Case AUTH/2808/12/15

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 occuring, 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 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 Miquest 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 Miquest 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.

<u>Products and interventions provided by the service provider to its nurses</u>

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.

<u>Further Relevant Information</u>

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**