meeting

The Daily Telegraph of Wednesday, 17 February 2016 carried an article criticising pharmaceutical companies in relation to payments to senior NHS staff ('NHS officials with second jobs at drugs firms' which continued under the heading 'How drugs firms give NHS officials trips abroad at top hotels for £1000 a day'). Hospira was named in relation to the arrangements for a meeting held at a five-star hotel in Zagreb which had a spa and casino. In accordance with Paragraph 6.1 of the Constitution and Procedure the matter was taken up as a complaint under the Code.

Hospira submitted that the trip included a manufacturing site visit and an advisory board. The company's detailed response is below.

The Panel noted that it was acceptable for companies to contract health professionals and others for advice. Nonetheless, the arrangements for such meetings had to comply with the Code. To be considered a legitimate advisory board the choice and number of participants should stand up to independent scrutiny with each chosen according to their expertise such that they would be able to contribute meaningfully to the purpose and expected outcomes. The number of participants should be limited to allow active participation by all. The agenda should allow adequate time for discussion. The number of meetings and the number of participants should be driven by need and not the invitees' willingness to attend. Invitations to participate should state the purpose of the advisory board meeting, the expected advisory role and the amount of work to be undertaken. If an honorarium was offered it should be made clear that it was a payment for such work and advice. Honoraria must be reasonable and reflect the fair market value of the time and effort involved.

Turning to the meeting at issue the Panel noted that it was wholly for UK health professionals (five pharmacists); two were from the same hospital's NHS trust. The Panel noted that the delegates were not paid any honoraria. In addition three Hospira staff attended and an employee of its communications agency. The Panel queried whether the ratio of Hospira staff to delegates was appropriate. The Panel noted Hospira's submission that the delegates were selected because they were UK pharmacists with a role in quality assurance and procurement of biologic/biosimilars. In the Panel's view the primary aim of trying to recruit 10-12 delegates for the meeting appeared to be driven by an attempt to maximise the number who could visit the manufacturing site rather than the number necessary to achieve the identified need of the advisory board. Hospira initially invited 17 potential delegates. The Panel queried, however, why no-

one from Wales or Northern Ireland was invited given Hospira's submission that the purpose of the advisory board was, *inter alia*, to seek advice on how to further facilitate the uptake of biosimilar products in the UK. The Panel further noted Hospira's submission that five delegates was sufficient to achieve the identified need of the advisory board and that if there had been 10-12, the additional input would have been welcomed but the feedback from five was useful.

The Panel noted Hospira's submission that the meeting would combine a site visit to Hospira's Zagreb biologics manufacturing site and an advisory board associated with Hospira's biosimilars. The Panel noted that it was in Hospira's interest for the NHS to be confident in the manufacture of its medicines. The Panel queried whether it was ever acceptable to combine two company meetings such that one part was promotional and the other part was an advisory board. The Panel noted that the invitation was to a site visit of the manufacturing facility, Monday to Wednesday (3 nights). The invitation further stated 'You will have a tour of the Hospira manufacturing facility and you will also take part in an advisory board during your visit'. The Panel noted that the agenda was entitled 'Agenda and Plan for Hospira UK, Zagreb Manufacturing Site Tour'. The expenses claim forms were entitled 'Hospira Manufacturing Facility Site Visit Expenses Form'. It appeared to the Panel that the visit to the manufacturing site and gaining confidence in the quality of that site was emphasised more than the advisory board.

The Panel noted that meetings which involved UK health professionals at venues outside the UK were not necessarily unacceptable provided there were valid and cogent reasons for holding meetings at such venues. As with meetings held in the UK, in determining whether such a meeting was acceptable or not, consideration must also be given to the educational programme, overall cost, facilities offered by the venue, nature of the audience, subsistence provided and the like. As with any meeting it should be the programme that attracted delegates and not the associated hospitality or venue.

The Panel was concerned that the primary justification for holding the meeting outside the UK appeared to be to allow UK pharmacists to conduct due diligence on Hospira's manufacturing facilities. In any event, in the Panel's view, the acceptability of the visit to the manufacturing site could not be considered separately to the rest of the meeting. The two elements were inextricably linked and the acceptability of the arrangements had to be considered in the round.

The Panel noted Hospira's submission that it manufactured and marketed a number of biosimilars. The Panel queried whether there was a *bona fide* need for advice such as to justify the advisory board meeting in question. The Panel noted that the advisory board ran from 2.30 – 6pm on Monday, 13 July. It was stated that the advisory board would focus on key issues including gaining advice and insights to uptake of biosimilars in the UK, including the recently licensed Inflectra; examining current challenges and perceived benefits of biosimilars that pharmacists experience; discussing educational and communication needs around biosimilars in the UK (eg new materials, communication, raising physician awareness and confidence in biosimilars etc); additional areas of interest to Hospira; and sharing what they hoped to achieve from the site tour the following day including questions that they would like to be answered. The Panel did not consider that sharing what delegates hoped to achieve from the site tour was a legitimate objective for an advisory board which should address *bona fide* questions of the company, not of the attendees. There did not appear to be a clear *bona fide* issue upon which Hospira had sought advice which necessitated an advisory board, nor had the anticipated role of the participants in the advisory board been made sufficiently clear in the invitation and elsewhere. In the Panel's view, despite the subheading 'Advisory Board planned agenda' some of the bullet points beneath including 'Discussing educational and communication needs ...' and 'sharing what you hope to achieve from the Zagreb tour ...' did not make it sufficiently clear that the company was seeking advice. Some recipients might have considered that they were being invited to participate in a discussion forum or such like. The Panel noted that the advisory board meeting notes listed no further actions for Hospira and there was an emphasis on finding out the position of delegates' NHS bodies in relation to switching to Inflectra. There appeared to be little substantive discussion of all of the stated objectives. In addition, the Panel noted Hospira's submission that in error the delegates had not been provided with a contract setting out the nature of the services to be provided as required by the Code. The Panel was concerned that the time spent obtaining advice appeared to be limited and further no preparation was needed. Hospira had not argued that this element of the meeting was anything other than an advisory board. Taking all the factors into account the Panel did not consider that the arrangements were such that the UK health professionals had attended a genuine advisory board meeting. A breach of the Code was ruled.

The Panel noted that whilst the manufacturing site visit took the whole day, it only included approximately three and a half hours of educational content. The Panel queried whether it was really necessary for the health professionals to travel to Croatia to be reassured about the manufacturing quality of Hospira products. In the Panel's view detailed information about the manufacturing facility could have been incorporated into a meeting held in the UK. The Panel considered that Hospira had effectively organised an overseas promotional meeting for UK health professionals.

The Panel noted that the average total cost of hospitality was approximately £450 per person plus economy airfares. The cost of the two evening meals in Croatia were £24.14 and £37.18 per head.

The hotel used was not appropriate. The Panel noted Hospira's submission that it understood that at the time, the hotel was a four-star hotel and there was no longer nor at the time of the meeting a casino; the only complimentary guest facilities were a gym and swimming pool/spa. The hotel was described in material provided by Hospira as 'the finest hotel in Zagreb' and that it was until recently a member of the 'Leading Hotels in the World'. The hotel was a 45 minute transfer from the manufacturing site; accommodation nearer to the manufacturer should have been used. In the Panel's view, the location and facilities were more akin to leisure travel than business purposes and would have attracted delegates to attend. The Panel was very concerned that the venue had been chosen without further assessment of its acceptability in the context of UK requirements.

The Panel considered that whilst the subsistence alone had not been excessive, the total hospitality provided was out of proportion to the occasion (ie overseas location, the venue and three nights' accommodation). The total educational content was approximately 7 hours including three and a half hours for the advisory board. The Panel noted its comments on the content of the meeting above. The Panel considered that hosting UK delegates for a two day promotional meeting in Croatia, in circumstances where the Panel did not consider that there was any clear and cogent reason for holding the meeting outside the UK was unacceptable and an inducement to prescribe or recommend Hospira products. A breach of the Code was ruled.

The Panel considered that, as it had ruled the arrangements did not meet the criteria for advisory boards, UK health professionals had been invited to attend a two day promotional meeting in Croatia, the primary objective of which appeared to be to increase their confidence in the manufacturing quality of Hospira products. The Panel noted its comments above and given the lack of a clear and cogent reason to hold the meeting outside the UK, ruled a breach of the Code.

The cost of the two dinners were each within the limits in the Croatian Code (HRK500 (£52)) and therefore no breach of the Code was ruled.

The Panel noted its criticisms of the meeting and rulings set out above and ruled a breach as high standards had not been maintained.

The Panel was very concerned to note that although the meeting (and materials) were approved and certified by Hospira at a European level, the meeting including the venue, the decision to take UK health professionals overseas and the majority of the materials were not reassessed and certified in the UK. The Panel noted that overall the company had exercised poor governance in relation to the arrangements including the failure to issue contracts and failure to certify an overseas meeting for health

**professionals. In addition health professionals had been taken overseas without there being valid and cogent reasons for so doing. This was compounded by the inclusion of an advisory board which failed to meet the requirements of the Code. The Panel considered that the overall arrangements was such as to bring discredit upon and reduce confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.**

The Daily Telegraph of Wednesday, 17 February 2016 carried an article critical of the activities of pharmaceutical companies in relation to payments to senior NHS staff ('NHS officials with second jobs at drugs firms' continued under the heading 'How drugs firms give NHS officials trips abroad at top hotels for £1000 a day'). The article named Hospira in relation to the arrangements for a meeting held in Croatia. In accordance with Paragraph 6.1 of the Constitution and Procedure the matter was taken up as a complaint under the Code.

## COMPLAINT

The Daily Telegraph article at issue named Hospira and stated that it hosted officials in a five-star hotel in Zagreb which had a spa and casino.

When writing to Hospira, the Authority provided it with a copy of The Daily Telegraph article at issue and asked it to respond in relation to Clauses 2, 9.1, 18.1, 22.1, 22.2 and 23.1 of the 2015 Code. The 2016 Constitution and Procedure applied.

## RESPONSE

Hospira submitted that the trip to Zagreb encapsulated a manufacturing site visit and an advisory board.

Hospira stated that with regard to the meeting in question it had engaged third party service providers in connection with its interactions with health professionals and/or corporate travel requirements:

- a healthcare communications agency, to assist with the logistical arrangements for the meeting including travel arrangements for delegates and paying for travel, accommodation, food and beverages and other reasonable expenses for the delegates (in accordance with Hospira's policy on interactions with health professionals) on Hospira's behalf. These costs and expenses were then reimbursed by Hospira.
- a corporate travel agent, to book the Zagreb hotel.
- a company signatory, to assist with the review and approval of the interactions with health professionals and the associated materials. In particular the agency acted as business signatory from a Code perspective. The named signatory notified to the PMCPA and the MHRA, was a licensed medical practitioner.

Hospira submitted that, neither it nor its communications agency paid any fees or honoraria to the delegates; the only transfers of value

to the delegates were the payment of travel, accommodation and food/beverage costs and other reasonable expenses. Although the Daily Telegraph referred to a five-star luxury spa hotel with casino, Hospira noted that there was no longer, nor at the time of the meeting, a casino at the hotel and the only complimentary guest health facilities were a gym and swimming pool/sauna. The agreed bed and breakfast rate was €130/night. The hotel currently described itself as a five-star venue (there was no longer an independent international star classification for hotels) but when the meeting was held Hospira understood that the hotel was a four-star hotel and it was still assessed as a four-star hotel by some booking websites.

Hospira explained that it held the meeting in Zagreb because one of its key biosimilar product manufacturing sites was located there. Biosimilar products were relatively novel and so awareness of, and confidence in them was still being established amongst health professionals. Hospira therefore generally considered it was an important and valuable educational opportunity (for all stakeholders) for the prescribers and procurers of these products in different countries to have the opportunity to gain confidence as to the quality of Hospira's biosimilar manufacturing sites (such as that in Zagreb). Likewise, with respect to the advisory board element of the meeting, it was helpful to Hospira to further understand the professional barriers and/or challenges health professionals might have with respect to the purchasing and/or prescription of biosimilar products. The discussions during the manufacturing site visit generally focussed on Hospira as a manufacturer of biosimilar products, the manufacturing processes for those products and biosimilars as a class of products as a whole.

### Clause 23.1

Hospira submitted that due to an employee's misunderstanding of the relevant corporate policy, no contracts were agreed with the delegates in connection with this meeting. The employee mistakenly considered that as no fee and/or honorarium was paid, no contract was required. Hospira accepted that this was not in compliance with Clause 23.1, however it emphasised that it had a clear corporate policy requiring appropriate written contracts to be entered into with all health professionals who acted as consultants to the company. Template contracts for this purpose were readily available to all Hospira employees on an easy to use self-service website.

Hospira submitted that its internal policy on advisory boards required a legitimate need to be identified in advance and approved by the applicable country manager as part of the overall approval process for advisory boards. In this case the legitimate need was for Hospira, which manufactured and marketed a number of biosimilars to gain insight from key stakeholders within significant NHS trusts with respect to challenges facing biosimilars and ways to facilitate their future uptake. Hospira submitted that given the above identified



need the selected consultants were chosen based on their standing as NHS procurement/ logistics pharmacists with a significant role in the commissioning process for biosimilar products.

Hospira submitted that it intended to have 10 to 12 delegates and so assuming that some invitations would be declined, 17 were issued (a list of invitees was provided). Ultimately 5 delegates (names provided) attended the meeting which was sufficient to achieve the identified need with respect to the advisory board. Also at the meeting were three Hospira employees and one employee from the healthcare communications agency.

Hospira submitted that the meeting notes it took with respect to the delegates' discussions and comments had been retained for future reference (copy provided).

Hospira submitted that the invitation to each delegate (copies provided) made it clear that the invitation was not offered as an inducement, furthermore the delegates were not paid for their participation in the advisory board or manufacturing site visit. The hospitality provided to the delegates was not excessive, it was in accordance with the Code and not an inducement to prescribe.

Hospira submitted that its written contracts contained a provision regarding the obligation of the consultant to declare that he/she was a consultant to the company whenever he/she wrote or spoke in public about a matter that was the subject of the agreement or any other issue relating to that company (template contract provided). However, as stated above, due to an employee's error, no contracts were put in place in this instance. Moreover, the consultants who participated in the meeting at issue were not retained to write or speak in public with regard to the meeting.

## **Clause 22**

As further detailed below Hospira accepted that there was an omission in terms of the approval and certification process for the meeting at issue (and the associated materials used in connection with it) in that the meeting (and materials) were approved and certified by Hospira at a European level in accordance with the principles of the EFPIA Code of Conduct, however, the majority of the materials were not reassessed and recertified under the UK Code. However, Hospira submitted that the requirements of the Code as set out in Clause 22.1 were nevertheless met with respect to this event.

All hospitality provided to the delegates (who were all health professionals) was in association with the advisory board and manufacturing site visit. The venues for the meeting were a meeting room within the hotel for the advisory board and Hospira's Zagreb manufacturing facility for the site visit. Hospira noted that careful consideration was given at a European level to the selection of an appropriate hotel for this event (in accordance with Hospira's policy on interactions with health professionals). As noted above, at the time, Hospira's understood that

the hotel was a four-star hotel and was both the most centrally located and offered the cheapest bed and breakfast rate of the three hotels considered at €130/night. Hospira listed two other hotels considered in planning for the meeting and stated that one was rejected from further consideration as it was a five-star hotel. The hotel used was then selected by the Hospira UK team without further assessment of its acceptability in the context of UK requirements.

Hospira noted that the timing of the single Zagreb/UK return flight each day (12.30pm) was such that a second night of accommodation was required as it would not have been possible to conclude the second day's planned activities in time for that day's return flight. The UK departure flight at 8.35am required delegates to stay overnight (Sunday) at a Heathrow hotel. The Heathrow hotel was a four-star hotel and the room rate for the delegates was £110 a night. Hospira considered this further supported the company's appropriate approach to the provision of hospitality to health professionals.

Hospira noted that advisory boards and manufacturing site visits were described in the supplementary information to Clause 22.1 in the Code as being appropriate meetings for a company to have with health professionals.

Hospira confirmed that the costs of meals provided to the delegates at the Zagreb hotel did not exceed the amount referred to in Clause 22.1 as evidenced by the hotel invoice (copy provided). With respect to the two evening meals at restaurants in Zagreb, the healthcare communications agency confirmed payments to the two restaurants of £217.30 and £302.25. Hospira confirmed that the costs per person for those meals (£24.14 and £37.78 respectively) did not exceed the amount referenced in Clause 22.2 of the Code.

## **Clause 18**

Hospira submitted that no gifts, pecuniary advantages or benefits were supplied, offered or promised to the delegates other than the value of the travel, accommodation and expenses in connection with the meeting which were paid for by Hospira – none of which were supplied, offered or promised as an inducement to prescribe, supply, administer, recommend, buy or sell any medicines. In particular no fees or honoraria were paid to the delegates in connection with any aspect of the meeting.

## **Clause 9**

Hospira submitted that while it always strove to maintain high standards, it recognised that there were some specific compliance errors that had occurred. Nevertheless Hospira submitted that it maintained high standards with respect to its interactions with health professionals in general and specifically with respect to this meeting as a whole as evidenced in part by Hospira's detailed policies and procedures which were established to maintain those high standards.

## Clause 2

Hospira submitted that with a few specific exceptions it had generally organised and undertaken the advisory board and manufacturing site visit in accordance with the Code. It took compliance with the Code (and other applicable laws, regulations and industry codes of practice) very seriously and had implemented systems and procedures and trained its employees to ensure that it was compliant. By way of example, Hospira provided attendance records for an external training session on the Code for UK employees in September 2015.

Hospira submitted that the meeting did not prejudice patient safety or public health, the hospitality offered was not excessive, there were no inducements to prescribe, delegates were not paid and the conduct of its employees and agents was generally competent.

Hospira submitted that The Daily Telegraph article was misleading in that it mistakenly stated that the hotel had a casino when the meeting was held, it implied that the Hospira delegates were paid fees when they were not and that the delegates might have had spa treatments at Hospira's expense which they did not; the article ignored the fact that manufacturing site visits and advisory boards were entirely legitimate interactions between industry and health professionals and in this case the manufacturing site provided a rare and valuable opportunity for the delegates to further their scientific and professional understanding of biosimilar products which would have an important role to play in the UK healthcare system. Hospira thus denied a breach of Clause 2.

Hospira submitted that the delegates were selected on the basis of their status as pharmacists in the UK whose roles encompassed quality assurance and procurement of pharmaceutical products, and in particular biologic/biosimilar products.

Hospira submitted that the meeting was held for two reasons, to combine a site visit to Hospira's biologics manufacturing site and an advisory board about Hospira's biosimilar products. Hospira intended that the delegates would share the training received during the site visit on the high standards of the manufacturing of Hospira biologics with their peers and communicate Hospira's adherence to those high standards. Hospira's intention was that the advisory board would enable it to obtain advice from the delegates about how to further facilitate the uptake of biosimilar products in the UK and allow it to understand the challenges these pharmacists faced in daily practice, the likely challenges relating to biosimilar use and educational and communication needs related to biosimilar use in the UK.

Hospira submitted that no contracts were entered into with the delegates on the basis that no honorarium or fee was paid to any delegate. Hospira explained that its policy on interactions with health professionals was very clear in its absolute requirement for detailed contracts to be entered into with attendees at advisory boards (Hospira

had template contracts for this purpose which were readily available to all employees). Accordingly the decision not to implement contracts with these delegates was a mistaken interpretation of the policy by the individual who arranged this aspect of the advisory board and site visit.

Hospira submitted that it was 'valid and cogent' to invite the delegates to its Zagreb manufacturing site in order that they could be directly exposed to, and experience the high standards of the manufacturing of Hospira biologics, which could then be shared with their peers to communicate Hospira's adherence to those high standards.

Hospira submitted that no materials were sent out to the delegates after the event – internal notes of the advisory board which were distributed in-house were provided.

Hospira noted that the meeting (and the associated materials shared with the delegates – copies provided) was fully approved and certified at a European level but only partially approved and certified from a UK Code perspective.

The programme was as set out in an agenda (copy provided). Hospira submitted that there was minimal leisure time for the delegates and there were no Hospira organised leisure activities.

Hospira reiterated that no fees or honoraria were paid to the delegates. All airfares, accommodation and meals in-country were paid for by the communications agency and subsequently reimbursed by Hospira. The only expenses incurred directly by the delegates (and subsequently reimbursed by the communications agency on behalf of Hospira) were train tickets, taxi or personal mileage and airport parking costs to cover the delegates' journeys to and from the UK airport from their home address.

Hospira reiterated that no fees were paid and economy airfare was provided. The advisory board was held in a private meeting room at the hotel and the manufacturing site visit was held in private at Hospira's Zagreb manufacturing site. Dining was in public in a quiet section of the relevant restaurant. Neither Hospira nor the communications agency paid for any services from the hotel on behalf of the delegates (or reimbursed any expenses to delegates in connection with the hotel) other than room and food/beverage costs as detailed in the hotel invoice and expenses spreadsheet.

Hospira submitted that in accordance with typical market practices certain aspects of the hotel leisure facilities were complimentary to all guests (in particular use of gym facilities and swimming pool/sauna), however Hospira did not know if any of the delegates made use of any of the hotel leisure facilities. Hospira understood that use of the hotel leisure facilities or services other than the gym or swimming pool/sauna (ie spa treatments or similar) required payment by guests and was not included in room rates.

Hospira submitted that it had not organised any other similar Zagreb manufacturing site visits and advisory boards meetings.

In response to a request for further information, Hospira submitted that the advisory board produced a productive and valuable discussion which might have slightly over-run the allocated time; Hospira attendees recollected that it might have finished closer to 7pm than 6pm. Hospira did not have a breakdown of timings for each of the topics however the advisory board was a roundtable discussion in which each of the topics received approximately equal discussion. The meeting started with a short 30 minute presentation to the delegates (copy provided) and the remaining time was spent receiving feedback from the delegates.

Whilst two delegates attended from the same NHS trust, they had very different roles and so it was valid and cogent reasons for both to attend. One attendee was a deputy director of pharmacy with an over-arching role and able to provide feedback from a more strategic perspective. In contrast, the other delegate was a pharmacist who focused on more operational issues.

The primary rationale for holding the meeting in Zagreb was the manufacturing site visit for which Hospira approached 17 potential delegates on the assumption that, following the likely decline of some invitees (due to prior commitments, potential lack of interest etc), approximately 10-12 would be able to attend, which would allow for two groups of up to 6 at the manufacturing site. In certain parts of the facility (ie viewing windows onto clean rooms etc) a group of more than 6 was impractical. Similarly, due to the sterile nature of the manufacturing facility, all visitors had to change in and out of protective clothing which was time-consuming. Therefore, there was a maximum number of visitors for whom this was practical. The primary aim of trying to recruit 10-12 delegates for the meeting was therefore to attempt to maximise the number of individuals who could participate in this educational opportunity. Ultimately 6 delegates accepted the invitation although one subsequently dropped out.

Separately, Hospira considered five delegates was sufficient to achieve the identified need of the advisory board; if 10-12 had accepted, the additional perspectives in the advisory board meeting would have been welcomed but the feedback from the five who attended was useful. As stated above, no fees were paid to any of the advisory board participants.

Hospira noted that differences in timings noted in the documentation provided related to the agenda set out on the initial delegate invitation and the final updated agenda (copy provided) which was produced once delegates had responded to the invitation and (given the number of acceptances) it was confirmed that the manufacturing site tour would be undertaken by a single group.

Hospira understood that the delegates arrived back at the hotel on Tuesday, 17 July approximately in accordance with the final agenda (ie at around

4.15pm). The intention was that between 4.15-7pm, delegates could catch up with work commitments (ie check and respond to emails, take telephone calls etc). Hospira did not arrange any additional services at the hotel or any tours of Zagreb.

Hospira noted that the final agenda confirmed that the time allotted for lunch during the factory tour was 1 hour 15 minutes. This time was necessary because the lunch was served in an office building onsite but separate to the manufacturing facilities. Additionally, the delegates had to have time to take off protective clothing before lunch. The lunch menu was exactly the same as the staff lunch (this was not an out of pocket cost paid to a third party as the delegates were simply offered a staff meal that was paid for as part of the manufacturing site's normal operating expenses). Hospira could not state what was specifically provided to the delegates but there was usually a salad or vegetable choice and a meat and vegetarian option, bread and fruit or cake as dessert with water, soft drinks, tea or coffee.

Hospira was unable to retrospectively state what other flight times were available to it – however as stated above, the only realistic return flight time was 12.30pm. It appeared that there were currently two carriers operating directly between London Heathrow and Zagreb. One of these appeared to offer a later daily return flight at 5.50pm, however, in Hospira's view, this would be unworkable in terms of ensuring the manufacturing site visit could be completed and an airport transfer undertaken in time to check-in and board for this flight on the same day as the manufacturing site visit; and if this flight was available at the time of the meeting it would have meant returning with a different carrier to the outbound journey which would have significantly increased the delegate travel costs.

Hospira stated that no subsistence was provided to the delegates during the overnight stay at Heathrow and no Hospira or communications agency personnel met the delegates on the Sunday night. The first interactions between Hospira/communications agency personnel and the delegates were during the hotel check-out and/or airport check-in on the Monday morning.

Hospira stated that the Croatian Code was not specifically considered during the approval process for the meeting. However, having now reviewed the Croatian Code, Hospira considered that it had complied with its provisions in relation to subsistence. The Croatian Code required the use of 4-star (rather than 5-star) hotels, but as explained above, Hospira colleagues believed that the hotel at issue was a 4-star hotel when it was selected.

Hospira stated that it had not arranged any other such meetings for UK health professionals and has not arranged any similar standalone advisory boards either in the UK or elsewhere.

Hospira stated that it realised in September 2015 that no consultancy agreements had been issued to the delegates.

Hospira stated that no breakdown of beverage costs was available, however the only bar beverages purchased for delegates (ie drinks provided to delegates not directly in association with a meal or the advisory board or manufacturing site visit) were those on the hotel invoice on 13 July and these were just hot and cold soft drinks purchased for the delegates and Hospira/communications agency attendees on arrival at the hotel. The only drinks provided to delegates during the advisory board and/or manufacturing site visit were hot and cold soft drinks.

Hospira submitted that the hotel was primarily chosen on the basis of a pre-planning visit by Hospira regional personnel who considered different Zagreb hotels against various criteria including suitability from the perspective of Hospira's compliance with applicable regulations and codes, location (for example convenience for walking to evening meal venues rather than incurring taxi costs and off-road parking facility for bus transfer drop-off/pick-up) and quality of meeting room/business facilities.

Hospira stated that having considered these criteria and ensured that they were satisfied, the final selection of the hotel was based on price (vs other options) however, as stated above, this was not the only criteria involved in its selection. There was a mistaken assumption by the Hospira UK team that because the acceptability of the hotel had already been considered at a European level (in relation to EFPIA Code requirements) there was no need to undertake a further assessment of its acceptability in the context of UK-specific requirements (such as the Code).

In conclusion, Hospira reiterated that with a few specific exceptions it generally organised and undertook this advisory board and manufacturing site visit in accordance with the Code. Hospira took its compliance with the Code (and other applicable laws, regulations and industry codes of practice) very seriously and had implemented systems and procedures and trained its employees to ensure that it was compliant.

## **PANEL RULING**

The Panel noted the allegations as set out in The Daily Telegraph article of 17 February and the company's responses. In the Panel's view, it had to consider the acceptability of the advisory board and tour of the manufacturing site, including their overseas location and the level of hospitality.

The Panel noted that it was acceptable for companies to contract health professionals and others for relevant advice. Nonetheless, the arrangements for such meetings had to comply with the Code, particularly Clause 23. To be considered a legitimate advisory board the choice and number of participants should stand up to independent scrutiny; each should be chosen according to their expertise such that they would be able to contribute meaningfully to the purpose and expected outcomes of the advisory board. The number of participants

should be limited so as to allow active participation by all. The agenda should allow adequate time for discussion. The number of meetings and the number of participants should be driven by need and not the invitees' willingness to attend. Invitations to participate should state the purpose of the advisory board meeting, the expected advisory role and the amount of work to be undertaken. If an honorarium was offered it should be made clear that it was a payment for such work and advice. Honoraria must be reasonable and reflect the fair market value of the time and effort involved.

Turning to the meeting at issue the Panel noted that it was wholly for UK health professionals; the delegates comprised five pharmacists. Two delegates were from the same hospital's NHS trust. The Panel noted that the delegates were not paid any honoraria. In addition three Hospira staff attended and an employee of the healthcare communications agency. The Panel queried whether the ratio of Hospira staff to delegates was appropriate. The Panel noted Hospira's submission that the delegates were selected on the basis of their status as UK pharmacists with a role in quality assurance and procurement of medicines, and in particular biologic/biosimilars. In the Panel's view the primary aim of trying to recruit 10-12 delegates for the meeting appeared to be driven by an attempt to maximise the number of individuals who could participate in the visit to the manufacturing site, rather than the number of consultants necessary to achieve the identified need of the advisory board. The Panel noted that in making allowance for the possibility that some invitations would be declined, Hospira initially invited 17 potential delegates. The Panel queried, however, why no-one from Wales or Northern Ireland was invited given Hospira's submission that the purpose of the advisory board was to seek advice on how to further facilitate the uptake of biosimilar products in the UK, the challenges these pharmacists faced in daily practice and the likely challenges relating to biosimilar use, and educational and communication needs related to biosimilar use in the UK. The Panel further noted Hospira's submission that five delegates was sufficient to achieve the identified need of the advisory board and that if 10-12 delegates had accepted, the additional perspectives in the advisory board meeting would have been welcomed but the feedback from the five who attended was useful. The Panel noted its general comments on the acceptable number of participants in an advisory board above.

The Panel noted Hospira's submission that the purpose of the meeting was to combine a site visit to Hospira's Zagreb biologics manufacturing site and an advisory board associated with Hospira's biosimilars. The Panel noted that it was in Hospira's commercial interest for the NHS to be confident in the manufacture of Hospira medicines. The Panel queried whether it was ever acceptable to combine two company meetings such that a company's products were promoted at part of the meeting and another part was a genuine advisory board. The Panel noted that the invitation for the meeting invited the reader to a site visit of the manufacturing facility at Zagreb, Croatia, on Monday 13 July to Wednesday

15 July. The invitation further stated 'You will have a tour of the Hospira manufacturing facility and you will also take part in an advisory board during your visit'. The Panel noted that the agenda was entitled 'Agenda and Plan for Hospira UK, Zagreb Manufacturing Site Tour'. All of the expenses claim forms were also entitled 'Hospira Manufacturing Facility Site Visit Expenses Form'. It appeared to the Panel that more emphasis was placed on the visit to the manufacturing site and gaining confidence in the quality of that site rather than the advisory board.

The Panel noted that the supplementary information to Clause 22 stated that meetings organised by pharmaceutical companies which involved UK health professionals at venues outside the UK were not necessarily unacceptable. There had, however, to be valid and cogent reasons for holding meetings at such venues. These were that most of the invitees were from outside the UK and, given their countries of origin, it made greater logistical sense to hold the meeting outside the UK or, given the location of the relevant resource or expertise that was the object or subject matter of the meeting, it made greater logistical sense to hold the meeting outside the UK. As with meetings held in the UK, in determining whether such a meeting was acceptable or not, consideration must also be given to the educational programme, overall cost, facilities offered by the venue, nature of the audience, subsistence provided and the like. As with any meeting it should be the programme that attracted delegates and not the associated hospitality or venue.

The Panel was concerned that the primary justification for holding the meeting outside the UK appeared to be to allow UK pharmacists to conduct due diligence on Hospira's manufacturing facilities. In any event, in the Panel's view, the acceptability of the visit to the manufacturing site could not be considered separately to the rest of the meeting. The two elements of the meeting were inextricably linked and the acceptability of the arrangements had to be considered in the round.

The Panel noted Hospira's submission that it manufactured and marketed a number of biosimilars. The Panel queried whether there was a *bona fide* need for advice such as to justify the advisory board meeting in question. The Panel noted that the advisory board ran from 2.30-6pm on Monday, 13 July. It was stated that the advisory board would focus on key issues including gaining advice and insights to uptake of biosimilars in the UK, including the recently licensed Inflectra; examining current challenges and perceived benefits of biosimilars that pharmacists experience in daily practice; discussing educational and communication needs around biosimilars in the UK (eg new materials, communication, raising physician awareness and confidence in biosimilars etc); additional areas of interest to Hospira; and sharing what they hoped to achieve from the site tour the following day including questions that they would like to be answered. The Panel did not consider that sharing what delegates hoped to achieve from the site tour the following day was a legitimate objective for an advisory board which should address *bona*

*fide* questions of the company, not of the attendees. On the material before the Panel there did not appear to be a clear *bona fide* issue upon which Hospira had sought advice which necessitated an advisory board, nor had the anticipated role of the participants in the advisory board been made sufficiently clear in the invitation and elsewhere. In the Panel's view, despite the subheading 'Advisory Board planned agenda' some of the bullet points beneath the subheading including 'Discussing educational and communication needs ...' and 'sharing what you hope to achieve from the Zagreb tour ...' did not make it sufficiently clear that the company was seeking advice. Some recipients might have considered that they were being invited to participate in a discussion forum or such like. The Panel noted that the advisory board meeting notes listed no further actions for Hospira and there was an emphasis on finding out the position of delegates' NHS bodies in relation to switching to Inflectra. There appeared to be little substantive discussion of all of the stated objectives. In addition, the Panel noted Hospira's submission that in error the delegates had not been provided with a contract setting out the nature of the services to be provided as required by Clause 23.1. The Panel was concerned that the time spent obtaining advice appeared to be limited and further no preparation was needed. Hospira had not argued that this element of the meeting was anything other than an advisory board. Taking all the factors into account the Panel did not consider that the arrangements were such that the UK health professionals had attended a genuine advisory board meeting. It therefore ruled a breach of Clause 23.1.

The Panel noted that delegates departed for the manufacturing site at 9.15am on Tuesday, 14 July and arrived back at the hotel at 4.15pm. The Panel noted that the tour of the manufacturing facility lasted two hours following a half hour introductory video which described the tour and a half hour welcome. After lunch on-site there was a 1 hour discussion about the development of the manufacturing facility and production in Zagreb and other feedback/queries following the tour. The Panel noted that whilst the manufacturing site visit took the whole day, it only included approximately three and a half hours of educational content. The Panel queried whether it was really necessary for the health professionals to travel to Croatia to be reassured about the manufacturing quality of Hospira products. In the Panel's view detailed information about the manufacturing facility could have been incorporated into a meeting held in the UK. The Panel considered that Hospira had effectively organised an overseas promotional meeting for UK health professionals.

The Panel noted that the average total cost of hospitality was approximately £449.40 per person plus economy airfares. The cost of the two evening meals in Croatia were £24.14 and £37.18 per head. The Panel noted Hospira's submission that it had not provided any subsistence on the night of Sunday, 12 July.

The hotel used was not appropriate. The Panel noted Hospira's submission that it understood that at the

time, the hotel was a four-star hotel and there was no longer nor at the time of the meeting a casino and the only complimentary guest facilities were a gym and swimming pool/spa. The hotel, however, was described in material provided by Hospira as 'the finest hotel in Zagreb' and that it was until recently a member of the 'Leading Hotels in the World'. The hotel was a 45 minute transfer from the manufacturing site; accommodation nearer to the manufacturer should have been used. In the Panel's view, the location and facilities were still more akin to leisure travel than business purposes and would have attracted delegates to attend. The Panel was very concerned that the venue had been chosen without further assessment of its acceptability in the context of UK requirements.

The Panel considered that whilst the subsistence alone had not been excessive, the total hospitality provided was out of proportion to the occasion (ie overseas location, the venue and three nights' accommodation). The total educational content was approximately 7 hours including three and a half hours for the advisory board for which three nights' accommodation was provided. The Panel noted its comments on the content of the meeting above. The Panel considered that hosting UK delegates for a two day promotional meeting in Croatia, in circumstances where the Panel did not consider that there was any clear and cogent reason for holding the meeting outside the UK was unacceptable in relation to the requirements of Clause 18.1 and an inducement to prescribe or recommend Hospira products. A breach of Clause 18.1 was ruled.

The Panel considered that, as it had ruled the arrangements did not meet the criteria for advisory boards, UK health professionals had been invited to attend a two day promotional meeting in Croatia, the primary objective of which appeared to be to increase their confidence in the manufacturing quality of Hospira products. The Panel noted its comments above and given the lack of a clear and cogent reason to hold the meeting outside the UK, ruled a breach of Clause 22.1.

The Panel noted the supplementary information to Clause 22.2, Maximum Cost of a Meal, which included that the maximum of £75 plus VAT and gratuities (or local equivalent) and that this would only be appropriate in very exceptional circumstances such as a dinner at a residential meeting for senior consultants or a learned society conference with substantial educational content. It also made it clear that the limit did not apply when a meeting was held outside UK in a European country where the national association was a member of EFPIA and thus covered by EFPIA Codes. In such circumstances the limits in the host country code would apply. The Panel noted the limits in the Croatian Code were relevant. The Panel noted the Croatian limit of HRK500 (£52) and that £24.14 and

£37.18 was spent per head for dinner (excluding tax and gratuities) on the two evening meals. This was in line with the local limit for a meal and therefore no breach of Clause 22.2 was ruled.

The Panel noted its criticisms of the meeting and rulings set out above and considered that high standards had not been maintained. A breach of Clause 9.1 was ruled.

The Panel was concerned to note that although the meeting (and materials) were approved and certified by Hospira at a European level against the principles of the EFPIA Healthcare Professional Code the meeting including the decision to take UK health professionals overseas and the majority of the materials were not reassessed and certified at a UK-specific level in accordance with the UK Code. The Panel was very concerned to note that the hotel used was selected by the Hospira UK team without further assessment of the acceptability of that hotel in the context of UK requirements. The Panel noted that overall the company had exercised poor governance in relation to the arrangements including the failure to issue contracts and failure to certify an overseas meeting for health professionals. In addition health professionals had been taken overseas without there being good and cogent reasons for so doing. This was compounded by the inclusion of an advisory board which failed to meet the requirements of the Code. The Panel noted that the supplementary information to Clause 2 stated that, *inter alia*, one activity likely to be in breach of Clause 2 was an inducement to prescribe. The Panel noted its comments above and its ruling of a breach of Clause 18.1 and thus considered that the overall arrangements including holding the meeting in question in Croatia was such as to bring discredit upon and reduce confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

The Panel was very concerned about the arrangements and the apparent lack of governance as set out above. Nonetheless, the Panel also noted that the meeting happened some seven and a half weeks before the company was acquired by Pfizer Inc and approximately nine months before Hospira joined the list of non member companies that have agreed to comply with the Code. In the exceptional circumstances of this case, and on balance, the Panel decided not to report Hospira to the Code of Practice Appeal Board for it to consider in accordance with Paragraph 8.2 of the Constitution and Procedure.

During its consideration of this matter the Panel requested that Hospira be reminded of the disclosure requirements as set out in the Code.

**Complaint received**                      **17 February 2016**

**Case completed**                              **5 July 2016**

# BAYER v DAIICHI-SANKYO

## Promotion of Lixiana

Bayer Healthcare complained about a Lixiana (edoxaban) leavepiece produced by Daiichi-Sankyo UK.

The detailed response from Daiichi Sankyo is given below.

Bayer alleged that the imagery of a crossed-out blood test machine with the claim 'No regular anticoagulation level monitoring required' was misleading, not capable of substantiation and was inconsistent with the SPC as the Lixiana SPC listed several circumstances in which regular monitoring of anticoagulation levels might be needed. It suggested there was no need for any blood-testing at all whereas in contrast to some other NOACs, patients on Lixiana were required to undergo renal and liver function tests. Bayer alleged that it put patient safety at risk by undermining rational use of the medicine. Bayer further alleged that the image itself was in breach of the Code and the associated claim was inconsistent with the SPC. High standards had not been maintained.

The Panel noted that the leavepiece, headed 'Simple and convenient for patients and prescribers' followed by 'New Once-Daily Lixiana Another Step Ahead', referred to the indication on page 1, gave efficacy information on page 2 and set out the dosing regimens on page 3. The statement 'Liver function testing and renal function (CrCl) assessment should be carried out prior to initiating Lixiana and afterwards when clinically indicated ...' appeared on page 3 and referred readers to the SPC for more guidance.

With regard to the graphic, the Panel noted that beneath the illustration the claim referred to anticoagulation monitoring rather than blood monitoring. It noted Daiichi-Sankyo's submission that the graphic resembled the devices recommended by NICE for anticoagulation and no such hand held device existed for renal/liver function testing. In the Panel's view the graphic with the line through it would not be read as implying no blood testing at all was required as alleged. The claim immediately beneath referred to anticoagulation. In the Panel's view the graphic in its context was not misleading, nor did it fail to promote rational use of the medicine and no breaches of the Code were ruled. The Panel did not agree that the graphic was inconsistent with the SPC or that Daiichi-Sankyo had failed to maintain high standards and no breaches of the Code were ruled.

Bayer further alleged that the claim 'No scheduled high-to-low dose transition at initiation in VTE [venous thromboembolism] patients' beneath a graphic of what appeared to be a calendar was misleading, not capable of substantiation and was

inconsistent with the SPC because it disregarded the requirement for high-dose parenteral anticoagulation for the first 5 days after initiation of venous thromboembolism (VTE) treatment, before Lixiana therapy could start. Bayer alleged that it encouraged the irrational use of Lixiana and thus Daiichi Sankyo had failed to maintain high standards.

The Panel noted that Lixiana required at least 5 days' treatment with parenteral anticoagulant before it could be used for treatment of DVT, PE or prevention of recurrent VTE. Bayer's product Xarelto did not need pre-treatment with another product. Its dosing regimen changed from 15mg twice daily (Day 1-21) to 20mg once-daily from Day 22 onwards. The Panel noted that page 2 of the leavepiece in relation to DVT or PE patients referred to 'following initial use of heparin for at least 5 days' and page 3 stated 'VTE patients should receive heparin for at least 5 days before initiating Lixiana'. Page 4 was headed 'once-daily Lixiana' and the claim at issue was preceded by a claim 'Consistent Lixiana dosing regimen across both NVAF and VTE indications'.

The Panel considered that the claim 'No scheduled high to low dose transition in initiation in VTE patients' was an accurate description of the dosing regimen for Lixiana once the patient had started treatment with that product. There was no mention on page 4 of the need for pre-treatment with heparin when prescribing for VTE patients. Whilst there was mention of such use on pages 2 and 3, the page and claim in question had to be capable of standing alone with regard to compliance with the Code. The Panel did not consider that the claim was sufficiently clear that VTE patients could only be given once-daily Lixiana after at least 5 days of treatment with heparin. The phrase 'initiation in VTE patients' could be read in two ways: the whole treatment for VTE or that part of the treatment of VTE when Lixiana was initiated. It was not clear. In the Panel's view the page implied that the use of Lixiana in patients with NVAF and VTE were similar and further that the only difference in treating VTE patients with Lixiana or other NOACs was that Lixiana was the only once-daily treatment at the same dose for the whole treatment period. The claim was misleading and a breach of the Code was ruled. The Panel considered that the misleading implication was not capable of substantiation and thus ruled a breach of the Code. The claim did not promote rational use of Lixiana, it was inconsistent with the SPC and the Panel ruled breaches of the Code. The Panel also ruled a breach of the Code as high standards had not been maintained.

Bayer noted the claim 'Superior reduction in major bleeding vs well-controlled warfarin' [NVAF population] and alleged that there was no evidence that the major-bleeding reduction vs warfarin

conferred by Lixiana was in any way 'superior' to the reduction vs warfarin that was conferred by any other NOAC. Use of the phrase 'superior reduction' rather than the more conventional 'significant reduction' was ambiguous and appeared to be a deliberate choice that implied that the reduction in bleeding versus warfarin seen with Lixiana was greater than the significant reduction in major bleeding observed in other trials with NOACs in the atrial fibrillation indication which was misleading, not capable of substantiation; implied that Lixiana had some special merit which could not be substantiated and was disparaging of Bayer's product Xarelto. 'Superior' was also alleged to be a hanging comparison.

Bayer alleged that similarly, the claim 'Superior reduction in clinically relevant bleeding vs well-controlled warfarin' [VTE population] was misleading and disparaging; it was not clear what 'superior' was compared to. 'Reduction' was versus warfarin but 'superior reduction' indicated that the reduction was greater than some other reduction, implying a head-to-head comparison where one did not exist.

The Panel did not consider that the description in the leavepiece 'Superior reduction' would necessarily be read in the statistical sense as submitted by Daiichi-Sankyo. No p number was given. The layout and context could imply that superior reduction in major bleeding was broader than a comparison between Lixiana and warfarin. This was due to the use of upper case for the claim 'SUPERIOR REDUCTION IN MAJOR BLEEDING' and that the claim was highlighted in green. The Panel accepted that the claim was qualified by 'Vs. well-controlled warfarin'. This appeared in smaller black type beneath and was not highlighted in green but was, nonetheless, sufficiently prominent to qualify the claim in question. The Panel considered that, on balance, the claim was not misleading or ambiguous as alleged as it did not claim that the difference between Lixiana and warfarin was superior to that seen with other NOACs. There was no mention of other NOACs on the page. The comparisons were all with warfarin. The Panel therefore ruled no breaches of the Code. The Panel did not consider that the claim disparaged Xarelto or was a hanging comparison. No breaches of the Code were ruled.

The Panel noted its ruling above and considered that the position was similar in relation to the VTE claims. The Panel therefore ruled no breaches of the Code.

Bayer further alleged that the claims 'Once-daily Lixiana is simple and convenient' and 'Once-daily Lixiana is simple and convenient for patients and prescribers' underplayed the inherent complexity and inconvenience of needing 5 days of injected low molecular weight heparin (LMWH) prior to being able to start Lixiana in the VTE population. Bayer alleged that the above claims were misleading, incapable of substantiation and 'simple' was contrary to the SPC.

The Panel agreed with both companies that Lixiana like other similar medicines was not necessarily

simple to use. It noted Daiichi-Sankyo's submission that it was the once-daily dose which meant that Lixiana was simple to use. Page 3 set out the dosing regimen 60mg once-daily (or 30mg once-daily when a reduced dose was needed) for eligible NVAF and VTE patients. This page also referred to the need for pre-treatment for VTE patients with heparin. Page 5 set out the dosing regimens for Lixiana, rivaroxaban, dabigatran and apixaban.

The Panel noted that treatment of eligible NVAF patients with Xarelto was also once-daily and the other two products dabigatran and apixaban were dosed twice daily in this indication.

In VTE Lixiana was once-daily (following heparin pre-treatment) whereas whilst there was no heparin pre-treatment with Xarelto or apixaban there was a dose transition from 15mg twice-daily for 3 weeks to 20mg once-daily for Xarelto and from 10mg twice-daily for 7 days to 5mg twice-daily for apixaban. Dabigatran was 150mg twice-daily after requiring heparin for at least 5 days.

The Panel considered that it was not unreasonable to claim that Lixiana's once-daily dosing regimen was simple and convenient including in VTE once treatment with Lixiana had commenced. The requirement to receive heparin for at least five days before initiating Lixiana in VTE patients was stated on pages 3 and 5. The Panel was concerned that on page 5 the requirement to receive heparin was only visible when, and if, the reader pulled a tab to reveal the VTE dosing regimens. However, on balance, the Panel did not consider that the claims as used on pages 3 and 5 were misleading as alleged, it was sufficiently clear that simple and convenient referred to once-daily dosing. The Panel ruled no breach of the Code. As such the claims at issue were capable of substantiation and therefore no breach of the Code was ruled. Lixiana was used for VTE patients once-daily after treatment with that product had commenced, ie after at least 5 days' treatment with heparin. The term 'simple' within the context of the claims in question and rulings of no breach of the Code above was not inconsistent with the SPC. The Panel thus ruled no breach of the Code.

Lastly Bayer alleged that a graph which compared Lixiana with rivaroxaban, dabigatran and apixaban in relation to dose and number of tablets for NVAF and VTE based on 30 days of treatment with a timescale from 0 to 6 months and the associated numerical claims for VTE were misleading, unsafe and defamatory to its product Xarelto. Calling the point of transition from LMWH to Lixiana 'time zero' was alleged to be misleading, unsafe and incompatible with the SPC. Time zero should be from the time of diagnosis/initiation of anticoagulation. Starting from the point of switch to Lixiana implied that the first 5 days of anticoagulation were not needed. This was essentially a 'suppressed zero' of the time axis, which specifically breached the Code. The omission of the first 5 days of injections furthermore downplayed the complexity, inconvenience and discomfort of using Lixiana relative to Xarelto which was pictured alongside and the comparison was alleged to be misleading and disparaging of Xarelto. Bayer had a further concern over the



choice of a 30-days' treatment horizon for the commercial comparison. The Lixiana SPC defined even 'short term treatment' as at least three months' duration. The choice of a 30-day treatment horizon was thus alleged to fail to promote rational prescribing in a manner contradictory to the SPC. In summary, the choice of 30 days was alleged to be inaccurate; misleading by comparison; visually misrepresentative; failed to promote rational use of any of the products; contrary to the SPC and was defamatory of Xarelto. Bayer alleged that overall this constituted a further failure to maintain high standards.

The Panel considered that the page was clear that time zero was the time of initiation of treatment with Lixiana and not when VTE was diagnosed and treatment commenced. The Panel did not accept that the first 5 days of injections had been omitted as alleged, the graph clearly referred to the need for treatment with heparin for Lixiana for VTE and thus it ruled no breaches of the Code in relation to Bayer's allegation that this omission downplayed the complexity, inconvenience and discomfort of using Lixiana compared to Xarelto. In that regard, Xarelto was not disparaged and no breach of the Code was ruled. The heading to the graph referred to the first 30 days of treatment with NOACs. The graph did not imply that pre-treatment with heparin was not necessary as alleged. The Panel ruled no breaches of the Code on this point. Nor did the Panel consider that there was a suppressed zero of the time axis as alleged; it was clear that the axis related to the start of treatment with a NOAC. No breach of the Code was ruled.

The Panel considered that it was misleading and unfair to compare dosing transition and pill burden for 30 days where Lixiana was indicated for at least 3 months ie 90 days. It was true that Lixiana had an advantage regarding the number of pills to be taken at either 30 days or 90 days but the difference at 90 days was less than at 30 days. When treating VTE there was an additional burden in that heparin for at least 5 days was also required to treat VTE. It was more complex to treat with heparin than with a tablet.

The Panel noted its comments about the 30 day treatment period above. The Panel considered the graph was misleading in relation to the 30 days and ruled a breach of the Code. The graph did not give a fair and balanced view of the pill burden and was ruled in breach of the Code. On balance, the Panel did not consider that the graph failed to promote rational prescribing as alleged and no breach of the Code was ruled.

The Panel considered that the 30-day treatment emphasis meant that rational prescribing had not been promoted as the leavepiece did not refer to the treatment with Lixiana as at least 3 months as set out in the SPC. The Panel ruled a breach of the Code as alleged. In this regard, the graph was inconsistent with the SPC and a breach of the Code was ruled.

The Panel noted its rulings above and considered that in relation to the graph Daiichi-Sankyo had not

**maintained high standards and a breach of the Code was ruled.**

Bayer Healthcare submitted a complaint about the promotion of Lixiana (edoxaban) by Daiichi-Sankyo UK Limited.

The material at issue (ref EDX/15/0090 June 2015) was a six-page gate-folded leavepiece used at the European Society of Cardiology meeting in London and which was for use by the sales team with health professionals either face-to-face or at meetings.

Lixiana was a novel oral anticoagulant (NOAC) for the prevention of stroke and systemic embolism in adults with non-valvular atrial fibrillation (NVAf) with one or more risk factors such as congestive heart failure (CHF), hypertension, over 75 years old, diabetes mellitus, prior stroke or transient ischaemic attack (TIA). It was also indicated for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and prevention of recurrent DVT and PE in adults.

The leavepiece was headed 'Simple and convenient for patients and prescribers' followed by 'New Once-Daily Lixiana (edoxaban) Another Step Ahead'. The indications were given beneath the heading.

Bayer marketed Xarelto (rivaroxaban) which was also a NOAC.

#### **1 Crossed-out image of a blood-test machine with the claim 'No regular anticoagulation level monitoring required'**

The claim appeared on page 4 which was headed 'Once-Daily Lixiana'. Five features of the product were illustrated with details of the feature below the illustration. The final graphic was of what appeared to be a hand held machine reading 2.8 with a line through it with the claim 'No regular anticoagulation level monitoring required' (referenced to the Lixiana summary of product characteristics (SPC)) beneath the graphic.

#### **COMPLAINT**

Bayer alleged that the use of the imagery of a crossed-out blood test machine was inappropriate for several reasons. Firstly, the Lixiana SPC listed several circumstances in which regular monitoring of anticoagulation levels might be needed. For instance, switching to or from a vitamin K antagonist (VKA); overdose; emergency surgery. The claim was alleged to be misleading in breach of Clause 7.2, not capable of substantiation in breach of Clause 7.4 and incompatible with the SPC in breach of Clause 3.2.

The prominent image of a crossed-out blood monitor was of particular concern as it suggested there was no need for any blood-testing at all – a *de facto* claim which was furthermore not qualified in any way by the text underneath which dealt only with anticoagulation monitoring. In contrast to some other NOACs, patients on Lixiana were required to undergo renal and liver function tests prior to initiation and periodically during treatment, as stated in Sections 4.2 and 4.4 of the Lixiana SPC.

Use of the graphic of a crossed-out blood monitor without mentioning the need for initial and regular liver and renal testing was alleged to be misleading in breach of Clause 7.2 in a way that put patient safety at risk through undermining rational use of the medicine in breach of Clause 7.10. The associated artwork was alleged to be in breach of Clause 7.8 and the *de facto* claim contrary to the label in breach of Clause 3.2. Furthermore, this cherry-picking of blood test information was an example of Daiichi-Sankyo putting commercially-favourable (but misleading) claims ahead of patient safety. Bayer alleged a failure to maintain high standards in breach of Clause 9.1.

## RESPONSE

Daiichi-Sankyo submitted that the imagery was appropriate in the context of the leavepiece. The graphic appeared on the fourth or fifth page of the leavepiece, on a summary page of the key features of edoxaban. It was not used in isolation in any other materials and should therefore be considered in the context of the leavepiece.

The graphic depicted a self-monitoring coagulometer international normalised ratio (INR) testing device, evidenced by the number '2.8' on the readout. Daiichi-Sankyo submitted that this type of device was becoming more and more common and had even been recommended by the National Institute for Health and Care Excellence (NICE).

The graphic very closely reassembled the devices that were in use and was not meant to mislead health professionals into believing that it represented a general blood test device. In addition, Daiichi-Sankyo UK submitted it had been very explicit with the wording 'No routine anticoagulation level monitoring required', as per the Lixiana SPC. The need to ascertain renal function and liver function prior to initiation of Lixiana was clearly stated on page 3 of the leavepiece. This 'dosing' page was discussed and agreed with the Medicines and Healthcare products Regulatory Agency (MHRA) as part of prevetting of materials. Finally, Daiichi-Sankyo UK had repeatedly pointed out to Bayer that the need to ascertain liver and renal function was common to all NOACs. Daiichi-Sankyo refuted breaches of Clauses 7.2, 7.4, 9.1 and 3.2.

In response to a request for further information, Daiichi-Sankyo submitted that the graphic representative of the device was meant to represent INR monitoring, a practice familiar to health professionals who managed patients on warfarin. While it was usually performed in a central laboratory, NICE (DG 14 2014) had issued recent guidance about the use of self-monitoring of INR by patients, two devices specifically, the Roche Coagucheck XS system and the InRatio 2 PT/INR. Daiichi-Sankyo submitted that the graphic closely resembled the devices that were recommended by NICE for use and there was no intention to claim that no other blood tests were required. The caption below the graphic clearly stated the reference to anticoagulation monitoring only.

No such handheld device existed for renal/liver function testing to Daiichi-Sankyo's knowledge and indeed there would not be a clinically relevant reason for a patient to self-test for those parameters. Monitoring of renal and liver function were part of the routine management of patients on anticoagulation (NICE CG 180) and would be performed on a regular basis by the physician via a central laboratory as part of the usual blood test panel via an automated instrument. An image of such a machine was provided which Daiichi-Sankyo submitted was unlikely to be confused with its graphic.

## PANEL RULING

The Panel noted that the leavepiece referred to the indication on page 1, gave efficacy information on page 2 and set out the dosing regimens on page 3. The statement 'Liver function testing and renal function (CrCl) assessment should be carried out prior to initiating Lixiana and afterwards when clinically indicated ....' appeared on page 3 and referred readers to the SPC for more guidance.

With regard to the graphic, the Panel noted that beneath the illustration the claim referred to anticoagulation monitoring rather than blood monitoring. It noted Daiichi-Sankyo's submission that the graphic resembled the devices recommended by NICE for anticoagulation and no such hand held device existed for renal/liver function testing. In the Panel's view the graphic with the line through it would not be read as implying no blood testing at all was required as alleged. The claim immediately beneath referred to anticoagulation. In the Panel's view the graphic in its context was not misleading, nor did it fail to promote rational use of the medicine. No breach of Clauses 7.2 and 7.10 was ruled and thus no breach of Clause 7.8 was also ruled.

The Panel did not agree that the graphic was inconsistent with the SPC and thus ruled no breach of Clause 3.2. Daiichi-Sankyo had not failed to maintain high standards as alleged and the Panel ruled no breach of Clause 9.1.

## 2 Claim 'No scheduled high-to-low dose transition at initiation in VTE [venous thromboembolism] patients'

The claim appeared on page 4 beneath a graphic of what appeared to be a calendar.

## COMPLAINT

Bayer alleged that this claim was deceptive and contrary to the label, because it disregarded the requirement for high-dose parenteral anticoagulation for the first 5 days after initiation of venous thromboembolism (VTE) treatment, before Lixiana therapy could start. In fact, what was required after initiation in VTE patients was far more than just a change in dose – a whole change of medicine class and mode as well as route of delivery was necessary. Bayer alleged that this claim was misleading in breach of Clause 7.2; not capable of substantiation

in breach of Clause 7.4 and contrary to the SPC, in breach of Clause 3.2 in a way that encouraged wrong and unsafe use of Lixiana in breach of Clause 7.10. Bayer alleged that the clear failure to maintain high standards was in breach of Clause 9.1.

## RESPONSE

Daiichi-Sankyo UK stated that the claim accurately reflected the posology of Lixiana for patients being treated for a VTE event ie at initiation with Lixiana, the selected dose did not need to be routinely altered. This was in contrast to eg rivaroxaban which required 21 days of an initial regimen of twice a day 15mg tablets followed by once a day 20mg (or 15mg depending on risk of bleeding) or apixaban (Eliquis, Bristol Myers Squibb product) which required an initial week course of two 5mg tablets twice a day, followed by one 5mg tablet twice a day for 6 months then one 2.5mg tablet twice a day.

Lixiana was the third factor Xa inhibitor to market and Daiichi-Sankyo wanted to ensure that this need for dose transition at initiation was not applied to patients on Lixiana as this would result in patients being under dosed and potentially put at risk of recurrent events. Daiichi-Sankyo denied that the need for a heparin lead-in was hidden. The need for a heparin lead-in was mentioned in four instances in the leavepiece. Daiichi-Sankyo refuted breaches of Clauses 3.2, 7.2, 7.4, 7.10 and 9.1.

## PANEL RULING

The Panel noted that Lixiana required at least 5 days' treatment with parenteral anticoagulant before it could be used for treatment of DVT, PE or prevention of recurrent VTE.

Bayer's product Xarelto did not need pre-treatment with another product. Its dosing regimen changed from 15mg twice daily (Day 1-21) to 20mg once-daily from Day 22 onwards.

The Panel noted that page 2 of the leavepiece in relation to DVT or PE patients referred to 'following initial use of heparin for at least 5 days' and page 3 stated 'VTE patients should receive heparin for at least 5 days before initiating Lixiana'.

Page 4 was headed 'once-daily Lixiana' and the claim at issue was preceded by a claim 'Consistent Lixiana dosing regimen across both NVAf and VTE indications'.

The Panel considered that the claim 'No scheduled high to low dose transition in initiation in VTE patients' was an accurate description of the dosing regimen for Lixiana once the patient had started treatment with that product. There was no mention on page 4 of the need for pre-treatment with heparin when prescribing for VTE patients. Whilst there was mention of such use on pages 2 and 3, the page and claim in question had to be capable of standing alone with regard to compliance with the Code. The Panel did not consider that the claim was sufficiently clear that VTE patients could only be given once-

daily Lixiana after at least 5 days of treatment with heparin. The phrase 'initiation in VTE patients' could be read in two ways: the whole treatment for VTE or that part of the treatment of VTE when Lixiana was initiated. It was not clear. In the Panel's view the page implied that the use of Lixiana in patients with NVAf and VTE were similar and further that the only difference in treating VTE patients with Lixiana or other NOACs was that Lixiana was the only once-daily treatment at the same dose for the whole treatment period. The claim was misleading and a breach of Clause 7.2 was ruled. The Panel considered that the misleading implication was not capable of substantiation and thus ruled a breach of Clause 7.4. The claim did not promote rational use of Lixiana and a breach of Clause 7.10 was ruled. It was inconsistent with the SPC and thus a breach of Clause 3.2 was ruled. Given its rulings above the Panel also ruled a breach of Clause 9.1 as high standards had not been maintained.

## 3 Claim 'Superior reduction in major bleeding vs well-controlled warfarin' [NVAf population]

The claim appeared on the left-hand side of page 2 beneath the heading 'For your patients with NVAf:' which was followed by 'Proven Efficacy' and 'Comparable to well-controlled warfarin in the prevention of stroke/SEE' [systemic embolic events]. Then followed the claim at issue 'Superior reduction in major bleeding' and 'Vs. well-controlled warfarin'. The page was designed such that 'Proven Efficacy' and 'Superior Reduction in major bleeding' were in upper case and highlighted in green. These claims were followed by 'Comparable to well-controlled warfarin in the prevention of stroke/SEE' and 'Vs. well-controlled warfarin' in smaller black type (with no highlighting) beneath each respectively.

## COMPLAINT

Bayer stated that this claim used in the leavepiece also appeared on the promotional stand. The company alleged there was no evidence that the major-bleeding reduction vs warfarin conferred by Lixiana was in any way 'superior' to the reduction vs warfarin that was conferred by any other NOAC. The use of the phrase 'superior reduction' rather than the more conventional 'significant reduction' was ambiguous and appeared to be a deliberate choice that implied that the reduction in bleeding versus warfarin seen with Lixiana was greater than the significant reduction in major bleeding observed in other trials with NOACs in the atrial fibrillation indication. Bayer alleged that this claim was therefore misleading in breach of Clause 7.2, not capable of substantiation in breach of Clause 7.4; implied that Lixiana had some special merit which could not be substantiated in breach of Clause 7.10 and was disparaging of Bayer's product Xarelto in breach of Clause 8.1. 'Superior' was also alleged to be technically a hanging comparison in breach of Clause 7.2.

## RESPONSE

Daiichi-Sankyo stated that the claims in points 4 and 5 (below) were very specific to the comparison of

Lixiana to warfarin and used the term 'superior' in its statistical sense. The claims referred to the primary safety endpoint of the registration trials of Lixiana and in both, Lixiana was superior to well-controlled warfarin at reducing the primary safety endpoint, with a very high degree of statistical significance (p=0.0009 for ENGAGE-AF trial and p=0.004 for HOKUS AI trial). No comparison to other NOACs was implied or intended.

At the face-to-face meeting, Bayer agreed that the claim 'Superior to well-controlled warfarin at reducing major/clinically relevant bleeding' would be acceptable. However, Daiichi-Sankyo decided against changing the claim as this would imply that the original claim was misleading. Daiichi-Sankyo stood by the original phrase. Daiichi-Sankyo refuted breaches of Clauses 7.2, 7.4, 7.10 and 8.1.

#### PANEL RULING

The Panel did not consider that the description 'Superior reduction' would necessarily be read in the statistical sense as submitted by Daiichi-Sankyo. No p number was given. The layout and context could imply that superior reduction in major bleeding was broader than a comparison between Lixiana and warfarin. This was due to the use of upper case for the claim 'SUPERIOR REDUCTION IN MAJOR BLEEDING' and that the claim was highlighted in green. The Panel accepted that the claim was qualified by 'Vs. well-controlled warfarin'. This appeared in smaller black type beneath and was not highlighted in green but was, nonetheless, sufficiently prominent to qualify the claim in question. The Panel considered that, on balance, the claim was not misleading or ambiguous as alleged as it did not claim that the difference between Lixiana and warfarin was superior to that seen with other NOACs. There was no mention of other NOACs on page 2. The comparisons were all with warfarin. The Panel therefore ruled no breach of Clauses 7.2 and 7.4. The Panel also ruled no breach of Clause 7.10. The Panel did not consider the claim disparaged Xarelto as alleged and no breach of Clause 8.1 was ruled. Nor did the Panel consider the claim was a hanging comparison. No breach of Clause 7.2 was ruled in this regard.

#### 4 Claim 'Superior reduction in clinically relevant bleeding vs well-controlled warfarin' [VTE population]

The claim appeared on the right-hand side of page 2 beneath the heading 'For your patients with DVT or PE, following initial use of heparin for at least 5 days:' which was followed by 'Proven Efficacy' and 'Comparable to well-controlled warfarin in the treatment and prevention of recurrent VTE events'. Then followed the claim at issue 'Superior reduction in clinically relevant bleeding and 'Vs. well-controlled warfarin'. The claim at issue was referenced to the Hokusai-VTE Investigators 2013.

The page was designed such that 'Proven Efficacy' and 'Superior Reduction in clinically relevant bleeding' were in upper case and highlighted in blue. These claims were followed by 'Comparable to well-

controlled warfarin in the treatment and prevention of recurrent VTE events' and 'Vs. well-controlled warfarin' in smaller black type with no highlighting beneath each respectively.

#### COMPLAINT

Bayer alleged that similar to point 3 above, this claim was disparaging in breach of Clauses 7.2, 7.4, 7.9, 7.10 and 8.1. It was not clear what 'superior' was compared to. 'Reduction' was versus warfarin but 'superior reduction' indicated that the reduction was greater than some other reduction, implying a head-to-head comparison where one did not exist.

#### RESPONSE

Daiichi-Sankyo made no separate submission for this point which it covered in point 3 above.

#### PANEL RULING

The Panel noted its ruling in point 3 above and considered that the position was similar in relation to the VTE claims. The Panel considered that, on balance, the claim 'SUPERIOR REDUCTION IN CLINICALLY RELEVANT BLEEDING' was not misleading or ambiguous as alleged as it did not claim that the difference between Lixiana and warfarin was superior to that seen with other NOACs. The claim 'Vs. well-controlled warfarin' was sufficiently prominent to qualify the claim in question. There was no mention of other NOACs on page 2. The comparisons were all with warfarin. The Panel therefore ruled no breach of Clauses 7.2 and 7.4. The Panel also ruled no breach of Clauses 7.9 and 7.10. The Panel did not consider the claim disparaged Xarelto as alleged and no breach of Clause 8.1 was ruled. Nor did the Panel consider the claim was a hanging comparison. No breach of Clause 7.2 was ruled in this regard.

#### 5 Claims 'Once-daily Lixiana is simple and convenient' and 'Once-daily Lixiana is simple and convenient for patients and prescribers'

The claim 'Once daily Lixiana is simple and convenient' appeared as the heading to page 5 which included a table showing dosing transitions and pill burden (further details appear in Point 7 below).

The claim 'Once daily Lixiana is simple and convenient for patients and prescribers' appeared as the heading to page 3 which set out the dosing regimens for NVAf and VTE and included 'VTE patients should receive heparin for least 5 days before initiating Lixiana'.

#### COMPLAINT

Bayer alleged that these claims underplayed the inherent complexity and inconvenience of needing 5 days of injected low molecular weight heparin (LMWH) prior to being able to start Lixiana in the VTE population. Many patients were likely to need nurse home visits or to attend clinic in order for this to be possible, or else to be trained on how to self-administer an injection. It was therefore clearly

not justified to suggest this was 'simple' for anyone concerned. The choice of Lixiana dosing was alleged to be far from simple. Multiple factors impacted on dose selection, so much so that a 15mg tablet had to be made commercially available to facilitate dosing transitions despite this dose not being licensed in isolation *per se*. Bayer alleged that Lixiana was not 'simple and convenient' for the patient or the prescriber, and both of the claims were therefore misleading in breach of Clause 7.2 and not capable of substantiation in breach of Clause 7.4. Furthermore, 'simple' was contrary to the SPC in breach of Clause 3.2.

## RESPONSE

Daiichi-Sankyo noted that Bayer only referred to the VTE indication for Lixiana as the need for a heparin lead-in did not apply to NVAF patients. Indeed, Bayer had successfully argued the use of the phrase 'one tablet, once daily, simple' in Case AUTH/2537/10/12.

As in that case, the phrase applied to the dosing regimen of Lixiana. On the front of the leavepiece, the claim was followed prominently by 'New ONCE-DAILY Lixiana'. The claim 'Once-daily Lixiana is simple and convenient for patients and prescribers' was on the dosing page. There was no indication generally that Lixiana was simple to use.

The posology of Lixiana was identical regardless of whether the patient was being treated for a VTE event or for prevention of stroke in NVAF. The other factor Xa inhibitors had different posologies depending on their indication.

With regard to Bayer's view that the use of LMWH was inherently complex and inconvenient, Daiichi-Sankyo noted that, like warfarin, heparin and LMWH had been on the market for decades and that their use in hospitals was routine, even mandated as prophylaxis for VTE events. Their use was still recommended in current guidelines (NICE CG92, SIGN 122, NICE TA 354, ESC PE guidelines 2014). Therefore, Daiichi-Sankyo did not shy away from the need for a heparin lead in prior to initiation of Lixiana and this was reiterated four times in the leavepiece. In those patients who had received heparin already, the decision to transition to Lixiana was made simple by the fact there was no further dose transition at initiation unlike other factor Xa inhibitors which required between one week and three weeks of a high dose treatment before reducing to another dose. As stated above, it was important that health professionals realised this difference as they might be under the impression that a similar transition was required for patients started on Lixiana.

The dosing criteria for the most commonly prescribed LMWH such as enoxaparin or dalteparin required a similar dosing adjustment according to body weight and renal function, meaning that these factors would already be known to the prescriber when initiating Lixiana. Given the need for at least 5 days of heparin lead-in, Daiichi-Sankyo was aware that patients initiated on Lixiana would be those who were likely to have

been hospitalised for more severe VTE events such as pulmonary embolism or extensive deep vein thrombosis. These patients were therefore in a hospital environment where the use of heparin was routine.

As for the availability of the 15mg tablet of Lixiana to temporarily protect patients should they need to transition back to warfarin from a 30mg daily dose of Lixiana, Bayer was aware that this regulatory requirement was as a result of the findings at the end of other NOAC trials where patients on the NOAC experienced a nearly 4-fold events increase in stroke and major bleeding due to the period of lack of anticoagulation as patients transitioned to warfarin. (HR 3.72,  $p=0.004$  Actual rate increase 4.7 per 100 Pt-Y for stroke and HR 3.62,  $p=0.0026$  Actual rate increase 5.19 per 100 Pt-Y for major bleeding). Similar increases in events were noted at the end of the apixaban trial. There were no excess of events at the end of the edoxaban ENGAGE-AF study as a result of this transition strategy. None of the other NOACs had a dose licensed to protect patients should they need to transition back to warfarin.

Daiichi-Sankyo always made the statement 'simple and convenient ...' in the context of the once-daily dosing of Lixiana, reflective of the posology of Lixiana. Daiichi-Sankyo refuted breaches of Clauses 3.2, 7.2 and 7.4.

## PANEL RULING

The Panel noted that the claim 'Simple and convenient for patients and prescribers' appeared as a banner claim at the top of page 1. This appeared to be contrary to Daiichi-Sankyo's submission that 'simple and convenient' was always in the context of once-daily dosing. The claim was followed by 'New once-daily Lixiana (edoxaban) another step ahead'. The second claim was in larger type size than the first claim. Nevertheless there was a claim that Lixiana was simple to use. However, Bayer had not complained about the claim 'Simple and convenient for patients and prescribers'.

The Panel agreed with both companies that Lixiana like other similar medicines was not necessarily simple to use. It noted Daiichi-Sankyo's submission that it was the once-daily dose which meant that Lixiana was simple to use. Page 3 set out the dosing regimen 60mg once-daily (or 30mg once-daily when a reduced dose was needed) for eligible NVAF and VTE patients. This page also referred to the need for pre-treatment for VTE patients with heparin. Page 5 set out the dosing regimens for Lixiana, rivaroxaban, dabigatran and apixaban.

The Panel noted that treatment of eligible NVAF patients with Xarelto was also once-daily and the other two products dabigatran and apixaban were dosed twice daily in this indication.

In VTE Lixiana was once-daily (following heparin pre-treatment) whereas whilst there was no heparin pre-treatment with Xarelto or apixaban there was a dose transition from 15mg twice-daily for 3 weeks to 20mg once-daily for Xarelto and from 10mg twice-daily for

7 days to 5mg twice-daily for apixaban. Dabigatran was 150mg twice-daily after requiring heparin for at least 5 days.

The Panel considered that it was not unreasonable to claim that Lixiana's once-daily dosing regimen was simple and convenient including in VTE once treatment with Lixiana had commenced. The requirement to receive heparin for at least five days before initiating Lixiana in VTE patients was stated on pages 3 and 5. The Panel was concerned that on page 5 the requirement to receive heparin was only visible when, and if, the reader pulled a tab to reveal the VTE dosing regimens. However, on balance, the Panel did not consider that the claims as used on pages 3 and 5 were misleading as alleged, it was sufficiently clear that simple and convenient referred to once-daily dosing. The Panel ruled no breach of Clause 7.2. As such the claims at issue were capable of substantiation and therefore no breach of Clause 7.4 was ruled. Lixiana was used for VTE patients' once-daily after treatment with that product had commenced, ie after at least 5 days' treatment with heparin. The term 'simple' within the context of the claims in question and rulings of no breach of the Code above was not inconsistent with the SPC. The Panel thus ruled no breach of Clause 3.2.

#### **6 Claim and graphic 'Dosing transitions and pill burden in the first 30 days' [VTE]**

Page 5 of the leavepiece was headed 'Once-daily Lixiana is simple and convenient' which was followed by 'Dosing transitions and pill burden in the first 30 days of treatment with NOACs for NVAf and VTE'. This was a heading to a graph which compared Lixiana with rivaroxaban, dabigatran and apixaban in relation to dose and number of tablets for NVAf and VTE based on 30 days of treatment. The timescale was from 0 to 6 months. The graphic included dotted lines at 30 days. The pill burden for VTE in the first 30 days of treatment was 30 for Lixiana (60 or 30mg once-daily after  $\geq 5$  days of heparin use. Rivaroxaban showed a pill burden of 51, 15mg twice daily for 3 weeks and 20mg (or 15mg) once-daily). Dabigatran was 60 at 150mg or 110mg twice-daily after  $\geq 5$  days of heparin use. The pill burden for apixaban was 74. Two x 5mg twice-daily for 7 days followed by 5mg (or 2.5mg) twice-daily followed by 2.5mg twice-daily for prevention.

The page included a tab which when pushed up changed the graphic from a comparison of the pill burden in NVAf to VTE.

#### **COMPLAINT**

Bayer alleged that the artwork and numerical claims for VTE were misleading, unsafe and defamatory to its product Xarelto. Calling the point of transition from LMWH to Lixiana 'time zero' was alleged to be misleading and misrepresentative. Time zero should be from the time of diagnosis/initiation of anticoagulation. Starting from the point of switch to Lixiana implied that the first 5 days of anticoagulation were not needed, which was alleged to be misleading in breach of Clause 7.2, unsafe in breach of Clause 7.10 and incompatible with the

SPC in breach of Clause 3.2. This was essentially a 'suppressed zero' of the time axis, which specifically breached Clause 7.8. The omission of the first 5 days of injections furthermore downplayed the complexity, inconvenience and discomfort of using Lixiana relative to Xarelto which was pictured alongside. This comparison was thus alleged to be misleading in breach of Clause 7.3, visually non-representative in breach of Clause 7.8 and disparaging of Xarelto in breach of Clause 8.1. Bayer had a further concern over the choice of a 30-days' treatment horizon for the commercial comparison. The Lixiana SPC defined even 'short term treatment' as at least three months' duration. The choice of a 30-day treatment horizon was alleged to thus fail to promote rational prescribing in breach of Clause 7.10 in a manner contradictory to the SPC in breach of Clause 3.2.

Bayer alleged that this clinically-incongruent choice of a 30-day treatment horizon was made in order to exaggerate the difference in pill burden vs other NOACs. Use of a 30 day cut-off made Xarelto appeared to have a pill burden 1.7x heavier than Lixiana (30 vs 51 tablets). In fact, over the minimum recommended treatment span of 90 days, the actual difference was only 1.22x (90 vs 111 tablets), which would be further off-set by the additional 5-10 injections needed for Lixiana had this been honestly represented in the graphic. In summary, the choice of 30 days was alleged to be inaccurate in breach of Clause 7.2; misleading by comparison in breach of Clause 7.3; visually misrepresentative in breach of Clause 7.8; failed to promote rational use of any of the products in breach of Clause 7.10; contrary to the SPC in breach of Clause 3.2 and was defamatory of Xarelto in breach of Clause 8.1. Bayer alleged that overall this constituted a further failure to maintain high standards in breach of Clause 9.1.

#### **RESPONSE**

Daiichi-Sankyo submitted that the 30 day pill count remained an important time point for both patients and prescribers when making their choice from the four available NOACs.

At around the 30 day mark, patients typically renewed their prescription. Indeed, some hospitals would provide the initial treatment pack to cover the first month especially for those with complicated regimes.

Studies tracking adherence in the area of anticoagulation as well as other chronic cardiovascular conditions showed a drop-off after the first 30 days. In various studies, treatment frequency and regimen complexity had been shown to have a significant impact on adherence/compliance. An example (Ingersoll *et al* 2008) was provided.

Daiichi-Sankyo submitted that Bayer had presented data showing patterns of use following initiation of rivaroxaban at its ESC satellite symposium (Monday, 31 August 2015) pointing to more relevant VTE persistence data. It could be seen from all the persistence curves that at 30 days, there was a consistent drop in adherence. Daiichi-Sankyo

provided graphs comparing rivaroxaban vs warfarin, NOAC vs VKA and rivaroxaban vs dabigatran for various indications.

As for the time horizon, Daiichi-Sankyo submitted that this was the most fair 'time zero' and clarified at the top of the graphic that the numbers referred to days of NOAC treatment. Had it included the heparin lead-in, the tablet count for 30 days of treatment would be 25 days or less. Instead it made the need for 5 or more days of heparin abundantly clear in the graphic itself as well as in three other instances in the leavepiece.

Daiichi-Sankyo submitted it represented the pill count accurately for each NOAC as per the SPCs at clinically relevant time points, not omitting the need for a heparin lead-in and had not disparaged or defamed Xarelto. Daiichi-Sankyo refuted breaches of Clauses 3.2, 7.2, 7.8 and 8.1.

### **PANEL RULING**

The Panel considered that the page was clear that time zero was the time of initiation of treatment with Lixiana and not when VTE was diagnosed and treatment commenced. The Panel did not accept that the first 5 days of injections had been omitted as alleged, the graph clearly referred to the need for treatment with heparin for Lixiana for VTE and thus it ruled no breach of Clauses 7.3 and 7.8 in relation to Bayer's allegation that this omission downplayed the complexity, inconvenience and discomfort of using Lixiana compared to Xarelto. In that regard, Xarelto was not disparaged and no breach of Clause 8.1 was ruled. The heading to the graph referred to the first 30 days of treatment with NOACs. The graph did not imply that pre-treatment with heparin was not necessary as alleged. The Panel ruled no breach of Clause 7.2 on this point. The Panel consequently ruled no breach of Clauses 7.10 and 3.2 on this point. Nor did the Panel consider that there was a suppressed zero of the time axis as alleged; it was clear that the axis related to the start of treatment with a NOAC. No breach of Clause 7.8 was ruled.

The Panel examined the page in question. It considered that it was misleading and unfair to compare dosing transition and pill burden for 30 days where Lixiana was indicated for at least 3 months ie 90 days, the Lixiana SPC referred to a minimum treatment period of at least 3 months, ie 90 days. It was true that Lixiana had an advantage regarding the number of pills to be taken at either 30 days or 90 days but the difference at 90 days was less than at 30 days. When treating VTE there was an additional burden in that heparin for at least 5 days was also required to treat VTE. It was more complex to treat with heparin than with a tablet.

The Panel noted its comments about the 30 day treatment period above. The Panel considered the graph was misleading in relation to the 30 days and ruled a breach of Clause 7.2. The graph did not give a fair and balanced view of the pill burden and was ruled in breach of Clause 7.8. On balance, the Panel did not consider that the graph failed to promote rational prescribing as alleged and no breach of Clause 7.10 was ruled.

The Panel considered that the 30-day treatment emphasis meant that rational prescribing had not been promoted as the leavepiece did not refer to the treatment with Lixiana as at least 3 months as set out in the SPC. The Panel ruled a breach of Clause 7.10 as alleged. In this regard, the graph was inconsistent with the SPC and a breach of Clause 3.2 was ruled.

The Panel noted its rulings above and considered that in relation to the graph Daiichi-Sankyo had not maintained high standards and a breach of Clause 9.1 was ruled.

**Complaint received**                      **23 February 2016**

**Case completed**                              **16 May 2016**

# VOLUNTARY ADMISSION BY BAXTER

## Failure to sit the examination for representatives within one year

**Baxter Healthcare voluntary admitted that one of its representatives had not taken the required examinations within one year of commencing his/her role.**

**In accordance with Paragraph 5.6 of the Constitution and Procedure, the Director treated the matter as a complaint.**

**Baxter explained that a review of its training database showed that one of its representatives had failed to take all of the modules of the appropriate representatives' examination within one year of commencing his/her role. The human resources (HR) administrator was unaware that examinations, although scheduled to be taken within the first year, had not been sat and so was unable to request an extension in time. The representative in question had booked further examination sittings and aimed to complete the qualification before the two year deadline.**

**The detailed response from Baxter is given below.**

**The Panel noted that the Code required that representatives take an appropriate examination within the first year of their employment as a representative and pass it within two years of starting such employment. The Panel noted that the representative in question had not taken the examination within his/her first year.**

**The Panel noted that the representative had sat and failed the elective modules within his/her first year and had booked but postponed, and therefore not sat, the compulsory modules within that year. The representative was scheduled to take the examinations (elective and compulsory modules) some 16-17 months after starting his/her employment but had resigned prior to taking them. The requirements of the Code had not been met as acknowledged by Baxter and the Panel ruled a breach of the Code.**

Baxter Healthcare voluntary admitted that one of its representatives had not taken the required examinations within one year of commencing his/her role.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Baxter.

### VOLUNTARY ADMISSION

Baxter stated that during a review of its training database, it found that one of its representatives had not taken all of the examinations for the ABPI representatives' qualification within one year of commencing the role. Baxter acknowledged a breach of Clause 16.3.

Baxter explained that the process used to monitor adherence to the training requirements relied on good communication between human resources (HR) and individual representatives. In this case, the HR administrator was aware that examinations had been scheduled prior to the representative's one year anniversary but was not informed that he/she had not taken them and was therefore not able to request an extension in time.

The tracking system proved to be highly effective in the past and this was the first time it had failed. Baxter stated that it would be taking steps to amend the process to reduce the likelihood of a recurrence.

In addition to being in breach of the Code, failure to attempt all modules of the representative's training within one year of commencing a sales role was in breach of the contract between Baxter and its representatives and the matter was being addressed.

Baxter understood that the representative in question had booked further examination sittings and aimed to complete the qualification before the two year deadline.

Baxter was asked to provide the PMCPA with any further comments in relation to the requirements of Clause 16.3.

### RESPONSE

Baxter provided a timeline of the representative's start date and attempts, bookings and postponements of the examination over the subsequent eighteen month period.

Baxter submitted that before and after each scheduled examination session, all candidates were emailed by HR; Baxter's manual examination tracker relied upon regular communication between the representatives and HR.

The representative did not respond to an HR email in November 2015, which requested an update on progress. Further follow-up in January 2016 elicited a response that he/she had not sat the compulsory module examinations and had rescheduled them for May 2016. Baxter submitted that had the representative responded to the November email, it would have had sufficient time to request an extension.

Baxter considered that the representative's personal reasons for postponement were reasonable grounds for postponement but not for the failure to advise HR which was a contractual requirement.

Baxter noted that the representative had planned to re-sit the elective module examinations in March



and the compulsory module examinations in May. However, he/she had subsequently resigned.

**PANEL RULING**

The Panel noted that Clause 16.3 stated that representatives must take an appropriate examination within the first year of their employment as a representative and pass it within two years of starting such employment. The Panel noted that the representative in question commenced employment in November 2014 and thus ought to have taken the examination by no later than November 2015.

The Panel noted that the representative in question had sat and failed the elective modules within his/her first year and had booked but postponed, and therefore not sat, the compulsory modules in November 2015. The representative was scheduled to take the examinations (elective and compulsory modules) by May 2016 but had resigned before taking the examinations. The requirements of Clause 16.3 had not been met as acknowledged by Baxter and the Panel ruled a breach of that Clause.

**Complaint received            4 April 2016**

**Case completed                27 April 2016**

# ALK-ABELLÓ v BAUSCH & LOMB

## Breach of undertaking

ALK-Abelló alleged that Bausch & Lomb had breached its undertaking given in Case AUTH/2802/11/15 for a second time.

ALK-Abelló stated that the material at issue was a presentation given by Bausch & Lomb to an allergy group in March 2016. The meeting was sponsored by Bausch & Lomb. A copy of the agenda was provided.

As the complaint concerned an alleged breach of undertaking it was taken up by the Authority in the name of the Director as the Authority was responsible for ensuring compliance with undertakings.

The detailed response from Bausch & Lomb is given below.

The Panel noted that a form of undertaking and assurance was an important document. Companies had to give an undertaking that the material in question and any similar material, if not already discontinued or no longer in use would cease forthwith and give an assurance that all possible steps would be taken to avoid similar breaches of the Code in the future. It was very important for the reputation of the industry that companies complied with undertakings.

The Panel noted that in Case AUTH/2802/11/15 ALK-Abelló had complained in November 2015 that the claim 'Emerade offers a new higher dose ...', which appeared in a Pulse Quick Guide, implied that a new higher dose of Emerade had been launched within the last 12 months. The Panel noted that this was not so. The Emerade 500mcg summary of product characteristics (SPC) stated that the date of the first marketing authorization/renewal of authorization was 3 January 2013. A breach of the Code was ruled which was accepted by Bausch & Lomb; the company's undertaking, signed in December 2015, stated that September 2015 was the last date the material was used or appeared.

In Case AUTH/2817/12/15, ALK-Abelló complained in December 2015 that Emerade continued to be described as 'new' on the product website. The Panel considered that Bausch & Lomb had failed to comply with its undertaking given in Case AUTH/2802/11/15 and breaches of the Code were ruled.

Turning to the case now before it, Case AUTH/2833/4/16, the Panel noted that a consultant had presented an update on adrenaline auto injectors at a third party meeting. One of the presentation slides was headed 'New Design' above a picture of Emerade 500mcg. The Panel noted Bausch & Lomb's submission that it had no knowledge of the meeting nor of the involvement of the consultant. The consultant was not authorized

by Bausch & Lomb to carry out field based activities and had been restricted to non-field based activities.

The Panel noted that the agenda which had been distributed to delegates stated that the consultant was from Bausch & Lomb and that 'You are all invited for complementary drinks immediately following the meeting, sponsored by Bausch and Lomb'. The meeting chair confirmed that prior to the meeting, but after the agenda had been circulated, the consultant had contacted him/her and confirmed that he/she was attending and presenting in a personal capacity. The consultant asked the chair to announce that his/her presentation and invitation for drinks afterwards was a personal one and not sponsored by Bausch & Lomb. The chairman stated that this had been done at the beginning and end of the presentation. In addition Bausch & Lomb provided a copy of an email from the consultant which stated that he/she had reiterated the chair's explanation before speaking. The Panel was not provided with a copy of the invitation to the meeting.

The consultant's explanation of the arrangements appeared to be inconsistent with the agenda. The consultant explained that he/she was invited to present on how current prescription regulations during medical emergencies could be interpreted which was subsequently extended to include the history and background of adrenaline auto-injector (AAI) design when another speaker did not attend. It was unclear when the previous speaker pulled out of the meeting, however this person's details did not appear on the agenda.

The Panel considered that it should have been possible to circulate a new agenda by email prior to the meeting and also at the meeting itself to make the position clear. ALK-Abelló did not refer to the change in arrangements. In addition it was apparent that the consultant had ample opportunity to raise this matter earlier than the day before the meeting when he/she saw the agenda.

Attendees at the meeting had been provided with material which did not comply with the Code. The question to be considered was whether Bausch & Lomb was responsible under the Code when the presenter, who was a consultant for Bausch & Lomb, was apparently acting in contravention of instructions from the company. The Panel considered that given there was a consultancy agreement between the parties at the time of the meeting and the impression given by the agenda and slides, Bausch & Lomb was responsible for the consultant's actions. The statement from the chair was insufficient to alter the company's responsibility in this regard. One of the slides referred to Emerade's 'New design'. The meeting was held after Bausch & Lomb had given its undertakings

**in Cases AUTH/2802/11/15 and AUTH/2817/12/15. Thus there had been a failure to comply with those undertakings. High standards had not been maintained. Breaches of the Code were ruled. The Panel noted its concerns about the clarity of the instructions given to the consultant but nonetheless considered that overall the company had been very badly let down by its consultant. The company had attempted to restrict the consultant's activities. The Panel noted the importance of complying with undertakings and that it had ruled that high standards had not been maintained. The Panel considered that in the exceptional circumstances of this case and on balance, Bausch & Lomb's failure to comply with its undertakings did not warrant a ruling of a breach of Clause 2 and thus no breach of that clause was ruled.**

ALK-Abelló Ltd alleged that Bausch & Lomb had breached its undertaking given in Case AUTH/2802/11/15 for a second time.

Case AUTH/2802/11/15 (ALK-Abelló v Bausch & Lomb) concerned the use of the word 'new' to describe Emerade (adrenaline auto-injector [AAI]) when the product had been available for more than 12 months. A breach of the Code was ruled which was accepted by Bausch & Lomb. Case AUTH/2817/12/15 (ALK-Abelló/Director v Bausch & Lomb) concerned a breach of undertaking given that Emerade continued to be described as new on the product website.

ALK-Abelló stated that the material now at issue was a presentation given by Bausch & Lomb to an allergy group in March 2016. The meeting was sponsored by Bausch & Lomb. A copy of the agenda was provided.

## COMPLAINT

ALK-Abelló noted that the Bausch & Lomb presentation included a slide headed 'New Design' beneath which was a prominent image of an Emerade auto-injector, despite the ruling in Case AUTH/2802/11/15. ALK-Abelló stated that it was particularly disappointing that this was the second time it had alleged a breach of undertaking.

As the complaint concerned an alleged breach of undertaking it was taken up by the Authority in the name of the Director as the Authority was responsible for ensuring compliance with undertakings.

When writing to Bausch & Lomb, the Authority asked it to respond in relation to Clauses 9.1 and 2 of the Code in addition to Clause 29 cited by ALK-Abelló.

## RESPONSE

Bausch & Lomb submitted that the person named on the meeting agenda, as an employee of the company and who would present the update on adrenaline auto-injectors was not an employee of Bausch & Lomb UK or any member of its group. The named person was a third party that another part of the Bausch & Lomb group had an agreement with to consult and support marketing activities with Emerade. This agreement was implemented

in March 2015 on the transfer of the sales and marketing rights of Emerade to Bausch & Lomb from a company where the named person had a role. This person had no rights to use the Bausch & Lomb name or act on behalf of the company outside of the terms of the consultancy agreement.

Bausch & Lomb stated that it was only on notification of the complaint that it knew of: any involvement by the company in the meeting held in March 2016; any arrangement between the organisers of the meeting and Bausch & Lomb; any attendance of any Bausch & Lomb personnel at the event; and the named individual's attendance. Bausch & Lomb submitted that the attendance at the meeting and use of the Bausch & Lomb name directly conflicted with the instructions provided by the company. The presentation given at the meeting was not approved by Bausch & Lomb.

The named individual was currently prohibited from attending any direct customer facing meetings and had been since the start of November 2015. Details were provided.

Since early November 2015, Bausch & Lomb had not instructed the named individual to carry out any activities on its behalf and was strictly prohibited from any face-to-face contact of the type facilitated by the meeting in question.

Bausch & Lomb stated that the named individual had confirmed that he/she did not attend or sponsor the meeting as a representative of Bausch & Lomb. The chairman and organiser of the meeting in question was made aware that the reference to Bausch & Lomb on the meeting agenda was inaccurate and this was disclosed from the platform to the attendees at the start of the meeting. This description of events had been confirmed as accurate by the chairman and organiser of the meeting.

Bausch & Lomb accepted that its relationship with the third party placed responsibility on Bausch & Lomb in the eyes of third parties. The company accepted that the named individual's attendance at the meeting and the agenda had given the impression to attendees that he/she represented Bausch & Lomb irrespective of the instructions provided. However, given the specific restrictions placed on the named individual by Bausch & Lomb, it did not foresee that he/she would contravene such instructions.

Bausch & Lomb's internal approval processes in respect of expenses was such that expense claims for an engagement such as the meeting in question must be pre-approved before they could be incurred. The named person was fully aware of this process and had used it on many occasions. Following the suspension he/she had not submitted any expenses for approval and therefore the company had no reason to believe that there had been a breach of the restrictions. The named person did not submit an expenses application in respect of the meeting in question or request permission to attend.

With the benefit of hindsight Bausch & Lomb now saw that potentially additional measures could

have been taken to ensure compliance with its instructions. However, at the relevant times, nothing in the named individuals' communications with the company or behaviour indicated an intention not to comply with the company's instructions.

Bausch & Lomb stated that it clearly took the named individual's actions extremely seriously.

With regard to the presentation given at the meeting, Bausch & Lomb stated that it was created without its knowledge and so there was no certificate approving it; it was not a Bausch & Lomb document.

Bausch & Lomb stated that the situation was deeply regrettable.

In response to a request for further information, Bausch & Lomb stated that the instruction not to engage in 'non-field based marketing activities' meant no customer contact face to face or otherwise and only if requested by Bausch & Lomb to be involved in any internal strategy discussions. The company had not instructed the named individual to take part in any activities non-field based or otherwise since November 2015.

Bausch & Lomb wrote to the named individual in November and December 2015. In addition, this position was reinforced by another named person from the third party.

With regard to pending field based activities the named individual was advised that all meetings and appointments should be handed over to the sales manager and that he/she should have no direct contact with the sales force. Bausch & Lomb sales teams were also advised to have no direct contact with the named individual who was compliant in handing over the relevant information on upcoming events and Bausch & Lomb had no reason to believe that this had changed.

Bausch & Lomb was not aware of the meeting in question prior to receiving the complaint letter. On writing to the named individual to request a response to a number of questions including about when the meeting arrangements were made the named individual stated that the meetings were held quarterly. He/she regularly attended these meetings and spoke. He/she was invited to give an update on how current prescription regulations during medical emergencies could be interpreted, a subject of current discussion amongst the group and an issue of interest to the individual. When another speaker had to pull out of the March date, he/she was asked to cover this slot. The individual agreed and extended the talk to include the history and background of AAI design.

Bausch & Lomb stated that its sales manager and the other named person from the third party had regular contact with the individual to monitor and ensure that he/she complied with the terms of the suspension. Bausch & Lomb submitted that there had been no claim on expenses from November 2015 which would indicate compliance with Bausch & Lomb's instruction.

Neither of these individuals were aware of this meeting. The first Bausch & Lomb became aware of this meeting was upon receipt of the complaint letter in April 2016. The individual stated that no one at Bausch & Lomb was aware of the meeting. He/she had never planned to attend in Bausch & Lomb's name or as its representative. Since leaving a previous company a number of years ago, he/she had continued to attend these meeting as a private individual, for educational and social reasons. A representative from another company was supposed to be in attendance and host the meeting, but was waylaid and did not make it.

The response to the question when did the named individual contact the meeting chairman and advise him that the reference to Bausch & Lomb on the agenda was inaccurate was that the chairman and organiser of the meeting, was made aware of the inaccuracy in the agenda prior to the meeting and the error in the agenda and Bausch & Lomb's non-involvement was further disclosed from the platform at the start of the meeting.

The individual's response to the question why an updated agenda was not provided to the delegates was that in hindsight that should have been the correct course of action, but instead the error was disclosed the following day by the chairman from the platform, before and during the meeting. He/she clearly explained that the individual was not there on behalf of Bausch & Lomb but as a personal member of the group. The individual also reiterated this before speaking and clarified and apologised for the error in the programme.

According to the individual the complementary drinks were organised between the sponsoring company and group organising the meeting.

Bausch & Lomb did not provide or have any knowledge of monies being paid for the drinks. No expenses were claimed from Bausch & Lomb. Bausch & Lomb assumed therefore that these were paid by the individual.

Bausch & Lomb submitted that it seemed that the named individual intentionally proceeded with this meeting without the knowledge or permission of Bausch & Lomb. He/she deliberately acted outside the scope of his/her authority and knowingly failed to comply with his/her contractual obligations. As a result, the company had taken immediate remedial action.

## **PANEL RULING**

The Panel noted that a form of undertaking and assurance was an important document. Companies had to give an undertaking that the material in question and any similar material, if not already discontinued or no longer in use would cease forthwith and give an assurance that all possible steps would be taken to avoid similar breaches of the Code in the future (Paragraph 7.1 of the Constitution and Procedure). It was very important for the reputation of the industry that companies complied with undertakings.

The Panel noted that in Case AUTH/2802/11/15 ALK-Abelló had complained in November 2015 that the claim 'Emerade offers a new higher dose ...', which appeared in a Pulse Quick Guide, implied that a new higher dose of Emerade had been launched within the last 12 months. The Panel noted that this was not so. The Emerade 500mcg summary of product characteristics (SPC) stated that the date of the first marketing authorization/renewal of authorization was 3 January 2013. A breach of Clause 7.11 was ruled which was accepted by Bausch & Lomb; the company's undertaking, signed in December 2015, stated that September 2015 was the last date the material was used or appeared.

In Case AUTH/2817/12/15 ALK-Abelló complained on 23 December 2015 that Emerade continued to be described as 'new' on the product website. The Panel considered that Bausch & Lomb had failed to comply with its undertaking given in Case AUTH/2802/11/15 and breaches of Clauses 2, 9.1 and 29 were ruled.

Turning to the case now before it, Case AUTH/2833/4/16, the Panel noted that a consultant had presented an update on adrenaline auto injectors at a third party meeting. The presentation mentioned EpiPen, JEXT, and Emerade with an emphasis on Emerade. Slide 8 of the presentation was headed 'New Design' above a picture of Emerade 500mcg. The Panel noted Bausch & Lomb's submission that it had no knowledge of the meeting nor of the involvement of the consultant. As a result of a separate conduct matter the consultant was not authorized by Bausch & Lomb to carry out field based activities. He/she was restricted to non-field based activities.

The Panel noted that the agenda which had been distributed to delegates stated that the consultant was from Bausch & Lomb and concluded by stating that 'You are all invited for complementary drinks immediately following the meeting, sponsored by Bausch and Lomb'. The meeting chair confirmed that prior to the meeting but after the agenda had been circulated the consultant had contacted him/her and confirmed that he/she was attending and presenting in a personal capacity. The consultant asked the chair to announce that his/her presentation and invitation to go out for drinks afterwards was a personal one and was not sponsored by Bausch & Lomb. The email from the chair stated that he/she did this at the beginning and end of the presentation. In addition Bausch & Lomb provided a copy of an email from the consultant wherein he/she stated that he/she had reiterated the chair's explanation before speaking. The Panel was not provided with a copy of the invitation to the meeting.

The consultant's explanation of the arrangements appeared to be inconsistent with the agenda. The consultant explained that he/she was invited to present on how current prescription regulations during medical emergencies could be interpreted which was subsequently extended to include the history and background of AAI design when another speaker had to pull out/was waylaid. It was

unclear when the previous speaker pulled out of the meeting, however his/her details did not appear on the agenda.

The Panel considered that it should have been possible to circulate a new agenda by email prior to the meeting and also at the meeting itself to make the position clear. ALK-Abelló did not refer to the change in arrangements. In addition it was apparent that the consultant had ample opportunity to raise this matter earlier than the day before the meeting when he/she saw the agenda.

The Panel considered that Bausch & Lomb had made it clear to the named individual that he/she was restricted to non-field based marketing activities in letters dated in November and December 2015. There was however no explanation of what Bausch & Lomb meant by non-field based activities. In its response to the Panel Bausch & Lomb referred to an apparently narrower prohibition on attending any direct customer facing meetings and no contact with customers face to face or otherwise. The Panel considered that the company could have been clearer about the nature of the prohibition in its aforementioned letters.

Attendees at the meeting had been provided with material which did not comply with the Code. The question to be considered was whether Bausch & Lomb was responsible under the Code for the activity when the presenter, who was a consultant for Bausch & Lomb, was apparently acting in contravention of instructions from the company. The Panel considered that given there was a consultancy agreement between the parties at the time of the meeting and the impression given by the agenda and slides, Bausch & Lomb was responsible for the consultant's actions. The statement from the chair was insufficient to alter the company's responsibility in this regard. One of the slides referred to Emerade's 'New design'. The meeting was held after Bausch & Lomb had given its undertakings in Cases AUTH/2802/11/15 and AUTH/2817/12/15. Thus there had been a failure to comply with those undertakings. The Panel therefore ruled a breach of Clause 29. High standards had not been maintained and a breach of Clause 9.1 was also ruled. The Panel noted its concerns about the clarity of the instructions given to the consultant but nonetheless considered that overall the company had been very badly let down by its consultant. The company had attempted to restrict the consultant's activities. The Panel noted the importance of complying with undertakings and that it had ruled a breach of Clause 9.1. The Panel considered that in the exceptional circumstances of this case and on balance, that Bausch & Lomb's failure to comply with its undertakings did not warrant a ruling of a breach of Clause 2 and thus no breach of that clause was ruled.

**Complaint received**      **4 April 2016**

**Case completed**         **31 May 2016**

# TAKEDA v AMDIPHARM MERCURY

## Promotion of Lutrate

Takeda UK complained about a Lutrate (leuprorelin acetate depot injection) promotional email (ref AMCo/LUT/1115/0027) sent by Amdipharm Mercury Company (AMCo) to health professionals and budget holders in the NHS about the availability of a new formulation of leuprorelin with the potential for cost savings to the NHS.

The detailed response from AMCo is given below.

Takeda alleged that AMCo had falsely implied that Lutrate and Prostav DCS were interchangeable and could be used for the same indications in prostate cancer. Lutrate had a much narrower licensed indication which Takeda alleged could lead to patients being prescribed Lutrate inappropriately. This was promotion outside the marketing authorization and only a limited number of Prostav DCS patients would be eligible for Lutrate. The email was likely to lead GP practices to overestimate the cost savings they could achieve by using Lutrate in place of Prostav DCS which was alleged to be misleading and did not encourage rational use.

The Panel noted that Prostav and Lutrate were both leuprorelin depot injections and in the Panel's view, the email implied that the two medicines were interchangeable. The Panel noted however that the indications for Prostav were broader than those for Lutrate. The Panel did not accept that the differences in indication were made clear. The impression was that the only difference between the medicines was the cost. No detail had been provided regarding the cost comparison but it again implied the products were interchangeable, ie Lutrate could be used whenever Prostav was used. This was not so. The Panel considered that the impression from the cost comparison and a poll was that Lutrate and Prostav were interchangeable. This was inconsistent with the Lutrate SPC and the Panel ruled a breach of the Code. This impression was not negated by the use of the term 'for eligible patients'.

Neither Takeda nor AMCo provided details about the basis of the cost comparison, the number of patients and what proportion of patients could be changed from Prostav to Lutrate. The impression was that all Prostav patients could be changed to Lutrate which was not so. The Panel considered that the claims for cost savings were misleading and did not promote the rational use of Lutrate as alleged and breaches of the Code were ruled.

Further only efficacy data regarding Lutrate's testosterone suppression was included with no balance of safety information regarding common adverse events or withdrawals due to adverse events which was alleged to be an unbalanced view of the evidence.

The Panel noted that there was no mention of adverse events in the body of the email. The only information about common adverse events or withdrawals due to adverse events was in the prescribing information. The Panel did not consider that this necessarily meant that the email was an unbalanced view of the evidence as alleged. It noted that the material at issue was not lengthy and that leuprorelin was not a new medicine, the formulation was new. The SPC stated that most of the treatment related adverse events reported were mainly subject to the specific pharmacological action of leuprorelin and associated with testosterone suppressing therapy. Local adverse reactions reported after injection were similar to those with similar products administered via intra-muscular [injection]. The email did not state nor imply that there were no adverse events etc. The Panel did not consider that the email was unbalanced as alleged and ruled no breach of the Code.

Takeda further alleged that the claim 'A novel leuprorelin formulation to maintain effective testosterone suppression' was misleading and disparaging since it implied that Lutrate offered some advantage over other leuprorelin formulations in terms of testosterone suppression. This had never been established.

The Panel considered that the claim 'Novel formulation to maintain effective testosterone suppression' implied that the novel formulation maintained testosterone suppression rather than the leuprorelin. Although there was no mention of Prostav in this section as the active ingredients of both medicines was leuprorelin, there was an implication that Lutrate was an improvement over Prostav in relation to maintenance of effective testosterone suppression. The Panel considered that the claim implied a special merit which had not been established and that the claim disparaged other formulations of leuprorelin. Breaches of the Code were ruled.

Takeda alleged that the claim 'Lutrate is simple and easy to administer' had not been substantiated and was a hanging comparison. Takeda stated that since Prostav DCS was the obvious alternative treatment for patients eligible for Lutrate, the claim would likely be interpreted by prescribers as indicating that Lutrate was at least as simple and easy to administer as Prostav DCS. No evidence to support this assertion was referenced in the email, or by AMCo during inter-company dialogue. Takeda alleged that administration of Lutrate was, in fact, a more complex process than administration of Prostav DCS.

The Panel noted that the claim 'Lutrate: simple and easy to administer' was followed by 8 illustrations

**of the steps needed to prepare the medicine and the injection area for administration. There was no mention of Prostav in this section. The first mention of Prostav in the email was in the following section. The Panel noted that the complainant had the burden of proving their complaint on the balance of probabilities. The Panel did not accept that the claim was a comparison; it was therefore not a hanging comparison as alleged. Readers would not necessarily interpret the claim as being that Lutrate was at least as simple and easy to administer as Prostav. The Panel ruled no breaches of the Code.**

**Takeda alleged that given its continued concerns and the range of clauses alleged to have been breached, AMCo's conduct in relation to this material suggested a failure to maintain high standards and brought discredit to and reduced confidence in the industry.**

**The Panel noted its rulings above. It considered that the lack of clarity regarding the comparison of Lutrate's indications and how these compared to Prostav and the general claim for cost savings ruled in breach meant that high standards had not been maintained and a breach of the Code was ruled.**

**The Panel noted that Clause 2 was a sign of particular censure. It did not consider that the material brought discredit upon or reduced confidence in the pharmaceutical industry. No breach of Clause 2 was ruled.**

Takeda UK Limited complained about a Lutrate (leuprorelin acetate depot injection) promotional email (ref AMCo/LUT/1115/0027) which was sent by Amdipharm Mercury Company Limited (AMCo) to health professionals and budget holders in the NHS. The email was to alert them about the availability of a new formulation of leuprorelin with the potential for cost savings to the NHS.

When printed the email consisted of three pages. Page 1 was headed 'Lutrate' 'new leuprorelin formulation' and Lutrate: A novel leuprorelin formulation' followed by details of the sustained delivery system with a 'click here to view email and prescribing information' link. Page 2 included details of how to prepare the injection and also referred to the link to the email and prescribing information. Page 3 referred to cost savings and included a brief survey. There were a number of links including to request a representative visit, view an administration guide and order a video.

Lutrate 1 month depot injection was indicated for palliative treatment of locally advanced or metastatic prostate cancer. Lutrate 3 month depot injection was indicated for palliative treatment of hormone dependent advanced prostate cancer.

Takeda's product Prostav DCS (leuprorelin depot injection) was indicated for: metastatic prostate cancer; locally advanced prostate cancer, as an alternative to surgical castration; as an adjuvant treatment to radiotherapy in patients with high-risk localised or locally advanced prostate cancer at high risk of disease progression and as an adjuvant

treatment to radical prostatectomy in patients with locally advanced prostate cancer; as neo-adjuvant treatment prior to radiotherapy in patient with high-risk localised or locally advanced prostate cancer. Prostav could also be used for a number of gynaecological indications.

#### **A Alleged lack of clarity on licence differences between Prostav DCS and Lutrate**

Page 3 of the email included a section headed 'A new leuprorelin formulation with significant cost savings compared to Prostav'. This was followed by 'Annual cost saving with Lutrate: £135 per patient' followed by 'NHS list price comparisons for available leuprorelin acetate formulations for Prostav SR DCS 3.75mg (monthly) and Prostav 3 DCS 11.25mg (3 monthly)'. Further down the email on the same page was a poll 'Based on the significant savings that can be made, which type of patients would you consider prescribing Lutrate for?'. The choices were 'New eligible prostate cancer patients who require treatment with a [luteinizing hormone releasing hormone] LHRH agonist' or 'Those eligible patients currently receiving Prostav'.

#### **COMPLAINT**

Takeda alleged that by including a direct comparison between the two medicines in terms of potential cost savings and a poll regarding the type of patients the prescriber would treat (ie new eligible prostate cancer patients who require LHRH agonist therapy or eligible patients currently receiving Prostav) AMCo had falsely implied that the two products were interchangeable and could be used for the same indications in prostate cancer. Lutrate had a much narrower licensed indication in prostate cancer compared with Prostav DCS, which could lead to patients being prescribed Lutrate inappropriately. Takeda alleged that this represented promotion outside the marketing authorization in breach of Clause 3.2.

Furthermore, because in reality only a limited number of Prostav DCS patients would be eligible for Lutrate, the email in question was likely to lead GP practices to overestimate the cost savings they could achieve by switching patients from Prostav DCS to Lutrate or using Lutrate in place of Prostav DCS. Takeda alleged breaches of Clauses 7.2, 7.3 and 7.10.

#### **RESPONSE**

AMCo stated that Takeda was concerned that a direct comparison between the two medicines with regards to cost saving implied that the products were interchangeable. AMCo did not understand how a *bona fide* and legitimate promotional activity targeted at health professionals and NHS decision makers whom would reasonably be entitled to know information regarding availability of Lutrate, could imply that the products were interchangeable as alleged.

AMCo noted that it had not used words such as 'interchangeable' or 'switch', and had further clarified that only 'eligible' patients could help realise the cost

savings shown. The prescribing information with the full licensed indications for Lutrate was prominently displayed. AMCo submitted that the promotion of Lutrate was in accordance with the terms of its marketing authorization and was not inconsistent with the particulars listed in the summary of product characteristics (SPC).

AMCo noted that in inter-company dialogue, Takeda accepted that the Code did not formally require competitor licences to be stated every time they were mentioned, yet it continued to request that AMCo provided an undertaking that whenever a comparison was made between Prostav DCS and Lutrate in any materials, that the difference in licensed indication was clearly stated. AMCo had twice requested clarity from Takeda as to exactly what was requested but had not received a response.

In addition, all internal materials and training of AMCo staff in relation to this piece as well as related budget impact models stated:

‘The selection of LHRH therapy based on efficacy is at the discretion of the prescribing physician following clinical assessment.....it would not be acceptable to state that all LHRHs are interchangeable based on efficacy.’

‘Representatives should not discuss switching patients as it would be unacceptable if a patient’s medication was changed without prior clinical assessment.’

## **PANEL RULING**

The Panel noted that Prostav and Lutrate were both leuporelin depot injections. In the Panel’s view, the email in question implied that the two medicines were interchangeable. There appeared to be a heading to pages 3 and 4 ‘A cost-saving option in prostate cancer’. The Panel noted however that the indications for Prostav were broader than those for Lutrate. The Panel did not accept that the differences in indication were made clear either by the reference to ‘eligible patients’ or the inclusion of the prescribing information. It was not stated in the email which prostate cancer patients were eligible for Lutrate other than in the prescribing information. Nor did the email include the indications for Prostav or even imply that the two medicines had different indications. Pages 1 and 2 focussed on Lutrate’s formulation and administration. The impression from page 3 was that the only difference between the medicines was the cost. No detail had been provided regarding the cost comparison but it again implied the products were interchangeable, ie Lutrate could be used whenever Prostav was used. This was not so. The Panel considered that the impression from the cost comparison and the poll was that Lutrate and Prostav were interchangeable. This was inconsistent with the Lutrate SPC and the Panel ruled a breach of Clause 3.2. This impression was not negated by the use of the term ‘for eligible patients’.

Neither party provided details about the basis of the cost comparison, the number of patients and

what proportion of patients could be changed from Prostav to Lutrate. The impression was that all Prostav patients could be changed to Lutrate which was not so. The Panel considered that the claims for cost savings were misleading and did not promote the rational use of Lutrate as alleged. The Panel ruled breaches of Clauses 7.2, 7.3 and 7.10.

## **B Alleged lack of fair balance between efficacy claims and safety information**

### **COMPLAINT**

Takeda alleged that the reader was only presented with efficacy data regarding Lutrate’s testosterone suppression with no balance of safety information regarding common adverse events or withdrawals due to adverse events. Including prescribing information in this piece was not sufficient to address the requirement to provide a balance of efficacy and safety information in promotional materials. The result was an unbalanced view of the evidence in breach of Clause 7.2.

### **RESPONSE**

AMCo submitted that the email was intended to provide short succinct information about the availability of a new formulation of leuporelin and its efficacy regarding testosterone suppression in line with the licensed indication.

The entire email was only one page in length, and included the prescribing information in line with the Code requirements for digital communication. The material was all-inclusive and was programmed to display the prescribing information together with the promotional content on the same page. The prescribing information thus formed part of the promotional email and was presented in line with the Code requirements.

The information on withdrawals and common adverse events, which could be found within the prescribing information was placed in a position such that its relationship to the claims could be appreciated by the reader. Since this was a concise one page email with the prescribing information as an inherent part of that page. AMCo submitted that the safety information in the prescribing information sufficiently addressed the Code requirement regarding provision of fair and balanced information.

AMCo submitted that the information presented was sufficiently complete to enable the reader to form their own opinion of the value of the medicine. Therefore, AMCo denied that this breached Clause 7.2 as all safety requirements of the Code were met.

### **PANEL RULING**

The Panel noted that there was no mention of adverse events in the body of the email. The only information about common adverse events or withdrawals due to adverse events was in the prescribing information. The Panel did not consider that this necessarily meant that the email was an unbalanced view of the evidence as alleged. It noted



that the material at issue was not lengthy and that leuprorelin was not a new medicine, the formulation was new. The SPC stated that most of the treatment related adverse events reported were mainly subject to the specific pharmacological action of leuprorelin and associated with testosterone suppressing therapy. Local adverse reactions reported after injection were similar to those with similar products administered via intra-muscular [injection]. The email did not state nor imply that there were no adverse events etc. The Panel did not consider that the email was unbalanced as alleged and ruled no breach of Clause 7.2.

### **C Linking 'Lutrate A novel leuprorelin formulation', 'Sustained release delivery system' to 'a novel formulation to maintain effective testosterone suppression'**

The email was headed 'Lutrate' followed by 'Lutrate: A novel leuprorelin formulation sustained release delivery system' which was followed by three bullet points the third of which was 'Novel formulation to maintain effective testosterone suppression'. It was stated elsewhere in the email that Lutrate achieved effective suppression and maintenance of testosterone to castration levels.

#### **COMPLAINT**

Takeda alleged that the claim that a novel leuprorelin formulation '... to maintain effective testosterone suppression' was misleading and disparaging since it implied that Lutrate offered some advantage over other leuprorelin formulations in terms of testosterone suppression. To its knowledge, this had never been established. A breach of Clauses 7.10 and 8.1 was alleged.

#### **RESPONSE**

AMCo submitted that the claim did not disparage Prostav DCS nor did 'novel' imply that Lutrate was any more efficacious than Prostav DCS in this or any other regard. Acceptability of words such as 'new' or 'novel' were well established in the Code and pharmaceutical medicine. This was a clear situation where AMCo was entirely justified and entitled to use this terminology. AMCo did not accept that this constituted a breach of the Code.

AMCo submitted that Lutrate was a novel formulation of leuprorelin and had been available since its launch in December 2015. This was a clear and factually accurate statement and did not imply that Lutrate had any special merit, quality or property vs Prostav DCS and did not disparage any medicine. AMCo denied a breach of Clauses 7.10 or 8.1.

#### **PANEL RULING**

The Panel considered that the claim 'Novel formulation to maintain effective testosterone suppression' implied that the novel formulation maintained testosterone suppression rather than the leuprorelin. Although there was no mention of Prostav in this section as the active ingredients of both medicines was leuprorelin, there was an

implication that Lutrate was an improvement over Prostav in relation to maintenance of effective testosterone suppression.

The Panel considered that the claim implied a special merit and this had not been established. A breach of Clause 7.10 was ruled. The Panel considered that the claim disparaged other formulations of leuprorelin. A breach of Clause 8.1 was ruled.

### **D Lutrate administration guide**

#### **COMPLAINT**

Takeda alleged that the claim 'Lutrate is simple and easy to administer' had not been substantiated and was a hanging comparison. Since Prostav DCS was the obvious alternative treatment for patients eligible for Lutrate, the claim would likely be interpreted by prescribers as indicating that Lutrate was at least as simple and easy to administer as Prostav DCS. No evidence to support this assertion was referenced in the email, or by AMCo during inter-company dialogue. Takeda alleged that administration of Lutrate was, in fact, a more complex process than administration of Prostav DCS. A breach of Clauses 7.2 and 7.4 was alleged.

#### **RESPONSE**

AMCo submitted that the claim 'Lutrate is simple and easy to administer' was not a hanging comparison, simply an accurate statement of fact that did not require further substantiation. Lutrate had been specifically designed to be reconstituted and administered by health professionals with relative ease. Takeda had stated that since 'Prostav DCS was the obvious alternative treatment for patients eligible for Lutrate' (thus contradicting its own earlier concerns) then the claim would likely be interpreted by prescribers as indicating that Lutrate was as 'easy' to administer as Prostav DCS.

Consequently AMCo denied a breach of either Clauses 7.2, or 7.3.

#### **PANEL RULING**

The Panel noted that the claim 'Lutrate: simple and easy to administer' was followed by 8 illustrations of the steps needed to prepare the medicine and the injection area for administration. There was no mention of Prostav in this section (page 2). The first mention of Prostav in the email was in the following section. Neither party had provided a copy of the Lutrate administration guide referred to in the email so the Panel considered the allegation only in relation to the content of the email.

The Panel noted that the complainant had the burden of proving their complaint on the balance of probabilities. The Panel did not accept that the claim was a comparison; it was therefore not a hanging comparison as alleged. Readers would not necessarily interpret the claim as being that Lutrate was at least as simple and easy to administer as Prostav. The Panel ruled no breach of Clauses 7.2 and 7.3.

**E Alleged breach of Clauses 9.1 and 2**

**COMPLAINT**

Takeda stated that given its continued concerns and the range of clauses alleged to have been breached, AMCo's conduct in relation to this material suggested a failure to maintain high standards and brought discredit to and reduced confidence in the industry. Takeda alleged a breach of Clauses 9.1 and 2.

**RESPONSE**

AMCo submitted that it had maintained high standards throughout, in its conduct and the use of the materials. It remained disappointed by the actions and premature referral of these matters before the PMCPA and thus rejected by Takeda's allegation that there had been breach of Clauses 9.1 or 2.

**PANEL RULING**

The Panel noted its rulings at points 1- 4 above. It considered that the lack of clarity regarding the comparison of Lutrate's indications and how these compared to Prostag and the general claim for cost savings ruled in breach (point 2 above) meant that high standards had not been maintained. A breach of Clause 9.1 was ruled.

The Panel noted that Clause 2 was a sign of particular censure. It did not consider that the material brought discredit upon or reduced confidence in the pharmaceutical industry. No breach of Clause 2 was ruled.

**Complaint received            11 April 2016**

**Case completed                3 June 2016**

# VOLUNTARY ADMISSION BY JANSSEN

## Invokana email

Janssen-Cilag voluntarily admitted a breach of the Code in that a promotional email for Invokana (canagliflozin), with outdated prescribing information, was inadvertently sent to general practitioners by its mailing agency.

Invokana was indicated in adult patients with type 2 diabetes mellitus to improve glycaemic control in certain patients as monotherapy or as added-on therapy.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Janssen.

Janssen explained that the Invokana prescribing information was updated in December 2015 to reflect the addition of the uncommon side effect of 'renal failure (mainly in the context of volume depletion)' and consolidation of non-serious, uncommon side effects associated with renal failure previously listed in prescribing information (blood creatinine increased, blood urea increased, blood potassium increased, blood phosphate increased). Therefore Janssen did not believe that the outdated prescribing information had risked patient safety. A copy of the Invokana prescribing information from August 2015 and an annotated copy from December 2015, indicating the changes, were provided.

Janssen acknowledged a breach of the Code since the expired prescribing information included on the mailer was not consistent with the summary of product characteristics (SPC) at the time of publication.

The detailed response from Janssen is given below.

The Panel noted that on 7 January 2015, the agency emailed Janssen to confirm that all old versions of the Invokana prescribing information had been deleted from its system. As prescribing information was an integral part of the promotional material provided by the agency, it was assumed that deletion of old prescribing information would, at the same time, delete the materials at issue.

On 16 March there was an email exchange between the agency and Janssen regarding the 'Invokana Cost Change email'. Neither party referred to 'updated' material or cited the reference number so that the item at issue could be correctly identified. Having received confirmation that the email was approved for use it appeared that there was a verbal instruction from the agency's account team to its IT team to 'resend' the mailer. The Panel assumed that the little information given was sufficient to allow the correct item to be identified. The IT team retrieved the old mailer from the sent items on its mail server and resent it. The Panel considered that

although the agency had not previously realised that material was effectively archived on its mail server, both parties should have been clearer about the item at issue particularly given the importance of not sending outdated material.

The Panel noted that, Janssen's agency had resent a previous document which included prescribing information which Janssen submitted did not reflect the most recent SPC. The company had updated its prescribing information by consolidating a previous list of what it described as non-serious, uncommon side effects associated with renal failure into the statement 'renal failure (mainly in the context of volume deletion)'.

The Code required the prescribing information to be included in promotional material and the supplementary information stated that the prescribing information must be consistent with the SPC. Clause 4.2 listed the elements of the prescribing information and in relation to adverse reactions the requirement was for a succinct statement of common adverse reactions likely to be encountered in clinical practice, serious adverse reactions and precautions and contra-indications relevant to the indications in the advertisement, giving in abbreviated form, the substance of the relevant information in the SPC, together with a statement that prescribers should consult the SPC in relation to other adverse reactions.

The Panel noted that the adverse reaction at issue was neither common nor, according to Janssen, serious. In that regard it was not one of the required elements of prescribing information listed in Clause 4.2. Nonetheless, information even about uncommon side effects still had to be accurate. The Panel noted that the change made to the Invokana prescribing information in December 2015 was to consolidate a list of conditions symptomatic of renal failure. The email sent in error included that list instead of the consolidated statement 'renal failure (mainly in the context of volume depletion)'. The Panel considered that although the prescribing information on the email sent in March 2015 was not the most up-to-date version, prescribers had nonetheless been given the substance of the relevant information in the SPC as required. No breach was ruled.

Janssen-Cilag Ltd voluntarily admitted a breach of the Code in that a promotional email for Invokana (canagliflozin) (ref PHGB/VOK/1015/0078), with outdated prescribing information, was inadvertently sent to general practitioners by its mailing agency.

Invokana was indicated in adult patients with type 2 diabetes mellitus to improve glycaemic control in certain patients as monotherapy or as added-on therapy.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Janssen.

## **VOLUNTARY ADMISSION**

Janssen stated that a withdrawn mailing was sent in error. The mailing agency had taken complete responsibility for the error which was caused by miscommunication between its account team and its information technology (IT) team. The agency brought the error to Janssen's attention almost immediately after the mailer was sent.

On 22 March, the agency apologised sincerely to Janssen for distributing a previously withdrawn campaign mailer with outdated prescribing information instead of the updated version with current prescribing information (ref PHGB/VOK/1015/0078(1)).

Janssen explained that the Invokana prescribing information was updated in December 2015 to reflect the addition of the uncommon side effect of 'renal failure (mainly in the context of volume depletion)' and consolidation of non-serious, uncommon side effects associated with renal failure previously listed in prescribing information (blood creatinine increased, blood urea increased, blood potassium increased, blood phosphate increased). Therefore Janssen did not believe that the outdated prescribing information had risked patient safety. A copy of the Invokana prescribing information from August 2015 and an annotated copy from December 2015, indicating the changes, were provided.

The timeline was as follows:

- 7 January – The agency wrote to confirm that all digital and print material had been updated with the latest prescribing information and the old prescribing information had been deleted from its systems. This confirmation was within the timeline specified in the Janssen Withdrawal of Materials standard operating procedure (SOP).
- 14 March – Janssen certified the updated mailer (ref PHGB/VOK/1015/0078(1))
- 16 March – Janssen emailed the agency to confirm that the updated material was certified and ready to be distributed.
- 22 March – Agency incorrectly sent outdated mailer
- 23 March – Agency sent out version with current prescribing information and subject line to highlight previous version was sent in error (ref PHGB/VOK/1015/0078 (1)a).

Janssen stated that it requested immediate investigations and corrective and preventative actions from its agency to prevent similar mistakes in the future. The agency reported that the error had resulted from confusion between its account and IT teams, where the account team requested the mailer to be 'resent' and the IT team resent the previous mailer instead of the certified updated version. As preventative measures the agency confirmed all client sponsored emails would be deleted from its email server one week post-send to prevent an

outdated mailer mistakenly being sent again. The agency also confirmed a process was in place where all client sponsored emails would be classed as new and any allusion to 'resent' would only be reflected in the data to match the requirements.

Janssen acknowledged a breach of Clause 4.1, since the expired prescribing information included on the mailer was not consistent with the summary of product characteristics (SPC) at the time of publication. Janssen had contacted the PMCPA proactively about this incident. To date it had not received any complaints from recipients or ABPI member companies.

Janssen submitted that it took its responsibilities under the Code very seriously and sincerely regretted the actions taken by its agency. It had registered its dissatisfaction with the agency which had confirmed in writing that a process was in place to prevent future outdated mailers being emailed in error.

Following its internal review Janssen was satisfied that its SOP for Withdrawal of Materials and Re-Approval had been adhered to and that this incident had occurred due to a mistake by its agency.

## **RESPONSE**

Janssen provided a copy of the email sent to the agency on 16 March, confirming that the updated job bag was certified and approved for use. Additionally, Janssen hoped the following summary would aid clarification:

- 1 On 7 January the agency confirmed that new Invokana prescribing information was received and previous versions destroyed (see below).
- 2 The correct material (ref PHGB/VOK/1015/0078(1)) was created by the agency and review was commenced on 22 January 2016; the agency uploaded the final artwork on 29 February 2016. This artwork was subsequently reviewed, amended, approved then certified by Janssen on 14 March with the correct prescribing information.
- 3 Once certification had taken place, the agency was informed that the material (ref PHGB/VOK/1015/0078(1)) was approved for distribution on 16 March.
- 4 On 22 March, the agency distributed the old mailer (ref PHGB/VOK/1015/0078) which contained the outdated prescribing information retrieved by its IT team from the 'sent items' from previous email distribution.
- 5 The agency acknowledged that the 'Cost Change Email' (ref PHGB/VOK/1015/0078) should not have been sent on 22 March. The correct job bag number that Janssen requested to be sent was PHGB/VOK/1015/0078(1).
- 6 Subsequent to Janssen's voluntary admission above, the agency had confirmed that before sending a promotional email on behalf of a client, it usually confirmed certification of the

job bag firstly by email or telephone call to the sponsoring company to confirm approval to send and secondly, verification in Zinc Unitas approval system to confirm certification. Due to the error, the agency had now implemented an additional process, by which promotional items contained in emails in the 'sent items' were deleted after one week.

In relation to why an email from the agency dated 22 March to Janssen referred to deletion of old versions of the Invokana prescribing information rather than specific materials, Janssen submitted that the prescribing information for Invokana was changed in December 2015 and the agency was informed of this change on 7 January 2016, within the Janssen SOP timeframe for this process. This communication included a request to delete copies of the former prescribing information. The agency wrote to Janssen on 7 January to confirm compliance with this request.

Promotional items produced by the agency were approved with an integrated prescribing information and so an instruction to delete the prescribing information would mean the entire promotional item would be deleted.

On 22 March, the agency distributed the incorrect item (ref PHGB/VOK/1015/0078), because its IT team sourced a version of the previous item from the 'sent items' server. The agency identified the error immediately and instigated a process to resolve the hitherto unknown source of archived material by ensuring all client sponsored emails in the 'sent item' repository on the server were deleted one week post mailing.

Janssen reiterated that it took its responsibilities under the Code very seriously. It had worked with the agency to ensure its processes were corrected so similar errors did not affect Janssen or other industry partners in the future. It sincerely regretted that it might have breached Clause 4.1 and was acutely aware that this was its second voluntary admission regarding a breach of that Clause. In this case, the company was satisfied that its SOP was followed and that this unfortunate error occurred as a result of agency error.

#### **PANEL RULING**

The Panel noted that on 7 January 2015, the agency emailed Janssen to confirm that all old versions of the Invokana prescribing information had been deleted from its system. As prescribing information was an integral part of the promotional material provided by the agency, it was assumed that deletion of old prescribing information would, at the same time, delete the materials at issue.

On 16 March there was an email exchange between the agency and Janssen regarding the 'Invokana Cost Change email'. Neither party referred to 'updated' material or cited the reference number of the updated email so that the item at issue could be

correctly identified. Having received confirmation that the email was signed off and approved for use it appeared that there was a verbal instruction from the agency's account team to its IT team to 'resend' the mailer. The Panel assumed that the little information given was sufficient to allow the correct item to be identified. The IT team retrieved the old mailer from the sent items on its mail server and resent it. The Panel considered that although the agency had not previously realised that material was effectively archived on its mail server, both parties should have been clearer about the item at issue particularly given the importance of not sending outdated material.

The Panel noted that, Janssen's agency had resent a previous document which included prescribing information which Janssen submitted did not reflect the most recent SPC. The company had updated its prescribing information by consolidating a previous list of what it described as non-serious, uncommon side effects associated with renal failure into the statement 'renal failure (mainly in the context of volume deletion)'.

The Panel noted that Clause 4.1 required the prescribing information to be included in promotional material and the supplementary information stated that 'The prescribing information must be consistent with the summary of product characteristics for the medicine'. Clause 4.2 listed the elements of the prescribing information and in relation to adverse reactions the requirement was for a succinct statement of common adverse reactions likely to be encountered in clinical practice, serious adverse reactions and precautions and contra-indications relevant to the indications in the advertisement, giving in abbreviated form, the substance of the relevant information in the SPC, together with a statement that prescribers should consult the SPC in relation to other adverse reactions.

The Panel noted that the adverse reaction at issue was neither common nor, according to Janssen, serious. In that regard it was not one of the required elements of prescribing information listed in Clause 4.2. Nonetheless, information even about uncommon side effects still had to be accurate. The Panel noted that the change made to the Invokana prescribing information in December 2015 was to consolidate a list of conditions symptomatic of renal failure. The email sent in error included that list instead of the consolidated statement 'renal failure (mainly in the context of volume depletion)'. The Panel considered that although the prescribing information on the email sent in March 2015 was not the most up-to-date version, prescribers had nonetheless been given the substance of the relevant information in the SPC as required by Clause 4.2. No breach of Clause 4.1 was thus ruled.

**Complaint received**                      **13 April 2016**

**Case completed**                              **13 May 2016**

# ANONYMOUS, NON-CONTACTABLE EMPLOYEE v LEO

## In-house communications material and reporting line of a medical science liaison team

An anonymous, non-contactable employee complained about in-house material produced by Leo Pharma to engage staff in the forthcoming launch of Enstilar (calcipotriol/betamethasone) cutaneous foam. The complainant provided copies of two emails and photographs of cut-out aerosol cans of Enstilar placed around the office. The complainant stated that the product had no marketing authorization and the material at issue could potentially be viewed by visitors.

The detailed response from Leo is given below.

The Panel noted that the complainant could not be contacted for any more information; he/she had provided no evidence that visitors had seen any of the material at issue.

The Panel considered that it was not necessarily unacceptable for a company to display product material within its own offices, but displays of such material in areas routinely accessed by visitors, or even viewed by passers-by, needed to be appropriate. The Panel did not agree with Leo's submission that no-one who visited the offices for a legitimate business purpose could be considered a member of the public. In the Panel's view the status of the visitor, his/her reason for visiting and the arrangements for the visit would be relevant. Each example would have to be considered on its own merits. Companies should be aware of the impact and impression such material could have on visitors and the messages that might be conveyed. The Panel noted that Leo's offices were on the second floor; visitors would generally be taken to one of the meeting rooms, away from the staff areas where the cut-outs were displayed.

In the circumstances, the Panel considered that there was no evidence to support the complainant's allegation that Leo had promoted Enstilar to the public as alleged. No breach of the Code was ruled including no breach of Clause 2.

The complainant further alleged that the reporting line for the company's medical scientific liaison officers (MSLs) did not seem correct. The complainant provided a copy of an internal email announcing that a commercial manager in one therapy area would take on the additional responsibility as head of MSLs in another therapy area.

The Panel initially considered the case on the assumption that there were two separate MSL teams and considered that there was no evidence to support the complainant's allegation that the line management of the dermatology MSLs was necessarily unacceptable. Leo had provided draft

material to show that it had recognised the inherent conflicts of interest in its interim management arrangements but had taken steps to mitigate and manage these. The Panel noted Leo's submission that the product areas, thrombosis and dermatology were distinct and separate. The complainant had cited no examples of inappropriate conduct by either the interim manager or the MSLs.

Following notification of the outcome, Leo clarified the arrangements. The Panel's impression that there were two distinct MSL teams was wrong; there was only one MSL team carrying out activities in both therapy areas (dermatology and thrombosis).

The Panel noted that MSLs carrying out activities in thrombosis would report to the head of sales (thrombosis), albeit only in relation to their activities in dermatology, as did the thrombosis sales force. The interim dual role of the head of sales of (thrombosis) and the dual responsibilities and reporting lines of the MSLs needed to be very carefully managed. It did not appear that Leo had finalised the work instruction covering the new arrangement. It was important to consider whether the activities were compatible with each other if they were undertaken by one individual, and how the activities were perceived. The more functions combined into one role the more difficult it was to ensure compliance with the Code and generally promotional and non-promotional activities should be performed by separate staff. The Panel noted Leo's submission that the governance of the MSL function would remain the medical director's responsibility.

The Panel noted its concerns above but considered that there was still no evidence to support the complainant's allegation that the line management of the MSLs in relation to dermatology by the head of sales (thrombosis) was necessarily unacceptable. Leo had provided draft material to show that it had recognised the inherent conflicts of interest in its interim management arrangements but had taken steps to mitigate and manage these. The interim head of MSLs was required to ensure that all of his/her interactions with MSLs were related to dermatology activities only and to refer MSLs to the medical director if any matters were raised in relation to thrombosis activities. The complainant had cited no examples of inappropriate conduct by either the interim manager or the MSLs. The Panel therefore ruled no breach of the Code including Clause 2.

An anonymous, non-contactable, 'concerned' employee complained about the conduct of Leo Pharma.

## 1 Alleged promotion of an unlicensed medicine

### COMPLAINT

The complainant provided copies of internal communications about Enstilar (calcipotriol/betamethasone) cutaneous spray foam for the treatment of psoriasis, due to be launched in May. Photographs of a large cut-out aerosol can of Enstilar were provided as well as a screen image promoting the product. All of the material appeared to be displayed in an office setting. The complainant also provided copies of two emails briefing staff about the upcoming product launch. The complainant stated that the product had no marketing authorization and the material was on view in the offices and potentially to visitors.

When writing to Leo, the Authority asked it to respond in relation to the requirements of Clauses 2, 9.1 and 26.1 of the Code.

### RESPONSE

Leo strongly refuted the suggestion that it had promoted a prescription only medicine to members of the public as all of the material at issue was displayed within the company's private, secure office (in the open-plan and staff kitchen areas) and was directed at head office staff for the legitimate business purpose of internal engagement and familiarisation with a product launch campaign. Members of the public never had access to these secure offices and it would be physically impossible for them to see the materials in the offices.

Leo explained that its offices were on the second floor of a building in an isolated part of Berkshire which had no public use or access. The building housed 5 companies (including Leo) with a common reception area on the ground floor. Post, packages and the like were left at reception and visitors reported to the reception staff at this initial entry point into the building. Any visitor with a legitimate, pre-arranged business purpose within the Leo offices was announced by telephone to their Leo contact. Visitors were then collected from reception by Leo staff and accompanied to a specific area within the Leo offices for their meeting. Everyone else present within the areas shown on the complainant's photographs were employed or otherwise contracted by Leo.

Leo noted that entry to its offices was only possible through one of two entrance doors, both of which required staff security passes.

Leo submitted that the photographs provided by the complainant were of three cut-out can stands and one screen image. A number of the photographs were duplicates either as close-ups or different angles. Leo provided a table to show the location of the materials at issue and when they were first displayed in the building. All of the material at issue had been displayed in the staff lunch/kitchen area, in the open-plan work area or in an internal meeting room for Leo staff only.

Leo noted that its formal meeting rooms were grouped together at one end of the floor with their own coffee/refreshment area. Most visitors would be shown to a room in the meetings area, away from the open-plan office and staff lunch/kitchen area.

Although visitors were not physically barred from the Leo open-plan and staff kitchen area, those areas were not designed or intended primarily for the use of visitors. They were designed for and were used by Leo staff rather than business visitors and all those present in the offices at any given moment were highly likely to be all Leo employees only.

The stands displayed in the offices were to remind staff that Enstilar would be available in a can which was a new and innovative way to apply a psoriasis product. The purpose of the internal communications campaign was for employees to understand the work being undertaken by a cross-functional launch team in preparation for the product launch and to ensure that all employees were part of the company commitment to have a successful launch. Such internal communication was a common and routine means in the pharmaceutical and other industries to help communicate to employees what their priorities should be in an otherwise busy work schedule; in this case, support for a new product launch. This theme was reiterated in the TV screenshot which noted a new method of delivery. The TV was normally set to a news channel and would have been temporarily set to the image display.

Leo noted that none of the internal imagery stated a licensed indication for Enstilar (or even a therapy area) and was also marked for internal use. Leo therefore denied a breach of Clause 26.1 that prescription only medicines must not be advertised to the public. No members of the public would have had access to these materials and although the complainant referred to 'visitors', all visitors to the Leo offices were there for a legitimate business purpose and so could not be considered to be members of the general public for the purposes of Clause 26.1.

Leo further noted that the complainant had also provided a number of internal emails announcing progress in the licensing and launch plans for Enstilar. It was clear that these internal emails were not available to visitors or the public.

Leo submitted that in its view, it was legitimate to provide business information to current employees which might relate to both existing medicines and those not yet marketed.

As could be expected, there were a number of activities and projects within the company that would be undertaken to get a product to market. The internal Enstilar awareness campaign was to facilitate an environment of employee engagement and a collective means of working together towards a common goal – the forthcoming UK licence and subsequent launch of the product. This ensured that all company staff, regardless of function, recognised the need to prioritise support for the launch.

Furthermore, Leo noted that in all the emails, employees were consistently reminded that the product did not have an external licence and that they should not discuss this with external stakeholders unless specifically briefed to do so.

Leo submitted that its standards had been sufficiently high to prevent promotion of a prescription only medicine to the public. In this regard, the company thus denied breaches of Clauses 9.1 and 2.

## **PANEL RULING**

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure stated that anonymous complaints would be accepted, but that like all other complaints, the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties. The complainant could not be contacted for more information.

The Panel noted Leo's submission that the material provided by the complainant showed different components of an internal communications campaign designed to engage staff throughout the organisation in the forthcoming launch of a new medicine. The two emails provided had been distributed internally and reminded readers not to discuss Enstilar with external stakeholders unless briefed to do so. Leo had submitted that the large cut-out cans of Enstilar and the television screen were all displayed in the staff lunch/kitchen area, in the open-plan work area or in an internal meeting room for Leo staff only. Access to the offices was controlled. The Panel noted Leo's submission that visitors to the offices would generally be taken to one of the meeting rooms, away from the staff areas where the cut-outs were displayed.

The Panel considered that it was not necessarily unacceptable for a company to display product material within the confines of its own offices, but displays of such material in areas routinely accessed by visitors, or even viewed by passers-by, needed to be appropriate. The Panel did not agree with Leo's submission that no-one who visited the offices for a legitimate business purpose could be considered a member of the public. In the Panel's view the status of the visitor, his/her reason for visiting and the arrangements for the visit would be relevant. Each example would have to be considered on its own merits. In the Panel's view, companies had to be aware of the impact and impression such material could have on visitors and the messages that might be conveyed. The Panel noted that Leo's offices were on the second floor. The only people who had access to the offices were Leo staff and visitors.

The Panel considered that although most visitors to Leo's offices would be shown to a room in the meetings area away from the open plan office and staff lunch/kitchen area, some might, nonetheless, see the cut-outs and screen. The Panel considered that if a visitor had seen the hard copy material at issue they would be very aware that the company was shortly to launch a new product. The cut-outs of

the can included a green traffic light and the brand name; other material which included the brand name and the generic name, made it clear that the product was ready for launch. One piece referred to the global launch. Although the screen image showed the brand name and generic name, it did not refer to the forthcoming launch. The Panel noted that the complainant had provided no evidence that visitors had seen any of the material placed around the office or that the internal company emails had been provided to anyone other than Leo staff.

In the circumstances, the Panel considered that there was no evidence to support the complainant's allegation that Leo had promoted Enstilar to the public as alleged. No breach of Clauses 2, 9.1 and 26.1 were ruled.

## **2 Reporting line of medical scientific liaison officers (MSLs)**

### **COMPLAINT**

The complainant provided a copy of an internal email which announced that the head of sales (thrombosis) would take on the additional responsibility as head of MSLs dealing specifically with the dermatology side of the business. The head of sales (thrombosis) would continue to report to the business unit director of thrombosis and would have a dotted line responsibility to the medical director who would directly manage the thrombosis activities of the MSLs.

The complainant alleged that the report line of MSLs to a sales manager did not seem to be correct.

When writing to Leo, the Authority asked it to respond in relation to the requirements of Clauses 2 and 9.1.

### **RESPONSE**

Leo stated that its MSL function currently reported to the medical director (as indicated in the email submitted by the complainant) and would continue to report to the medical director even after the new interim head of MSLs was in position as of 1 May 2016. Moreover, the governance of the MSL function had been, and would remain, the medical director's responsibility.

Leo believed that this was in line with the PMCPA document 'Guidance about Clause 3' which stated 'the overall governance of the medical and scientific liaison executives and the like should be the responsibility of the medical director or similar, irrespective of reporting lines, rather than the commercial side of the company'.

Leo explained that dermatology MSLs would report into the medical director via the new, interim head of MSLs as of 1 May and thrombosis MSLs would report directly to the medical director. During the temporary period (of up to one year), the interim head of MSLs would continue to line manage the thrombosis regional business managers (RBMs) and report into the business unit director of thrombosis



for that purpose. Leo stated that its thrombosis and dermatology business units were so distinct and separate that such an arrangement was possible whilst retaining an acceptable level of governance over the MSL function. They were served by two distinct sales forces that did not promote products in both therapy areas and furthermore they did not have any routine local/regional interaction such as combined sales team meetings.

Furthermore, the head of sales (thrombosis) would look after the dermatology MSL team, a part of the business for which he had no sales targets delivery responsibility or incentives. This safeguard was already considered to ensure appropriate management structure for the MSLs reporting to the head of sales (thrombosis) and was communicated in the email announcement.

Leo was confident, given his/her length of time and seniority within the pharmaceutical industry, that the manager understood the important compliance requirements for managing an MSL team before this decision was taken and that this need could be appropriately managed by a senior member of Leo staff recognising the need to clearly separate non-promotional and promotional approaches.

To reiterate, the temporary reporting structure for the head of MSL role reflected the fact that the individual in the role would undertake two different roles for two completely different business units. This was a pragmatic and caretaking measure to meet business needs in a relatively small company such as Leo. For an interim period the head of MSL role would effectively be shared between the head of sales (thrombosis) and the medical director.

The complainant appeared to be concerned that such a reporting line arrangement, involving national level managers was, in and of itself, in breach of the Code. Leo did not consider this was so and such a reporting line arrangement, as long as the medical director retained overall responsibility for governance, was not in breach of the Code.

Leo noted that the complainant had not alleged that the MSLs had undertaken any activity that was in breach of the Code nor that they had been directed to undertake such activity in future.

Leo confirmed that it considered the MSL role was non-promotional and it had a strict internal policy on the activities of MSLs and a standard operating procedure (SOP) for the Medical Science Liaison functions (SOP 006445) made the non-promotional requirements of this function very clear. This was further supported by job descriptions for the two relevant roles within this medical function – the head of medical science liaisons and the medical scientific liaison officer. Copies of all these documents were provided.

Leo was confident that it had a strong culture of compliance which was supported by the Leo Code of Conduct which, together with the company's guidelines, procedures and policies, underpinned the ways of working within Leo. The Leo Code

of Conduct provided guidance to translate the values into consistent actions by resolving ethics and compliance issues arising in employees' daily work. Compliance with the Leo Code of Conduct was mandatory for all employees who had a shared responsibility to ensure compliance at Leo and this was also even more important for Leo managers who must ensure that Leo standards were followed at all times.

Leo stated that the MSLs' role and responsibilities centred around reactive responses to requests for information at either an individual level, presentations for senior health professionals with their team or medical presentations representing Leo at third party events. They would also engage with health professionals in relation to research projects. They might also be involved in advisory boards meetings as part of the medical function or provide internal disease/therapy area training to Leo employees including sales representatives. These activities might be in any disease or therapy area for Leo including dermatology and thrombosis.

Leo stated that MSLs were incentivised on individual performance and on company performance. They were not incentivised on local or regional sales performance or activity input metrics such as the number of visits to health professionals. For the interim head of MSLs/head of sales (thrombosis) a proportion of his/her bonus would be based on sales targets in the thrombosis division and the rest would be related to people management goals to include the management of the dermatology MSLs.

Leo stated that further safeguards had been developed as the change in reporting lines would not take effect until 1 May 2016 and a work instructions document had been prepared which was currently in draft awaiting approval to support this new internal caretaking position. A copy of the draft work instruction was provided.

Leo considered that it had taken adequate steps to safeguard and support both the head of sales (thrombosis) and the MSLs reporting to this manager for the short period. For these reasons Leo denied breaches of Clause 9.1 and Clause 2.

#### **PANEL RULING (initial)**

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure for the Prescription Medicines Code of Practice Authority stated that anonymous complaints would be accepted, but that like all other complaints, the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties. The complainant could not be contacted for more information.

The Panel noted that the email provided by the complainant stated that following an internal move by the then current head of MSLs, the dermatology MSLs would, for an interim period of one year, be line managed by the head of sales from a completely separate side of the Leo business. However,

given the inherent possible conflict of interest in a commercial manager line managing an MSL team, the Leo draft work instruction to cover this arrangement stated that to ensure compliance with Leo policies and with the Code, the overall governance of these MSLs, would remain the responsibility of the medical director. The draft work instruction set out in detail the relationships between the parties and, *inter alia*, required the interim head of MSLs (dermatology) to promptly raise any possible conflict of interest situations with the managers/medical director to ensure that these could be properly mitigated. Further, the interim head of MSLs (dermatology) was to meet twice monthly with the medical director to ensure appropriate governance and guidance was given to the interim manager.

The Panel considered that there was no evidence to support the complainant's allegation that the line management of the dermatology MSLs was necessarily unacceptable. Leo had provided draft material to show that it had recognised the inherent conflicts of interest in its interim management arrangements but had taken steps to mitigate and manage these. The Panel noted Leo's submission that the product areas, thrombosis and dermatology were distinct and separate. The complainant had cited no examples of inappropriate conduct by either the interim manager or the MSLs. The Panel therefore ruled no breach of Clauses 2 and 9.1.

#### **FURTHER COMMENTS FROM LEO**

Upon receiving details of the outcome of the Panel's consideration, Leo was concerned to note that the Panel referred to 'dermatology MSLs' and 'thrombosis MSLs' and 'dermatology MSL team' which were not terms used by Leo. There was one MSL team and not two distinct and separate MSL teams, one for dermatology and one for thrombosis.

Leo submitted that it was explicit in its response that its MSLs undertook activities in both dermatology and thrombosis. Leo had described the MSL role and stated '...the MSL officer role centres around.... These activities may be in any disease or therapy area for Leo including dermatology and thrombosis'. Leo submitted that it had a small MSL function (comprised of 4 positions) that worked as a single team supporting all therapy areas and who would all have shared reporting structure to both the new interim head of MSLs and the medical director.

Leo submitted that MSLs would report directly to the medical director for activities which involved thrombosis as a therapy area and to the interim head of MSLs (who was also national sales head (thrombosis) looking after the thrombosis sales team) for the dermatology areas of their activities. Leo submitted that this was made clear when it stated 'For an interim period the head of MSL role would effectively be shared between the head of sales (thrombosis) and the medical director'. Leo submitted that overall governance of the MSLs remained with the medical director who would also have governance over the interim head of MSLs for those specific medical affairs area related parts of the appointee's role.

Leo submitted that this additional clarification would not impact the Panel's ruling and furthermore that it demonstrated that the single MSL team would always be directly managed by a medical, non-commercial role.

Leo was confident that the information previously provided was accurate but apologized if it was not sufficiently explicit to avoid possible misunderstandings.

The Authority decided that the original Panel should reconvene to consider this matter in light of the clarification from Leo. Leo was so informed and asked to respond including in relation to the requirements of Clauses 2 and 9.1 of the Code.

#### **COMMENTS FROM LEO**

Leo submitted no additional information but highlighted the following points:

- the single MSL team would always be directly managed by a medical, non-commercial role. As there was a single MSL team all the MSLs would have both a direct reporting line and also direct access to the medical director. The governance of the activities of the MSLs would remain the responsibility of the medical director and consequently this should not impact the original Panel rulings.
- appropriate governance arrangements were covered by the work instruction previously provided. Leo was confident that the work instruction met the appropriate governance needs and correct support for the MSLs as well as the MSLs interim head/head of sales (thrombosis) to operate compliantly during this period.
- the interim reporting line decision was only taken after careful consideration of the compliance requirements to ensure the whole team (both MSLs and the interim head of MSLs) was adequately supported and that consideration was evidenced by the details within the email announcement, sent before the anonymous complaint was made.

Leo submitted that this clearly demonstrated its commitment to the requirements of the Code and it denied breaches of Clauses 9.1 and 2.

#### **PANEL RULING**

The Panel noted its previous rulings of no breaches of Clauses 9.1 and 2. The Panel had considered that there was no evidence to support the complainant's allegation that the line management of the dermatology MSLs was necessarily unacceptable. Leo had provided draft material to show that it had recognised the inherent conflicts of interest in its interim management arrangements but had taken steps to mitigate and manage these. The Panel noted Leo's submission that the product areas, thrombosis and dermatology were distinct and separate. The complainant had cited no examples of inappropriate conduct by either the interim manager or the MSLs.

The Panel noted Leo's subsequent clarification that there was a single MSL team that would carry

out activities in both dermatology and thrombosis therapy areas. Previously the Panel was under the impression that there were two distinct MSL teams. The Panel considered that although Leo had not actually stated in its original response that there were two separate MSLs teams, it did not clearly state that a single MSL team was responsible for activities in both the thrombosis and dermatology therapy areas. The Panel noted Leo's submission that '...its thrombosis and dermatology business units were so distinct and separate...' and that 'They were served by two distinct sales forces that did not promote products in both therapy areas' and considered that it was not explicitly clear that there was only one MSL team carrying out activities in both therapy areas. The Panel considered that the confusion was due to a misunderstanding and lack of clarity.

The Panel noted that MSLs carrying out activities in thrombosis would report to the head of sales (thrombosis), albeit only in relation to their activities in dermatology, as did the thrombosis sales force. The interim dual role of the head of sales (thrombosis) and the dual responsibilities and reporting lines of the MSLs needed to be very carefully managed. It did not appear that Leo had finalised the work instruction. It was important to consider whether the activities were compatible with each other if they were undertaken by one individual, and how the activities were perceived. The more functions combined into one role the more difficult it was to ensure compliance with the Code

and generally promotional and non-promotional activities should be performed by separate staff. The Panel noted Leo's submission that the governance of the MSL function would remain the medical director's responsibility.

The Panel noted its concerns above but considered that there was still no evidence to support the complainant's allegation that the line management of the MSLs in relation to dermatology by the head of sales (thrombosis) was necessarily unacceptable. Leo had provided draft material to show that it had recognised the inherent conflicts of interest in its interim management arrangements but had taken steps to mitigate and manage these. The interim head of MSLs was required to ensure that all of his/her interactions with MSLs were related to dermatology activities only and to refer MSLs to the medical director if any matters were raised in relation to thrombosis activities. When accompanying MSLs as a manager to visit a health professional in relation to dermatology, he/she would forego attendance in the unlikely event that the health professional was known to him/her in a sales capacity. The complainant had cited no examples of inappropriate conduct by either the interim manager or the MSLs. The Panel therefore ruled no breach of Clauses 2 and 9.1.

|                           |                      |
|---------------------------|----------------------|
| <b>Complaint received</b> | <b>11 April 2016</b> |
| <b>Case completed</b>     | <b>3 June 2016</b>   |

# ANONYMOUS, NON-CONTACTABLE v MERCK SHARP & DOHME

## Diabetes meeting sponsorship

An anonymous, non-contactable complainant complained about Merck Sharp & Dohme's involvement in a study day for community diabetes nurses.

The complainant alleged that all of the speakers were paid by Merck Sharp & Dohme. However, nowhere on the agenda was it clearly stated that this was fundamentally a Merck Sharp & Dohme meeting. Whilst it appeared as though the meeting was organized by the local community diabetes nurses, the complainant alleged that it was organised by Merck Sharp & Dohme and requested an investigation with a view to ensuring all future meetings were clear and transparent with regard to pharmaceutical company input.

The detailed response from Merck Sharp & Dohme is given below.

The Panel noted that the complainant had provided no evidence to support his/her allegations and could not be contacted for more information.

The Panel noted that the community diabetes nurses study day was not a Merck Sharp & Dohme meeting as alleged. A letter from Merck Sharp & Dohme to the meeting organisers which set out the terms of agreement for sponsorship, clearly stated that payment was for stand space. Further, the company considered that the amount paid for stand space was fair. Merck Sharp & Dohme had not organised the meeting or paid the speakers as alleged. The invitation/agenda clearly listed the meeting sponsors, of which Merck Sharp & Dohme was one.

The Panel considered that there was no evidence to support the complainant's allegations and no breach of the Code was ruled including no breach of Clause 2.

An anonymous, non-contactable complainant complained about Merck Sharp & Dohme Limited's involvement in a study day for community diabetes nurses. The complainant provided a copy of the invitation and agenda for the meeting.

### COMPLAINT

The complainant submitted that he/she was not happy about the meeting for several reasons. The main reason was that all of the speakers were paid by Merck Sharp & Dohme to, the complainant believed, the sum of approximately £8,000. However, nowhere on the agenda was it clearly stated that this was fundamentally a Merck Sharp & Dohme meeting. The complainant submitted that he/she would not have gone if he/she had

known. Secondly, it appeared as though the meeting was organized by the local community diabetes nurses. The complainant alleged that this was not true. It was organised by Merck Sharp & Dohme. The complainant queried why, if the meeting was organised by Merck Sharp & Dohme, and all the speakers were paid by Merck Sharp & Dohme, this was not made clear.

The complainant requested that the meeting be investigated with a view to ensuring all future meetings were clear and transparent with regard to pharmaceutical company input.

When writing to Merck Sharp & Dohme, the company was asked to consider the requirements of Clauses 2, 9.1, 9.10 and 22.4 of the Code.

### RESPONSE

Merck Sharp & Dohme noted that the meeting, entitled 'Treat yourself – Boost your confidence in managing type II diabetes', was conceived, organised, arranged and run by the community diabetes nurses group. Merck Sharp & Dohme submitted that in that regard the meeting was a third party meeting ie one that had no organisational involvement from the company and was independently conceived, administered and held.

Merck Sharp & Dohme explained that the community diabetes nurses group asked the local representative for sponsorship to pay for the speakers and to pay them directly. The representative declined as, under PMCPA guidance and internal standard operating procedures, this would make the meeting a company meeting and advised that Merck Sharp & Dohme would only be able to sponsor stand space. As such, the company paid fair market value (amount stated) for stand space only with the understanding that this was an independent, third party meeting. Merck Sharp & Dohme had no involvement in the organisation or content of the meeting or selection of speakers. Merck Sharp & Dohme noted that a number of other pharmaceutical companies also sponsored the event and had promotional stands at the meeting.

Three local representatives attended the meeting to staff the stand but had no other role in the meeting. The agreement between the community diabetes nurses group was covered in a sponsorship agreement which was signed by the nurses on 7 April 2016. This agreement contained the specific instruction to the third party to declare the involvement of Merck Sharp & Dohme on all papers relating to the meeting. A copy of the agreement was provided.

Merck Sharp & Dohme stated that as it did not organise the meeting, and was one of a number of stand sponsors, the company believed it was the organiser's responsibility to add an appropriate declaration of sponsorship to its invitation. Further, it was clear on the last page of the invitation that Merck Sharp & Dohme was one of a number of pharmaceutical companies which sponsored this independent meeting. As a result, Merck Sharp & Dohme considered that the sponsorship arrangements for this meeting met the requirements of Clauses 9.10 and 22.4.

Merck Sharp & Dohme explained that the invitations to the study day were sent by the community diabetes nurses group; the company had no role in selecting or inviting delegates or in the production of the invitations or their distribution. The invitation correctly made it clear that the meeting was a community diabetes nurses meeting.

Merck Sharp & Dohme noted that the community diabetes nurses ran similar third party meetings once or twice a year. Merck Sharp & Dohme had no influence on the creation of the meeting, its content, choice of speakers or organisation of the meeting. Merck Sharp & Dohme did not contact the speakers before the meeting or contact or brief them in any way.

Merck Sharp & Dohme was not clear where the £8,000 quoted by the complainant came from. Merck Sharp & Dohme paid significantly less than that for exhibition space and had not been involved with the selection and payment of the speakers, or the content of the meeting. The community diabetes nurses group used this money to fund part of the meeting which might have included payment to speakers, but this was done as part of an arm's length agreement without Merck Sharp & Dohme involvement.

In conclusion, Merck Sharp & Dohme stated that it did not organise or have involvement in the organisation of the meeting. Merck Sharp & Dohme sponsored stand space at fair market value and the

invitation made it clear that Merck Sharp & Dohme was one of a number of pharmaceutical companies to sponsor the meeting. For these reasons, Merck Sharp & Dohme did not consider there to be a breach of Clauses 2, 9.1, 9.10 or 22.4.

#### **PANEL RULING**

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure for the Prescription Medicines Code of Practice Authority, stated that anonymous complaints would be accepted but that like all other complaints, the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties. The complainant had provided no evidence to support his/her allegations and could not be contacted for more information.

The Panel noted that the complainant had alleged that the community diabetes nurses study day was effectively a Merck Sharp & Dohme meeting. This was not so. The letter from Merck Sharp & Dohme to the meeting organisers which set out the terms of agreement for sponsorship, clearly stated that payment was for stand space. Further, the company considered that the amount paid for stand space was in line with fair market value. Merck Sharp & Dohme had not organised the meeting or paid the speakers as alleged. Page 6 of the invitation/agenda clearly listed the meeting sponsors, of which Merck Sharp & Dohme was one.

The Panel considered that there was no evidence to support the complainant's allegation that Merck Sharp & Dohme had not been transparent with regard to its involvement in the community diabetes nurses study day at issue or that it had it paid for the speakers as alleged. No breach of Clauses 2, 9.1, 9.10 and 22.4 were ruled.

**Complaint received**                      **18 April 2016**

**Case completed**                              **10 May 2016**

## **VOLUNTARY ADMISSION BY JANSSEN**

### **Failure to sit the examination for representatives within one year**

**Janssen voluntarily admitted that one of its sales managers failed to take the required examination within one year of commencing that role.**

**As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Janssen.**

**Janssen explained that in Autumn 2014, one of its employees became a first line sales manager. Details of the manager's previous roles (which did not include sales), qualifications and training were provided.**

**In June 2015, the learning and development (L&D) department was asked to clarify whether the manager needed to complete the ABPI representatives examination. The advice was 'No' given the employee's qualifications and training to date. This was an error. In April 2016 this advice was re-questioned and the L&D team raised the matter with the medical director, who confirmed the examination was required.**

**Janssen stated that these events amounted to a breach of the Code, since the individual had been in a sales management role for more than 12 months without sitting the ABPI examination.**

**The detailed response from Janssen is given below.**

**The Panel noted that Janssen made no submission that the manager's role was not within the definition of a representative. It therefore followed that the sales manager in question, who commenced employment in that role in Autumn 2014, should have taken an appropriate examination for the first time by Autumn 2015.**

**The requirement of the Code to take an examination within 1 year had not been met as acknowledged by Janssen and the Panel ruled a breach of the Code.**

**The Panel was concerned that neither an experienced manager nor Janssen's L&D department were clear about the requirement to take an examination. It did not appear that anyone had referred directly to the Code. The Panel further noted that Janssen's procedure for training employees on the Code did not cover the situation where an existing employee moved to a role which newly required them to take an appropriate examination. On balance the Panel decided that the failure to take the examination or recognise that the employee needed to take an appropriate examination amounted to a failure to maintain high standards and thus a breach of the Code was ruled.**

Janssen voluntarily admitted that one of its sales managers failed to take the required examination within one year of commencing that role.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Janssen.

#### **VOLUNTARY ADMISSION**

Janssen stated that in September 2014, one of its employees moved into a sales management role, responsible for leading a team of sales representatives. The employee had previously worked as a product manager, in Janssen medical affairs, for other pharmaceutical companies and prior to that as a health professional.

During time in Janssen medical affairs the employee completed signatory training but before formally becoming a Janssen signatory moved to another role in Janssen. Details of the manager's qualifications and training were provided.

In June 2015 the learning and development (L&D) department was asked to clarify whether the manager needed to complete the ABPI representatives examination. Janssen had no written record of a follow up conversation but later that year after being prompted by its learning management system (LMS) to provide a copy of his/her ABPI certificate, the manager again contacted L&D and was advised that the examination was not required given his/her qualifications and training to date. This was in error and based on a misunderstanding that given the manager's background (as a health professional and signatory training), the ABPI representative's examination was not needed. The manager had been trained on the company's work instruction (WI) on a number of occasions but the WI was followed based on the incorrect advice received.

In April this advice was re-questioned within the L&D team, prompted by a gap in the training records on the company LMS, and L&D raised the question of exemption with the medical director, who confirmed the examination was required.

Janssen stated that these events amounted to a breach of Clause 16.3, since the individual had been a sales manager for more than 12 months without sitting the ABPI examination.

Janssen was asked to provide the PMCPA with any further comments in relation to the requirements of Clauses 9.1 and 16.3.

## RESPONSE

Janssen stated this was a case of an experienced employee with significant relevant training (registered health professional and signatory-trained) moving into a sales management role from within the company. The company's standard operating procedure (SOP) indicated that anyone in a sales role must have taken the ABPI Medical Representatives Examination. On this occasion, given the employee's background, the SOP was unfortunately incorrectly interpreted by L&D and incorrect advice given. This was an isolated incident and one of low risk to Code compliance given the individual's training on the Code and as a health professional; and his/her pharmaceutical industry experience. In this context Janssen submitted that it had not failed to maintain high standards.

The employee did not take the ABPI Medical Representatives Examination within one year of being a sales manager.

The manager's email to the company's L&D department was provided. The gap in timelines from June to October 2015 reflected the verbal discussion that took place during this period between the representative and an L&D manager. The manager's October email was prompted by his/her training on the Work Instruction WI08558, Procedure for Training Employees on the ABPI Code of Practice, issued as training by Janssen's learning management system. The manager referred to this training in an email as 'ABPI requirement training'. The response from the L&D manager detailed the incorrect advice.

Following an internal audit of training records, the individual was flagged as the company did not have a record of his/her ABPI Medical Representatives Examination certificate on file. The response to the request to provide the certificate to L&D, caused L&D to review the original advice given in 2015. Further advice on whether, given the manager's training and background, an exemption was possible was then discussed with the medical director who confirmed the examination certification requirement. Janssen then duly reported a potential breach of Clause 16.3 to the PMCPA.

## PANEL RULING

The Panel noted that Clause 16.3 stated that representatives must take an appropriate

examination within the first year of their employment as a representative and pass it within two years of starting such employment. A representative was defined in the Code as someone who called on members of the health professions and others in relation to the promotion of medicines.

The Panel noted that Janssen made no submission that the manager's role was not within the definition of a representative. It therefore followed that as the sales manager in question commenced employment in that role in Autumn 2014 he/she should have taken an appropriate examination for the first time by Autumn 2015.

The Panel noted that the manager in question had been in post for over 18 months and had not yet taken an examination. The requirement of Clause 16.3 to take an examination within 1 year had not been met as acknowledged by Janssen and the Panel ruled a breach of that clause.

With regard to Clause 9.1, the Panel was concerned that neither an experienced manager nor the L&D department were clear about the requirement to take an examination. It did not appear that anyone had referred directly to the Code. The Panel further noted that the work instruction detailing the procedure for training employees on the Code did not cover the situation where an existing employee moved to a role which newly required them to take an appropriate examination. The exemptions to taking the ABPI examination were removed from the Code in 2006 and so in that regard the examination requirements of the Code were very simple. The Panel noted an email in 2016 referred to 'exemption criteria' and implied that the manager's need to take an appropriate examination might be 'a local decision'. On balance the Panel decided that the failure to take the examination or recognise that the employee needed to take an appropriate examination amounted to a failure to maintain high standards and thus a breach of Clause 9.1 was ruled.

**Complaint received**            **23 May 2016**

**Case completed**                **4 July 2016**

# CODE OF PRACTICE REVIEW – August 2016

Cases in which a breach of the Code was ruled are indexed in **bold type**.

|                        |  |   |  |                             |                |
|------------------------|--|---|--|-----------------------------|----------------|
| <b>AUTH/2805/12/15</b> | <b>Bayer v Guerbet</b>                             | <b>Offer of equipment</b>   | <b>Breach Clause 2</b>   | <b>No appeal</b>            | <b>Page 3</b>  |
| AUTH/2806/12/15        | Bayer v Mallinckrodt                               | Offer of equipment  | No breach  | No appeal                   | Page 8         |
| <b>AUTH/2808/12/15</b> | <b>Anonymous, non-contactable v Napp</b>           | <b>Therapy review and advisory board</b>  | <b>Breaches Clauses 2, 9.1, 12.1, 18.1 and 23.1</b>  | <b>Appeal by respondent</b> | <b>Page 14</b> |
| <b>AUTH/2811/12/15</b> | <b>Anonymous, non-contactable v Daiichi-Sankyo</b> | <b>Exhibition stand design and hospitality</b>  | <b>Breach Clause 18.1</b>  | <b>Appeal by respondent</b> | <b>Page 34</b> |
| AUTH/2813/12/15        | Anonymous, non-contactable v Pfizer                | Exhibition stand design and hospitality   | No breach  | No appeal                   | Page 38        |
| <b>AUTH/2815/12/15</b> | <b>AbbVie v Piramal</b>                            | <b>Sevoflurane material</b>   | <b>Breaches Clauses 4.1, 4.9, 4.10 and 9.1</b>   | <b>No appeal</b>            | <b>Page 40</b> |
| <b>AUTH/2820/2/16</b>  | <b>Media/Director v Hospira</b>                    | <b>Arrangements for an overseas meeting</b>   | <b>Breaches Clauses 2, 9.1, 18.1, 22.1 and 23.1</b>  | <b>No appeal</b>            | <b>Page 46</b> |
| <b>AUTH/2822/2/16</b>  | <b>Bayer v Daiichi-Sankyo</b>                      | <b>Promotion of Lixiana</b>   | <b>Two Breaches Clause 3.2</b><br><b>Two Breaches Clause 7.2</b><br><b>Breaches Clauses 7.4 and 7.8</b><br><b>Two Breaches Clause 7.10</b><br><b>Two Breaches Clause 9.1</b> | <b>No appeal</b>            | <b>Page 55</b> |
| <b>AUTH/2832/4/16</b>  | <b>Voluntary admission from Baxter Healthcare</b>  | <b>Failure to sit the examination for representatives within one year</b>             | <b>Breach Clause 16.3</b>  | <b>No appeal</b>            | <b>Page 64</b> |
| <b>AUTH/2833/4/16</b>  | <b>ALK-Abelló v Bausch &amp; Lomb</b>              | <b>Breach of undertaking</b>  | <b>Breach Clauses 9.1 and 29</b>   | <b>No appeal</b>            | <b>Page 66</b> |
| <b>AUTH/2834/4/16</b>  | <b>Takeda v Amdipharm Mercury</b>                  | <b>Promotion of Lutrate</b>   | <b>Breaches Clauses 3.2, 7.2 and 7.3</b><br><b>Two Breaches Clause 7.10</b><br><b>Breaches Clauses 8.1 and 9.1</b>   | <b>No appeal</b>            | <b>Page 70</b> |
| AUTH/2835/4/16         | Voluntary admission from Janssen                   | Invokana email  | No breach  | No appeal                   | Page 75        |
| AUTH/2837/4/16         | Anonymous, non-contactable employee v Leo Pharma   | In-house communications material and reporting line of a medical science liaison team | No breach  | No appeal                   | Page 78        |
| AUTH/2839/4/16         | Anonymous, non contactable v Merck Sharp & Dohme   | Diabetes meeting sponsorship  | No breach  | No appeal                   | Page 84        |
| <b>AUTH/2846/5/16</b>  | <b>Voluntary admission by Janssen</b>              | <b>Failure to sit the examination for representatives within one year</b>             | <b>Breaches Clauses 9.1 and 16.3</b>   | <b>No appeal</b>            | <b>Page 86</b> |







The Prescription Medicines Code of Practice Authority was established by the Association of the British Pharmaceutical Industry (ABPI) in 1993 to operate the Code of Practice for the Pharmaceutical Industry at arm's length from the ABPI itself. Compliance with the Code is obligatory for ABPI member companies and, in addition, over sixty non member companies have voluntarily agreed to comply with the Code and to accept the jurisdiction of the Authority.

The Code covers the advertising of medicines to health professionals and other relevant decision makers and also covers information about prescription only medicines made available to the public.

It covers:

- journal and direct mail advertising
- the activities of representatives, including any printed or electronic material used by them
- the supply of samples
- the provision of inducements in connection with the promotion of medicines and inducements to prescribe, supply, administer, recommend, buy or sell medicines by the gift, offer or promise of any benefit or bonus, whether in money or in kind
- the provision of hospitality
- the organisation of promotional meetings
- the sponsorship of scientific and other meetings, including payment of travelling and accommodation expenses
- the sponsorship of attendance at meetings organised by third parties
- all other sales promotion in whatever form, such as participation in exhibitions, the use of audio or video-recordings in any format, broadcast media, non-print media, the Internet, interactive data systems, social media and the like.

It also covers:

- the provision of information on prescription only medicines to the public either directly or indirectly, including by means of the Internet
- relationships with patient organisations
- disclosure of transfers of value to health professionals and organisations
- joint working between the NHS and pharmaceutical companies

- the use of consultants
- non-interventional studies of marketed medicines
- the provision of items for patients
- the provision of medical and educational goods and services
- grants, donations and benefits in kind to institutions.

Complaints submitted under the Code are considered by the Code of Practice Panel which consists of three of the four members of the Code of Practice Authority acting with the assistance of independent expert advisers where appropriate. One member of the Panel acts as case preparation manager for a particular case and that member does not participate and is not present when the Panel considers it.

Both complainants and respondents may appeal to the Code of Practice Appeal Board against rulings made by the Panel. The Code of Practice Appeal Board is chaired by an independent legally qualified Chairman, Mr William Harbage QC, and includes independent members from outside the industry. Independent members, including the Chairman, must be in a majority when matters are considered by the Appeal Board.

In each case where a breach of the Code is ruled, the company concerned must give an undertaking that the practice in question has ceased forthwith and that all possible steps have been taken to avoid a similar breach in the future. An undertaking must be accompanied by details of the action taken to implement the ruling. Additional sanctions are imposed in serious cases.

Further information about the Authority and the Code can be found at [www.pmcpa.org.uk](http://www.pmcpa.org.uk)

Complaints under the Code should be sent to the Director of the Prescription Medicines Code of Practice Authority, 7th Floor, Southside, 105 Victoria St, London SW1E 6QT

telephone 020 7747 8880  
facsimile 020 7747 8881  
by email to: [complaints@pmcpa.org.uk](mailto:complaints@pmcpa.org.uk).