CASE AUTH/2978/9/17

ANONYMOUS NON-CONTACTABLE CONSULTANT DERMATOLOGIST v JANSSEN

Promotion of Tremfya

An anonymous, non-contactable consultant dermatologist complained about a Janssen symposium entitled 'Emerging Treatments for Psoriasis: Unlocking the IL-23 Pathway'. The symposium was part of the British Association of Dermatologists' (BAD) annual meeting held in Liverpool, July 2017.

The flyer for the symposium referred to emerging treatments for psoriasis and that the meeting would provide an opportunity for focussing on the pivotal role of IL-23. The similarities and differences in the mechanism of action of therapies which targeted this cytokine and the latest data for guselkumab and other IL-23 targeting molecules would be presented. The flyer stated at the bottom, in small blue font, that guselkumab was not licensed in the UK.

The complainant provided a copy of the flyer for the 'so called' symposium which he/she had been given at the Janssen exhibition stand. The complainant stated that although the symposium was entitled 'Emerging Treatments for Psoriasis: Unlocking the IL-23 Pathway', it was obviously a presentation about guselkumab (Tremfya) as the weight of discussion and evidence presented related mainly to that product. The complainant was surprised to see prescribing information at the end of the presentation. At the time, guselkumab was not licensed anywhere in the world and although the meeting appeared to be a 'scientific' symposium, it appeared to actually be mainly about guselkumab. The complainant alleged that it was unacceptable to discuss a medicine which was not licensed in that way.

The detailed response from Janssen appears below.

The Panel noted that promotion was defined as any activity undertaken by a pharmaceutical company or with its authority which promoted the administration, consumption, prescription, purchase, recommendation, sale, supply or use of its medicines. The Panel noted that although the Code prohibited the promotion of a medicine prior to the grant of its marketing authorization, certain activities with regard to unlicensed medicines were permitted such as the legitimate exchange of medical and scientific information during the development of a medicine provided that this did not constitute promotion which was prohibited.

The legitimate exchange of scientific information during the development of a medicine should involve debate that enhanced the current state of knowledge. To avoid being seen as promotional, it should not be a one way flow of information.

The Panel noted that the symposium started at 18:15 and consisted of two presentations on 'Leveraging IL-23 in psoriasis' and 'What next for IL-23 inhibition?' (from 18:20 until 18:50). Ten minutes were then set aside for Q&A and discussion and the seminar finished at 19:00. The Panel queried whether the agenda allowed for 'the exchange of information' given the very limited time for discussion and input from the audience.

The Panel noted that the first presentation (20 minutes) had a title slide of 'Selective blockade of IL-23 in psoriasis – A novel treatment concept'. Half of the 34 slides looked at selective IL-23 inhibition; risankizumab clinical trials featured on one slide, clinical trial results for tildrakizumab were discussed on 5 slides and data from guselkumab trials were on 8 slides.

The second presentation was entitled 'What next for IL-23 inhibition?'; the certificate for the material, however, described the item as 'Slide deck for 10 minute presentation titled 'What next for guselkumab?'. Focussing on how it could change clinical practice, what it would mean for patients and what trials are … [the text then became unreadable]'. Of the 19 slides, 12 were specifically about guselkumab clinical trials. The Panel noted the original title for the presentation had been changed. It queried whether such a product-specific slide deck would have been written by the speaker.

The second presentation included prescribing information for Stelara which was referred to in the briefing notes as IL-12/23 so it appeared that there was a promotional element to the symposium.

The Panel noted that the purpose of the symposium set out in the briefing document for speakers did not mention the exchange of information and there was very limited time for such.

The evaluation form asked attendees to assess the session in terms of overall interest, fulfilment of learning objectives and to rate 'the relevance of the content i.e. could it change your clinical practice?'. The evaluation form also invited attendees to ask for 'further information on the topics discussed during this meeting'. In that regard, Janssen appeared to be soliciting questions about its unlicensed medicine.

It appeared that the Janssen booth included a commercial section and medical information staff would be present at certain times to provide assistance on a number of issues including off-label indications/uses, pipeline products and investigator initiated studies (IIS).

In the Panel's view, it was reasonable to assume that, on the balance of probabilities, many of the booth visitors would ask about guselkumab. The briefing materials prepared staff for such questions and medical information staff were there to answer such questions.

The Panel considered that the symposium in July 2017 focussed on Janssen's product which was authorized by the FDA on 13 July. Although the term 'investigational' was not defined, the Panel queried whether a product for which a marketing authorization was applied for in the US and received just over a week after the symposium and was going through the EMEA process for a marketing authorization could be considered to be an 'investigational molecule' or being 'in development'. In the Panel's view, health professionals were likely to view guselkumab as a pre-licence product.

The Panel did not consider that the arrangements for the symposium would lead to an exchange of information. The limited time for discussion together with the balance of information presented being about Janssen's new product which would be likely to receive a marketing authorization within a few months meant that the medicine had been promoted prior to the grant of its marketing authorisation. A breach of the Code was ruled.

The Panel ruled a breach as high standards had not been maintained. Promotion of an unlicensed medicine brought discredit upon and reduced confidence in the pharmaceutical industry so a breach of Clause 2 was also ruled.

On appeal by Janssen of all of the Panel's rulings of breaches of the Code, the Appeal Board noted that under the objectives' the briefing for the speakers and chairman made no mention that discussion and an exchange of scientific information were essential; the stated objectives implied that data was being presented.

The Appeal Board noted from the transcript of the meeting that there were only two questions from the audience despite encouragement from the chair. The Appeal Board considered this was surprising given the data and the potential impact of a different treatment approach. The Appeal Board considered that the company should have done much more to engage the audience and to stimulate debate to enable two-way discussion and an exchange of medical and scientific information.

The Appeal Board considered that there was very little evidence of any legitimate scientific exchange. The Appeal Board did not consider whether the medicine was still in development; this had not been raised by the complainant. The Appeal Board considered that the balance of information presented in the second presentation was about Janssen's new product which would be likely to receive a marketing authorization within a few months and that this in conjunction with the points mentioned above meant that the medicine had been promoted prior to the grant of its marketing authorisation. The Appeal Board upheld the Panel's ruling of a breaches of the Code including Clause 2. The appeals on all points were unsuccessful.

An anonymous, non-contactable consultant dermatologist complained about a Janssen symposium entitled 'Emerging Treatments for Psoriasis: Unlocking the IL-23 Pathway'. The symposium was part of the British Association of Dermatologists' (BAD) annual meeting held in Liverpool, 4-6 July 2017.

The flyer for the symposium referred to emerging treatments for psoriasis and that the meeting would provide an opportunity for focussing on the pivotal role of IL-23. The similarities and differences in the mechanism of action of therapies which targeted this cytokine and the latest data for guselkumab and other IL-23 targeting molecules would be presented. The flyer stated at the bottom, in small blue font, that guselkumab was not licensed in the UK.

COMPLAINT

The complainant provided a copy of the flyer (ref PHGB/MEDed/0517/0010c) for the 'so called' symposium which he/she had been given at the Janssen exhibition stand. The complainant stated that although the symposium was entitled 'Emerging Treatments for Psoriasis: Unlocking the IL-23 Pathway', it was obviously a presentation about guselkumab (Tremfya), as the weight of discussion and evidence presented related mainly to that product. The complainant was surprised to see information at the end of the presentation which looked like the sort of material he/she would normally see at the end of a sales representative's documents, describing guselkumab prescribing features, side effects etc. The complainant did not think that, at the time, guselkumab was licensed anywhere in the world and certainly not in the UK and although the meeting appeared to be a 'scientific' symposium, it appeared to actually be mainly about guselkumab. The complainant alleged that it was unacceptable to discuss a medicine which was not licensed in that way.

When writing to Janssen, the Authority asked it to consider the requirements of Clauses 2, 3.1, 9.1 and 12.1 in relation to the symposium.

RESPONSE

Janssen submitted that no materials on its exhibition stand were about guselkumab or the Janssen symposium. The symposium flyer was only available in the BAD delegate bags at the conference; it was not available on the stand. The flyer clearly acknowledged Janssen's involvement, as it stated: 'This session is organised and funded by Janssen and intended for healthcare professionals only'.

Janssen submitted that commercial and medical activities were kept entirely separate and the exhibition stand at the BAD meeting was a promotional stand for Stelara (ustekinumab). The sales force briefing document (copy provided) was

clear and explicit in its instruction that commercial and sales staff were only to provide on-label product information for Stelara.

With regard to the symposium itself Janssen considered that it had acted in keeping with both the letter and the spirit of the PMCPA guidance about Clause 3 in that the fostering of legitimate exchange of medical and scientific information during the development of a medicine was permissible.

Janssen submitted that it had acted in accordance with the guidance, with the symposium's intent and structure being to foster legitimate scientific exchange. The audience was self-selected by virtue of being attendees at the UK's leading dermatological congress and the symposium was an integral part of the official congress programme, confirmed by the BAD programme committee.

Janssen submitted that when the symposium was held, (and still currently), guselkumab was not licensed in the UK for any indication.

On 13 July 2017, guselkumab was approved in the US by the FDA for the treatment of adults with moderate to severe plaque psoriasis who were candidates for systemic therapy or photo therapy.

On 15 September 2017, the Committee for Medicinal Products for Human Use (CHMP) gave a positive opinion for guselkumab in the treatment of adults with moderate to severe plaque psoriasis who were candidates for systemic therapy and the Final Commission Decision from the European Medicines Agency (EMA) was expected on 20 November 2017. There were two other selective IL-23 inhibitors in development for plaque psoriasis; tildrakizumab (Merck Sharp & Dohme, Sun Pharma, Almirall) and rizankizumab (Boehringer, Abbvie).

When the symposium was held, two phase III trials had been published on the use of tildrakizumab in this indication whilst only phase II data had been published on risankizumab. The development programs for both molecules were ongoing and data from these formed an integral part of the symposium. Janssen could not comment on the regulatory timelines of the other products. Guselkumab was also in development for pustular psoriasis, palmoplantar pustulosis, and psoriatic arthritis.

The speaker briefing guides included both general guidance around the Code clauses to be adhered to and additionally, specific guidance on inclusion of detailed analysis of the data from the development programmes of the other IL-23 inhibitors.

The presentations were prepared by the speakers and did not include any brand colours or logos or the brand name for guselkumab. Analyses of all 3 available IL-23 molecules were included and there were no case-based discussions or testimonials of the use of guselkumab outside of the clinical trial setting.

Janssen asserted that this was a scientific symposium on the role of IL-23 targeting molecules including guselkumab, with data for the other molecules presented in a fair and balanced manner.

The development program for guselkumab was more advanced compared with the other two molecules, in terms of timelines, number of studies and indications under investigation. The available data reflected this fact and informed the balance of information presented at the symposium.

Janssen provided a list and copies of the symposium material to include briefing documents, presentations and evaluation form. The company also provided a list of company employees who attended the meeting.

Janssen submitted that the symposium met the requirements of scientific exchange and as such it denied a breach of Clauses 3.1 and 12.1. Consequently, Janssen also believed that high standards had been maintained and that therefore it had not brought discredit upon, or reduced confidence in, the pharmaceutical industry. Janssen thus denied breaches of Clauses 9.1 or 2.

With regard to the complainant's comments about information seen at the end of the presentation, the deck presented by one of the speakers included Stelara prescribing information at the end of it, not as suggested by the complainant, guselkumab prescribing information which was not yet available. The Stelara prescribing information was included because Stelara data were shown and informed part of the discussion and it was a currently Janssen marketed product.

Janssen noted that there was no advertising of the symposium by commercial or sales staff, the speakers were all independent health practitioners and the speaker briefings demonstrated Janssen's commitment to the fair and balanced portrayal of the available data.

Janssen also noted that it had commented on the weighting of the data presented which reflected the more advanced clinical development program for guselkumab compared with the other selective IL-23 blocking agents. The company believed that the symposium met the requirements of scientific exchange and the activities surrounding it were therefore not in breach of Clauses 3.1 and 12.1. Janssen therefore denied breaches of Clauses 9.1 or 2.

Janssen repeated that it had maintained a high standard in all activities relating to the symposium and it would not be seen to either discredit, or reduce confidence in the industry.

In conclusion, Janssen denied any breach of Clauses 2, 3.1, 9.1 and 12.1 in relation to the symposium.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure for the Prescription Medicines Code of Practice Authority stated that anonymous complaints would be accepted but that like all other complaints,

the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties.

The Panel noted that Clause 1.2 defined promotion as any activity undertaken by a pharmaceutical company or with its authority which promoted the administration, consumption, prescription, purchase, recommendation, sale, supply or use of its medicines. The Panel noted that although Clause 3 prohibited the promotion of a medicine prior to the grant of its marketing authorization, the Code permitted companies to undertake certain activities with regard to unlicensed medicines. The supplementary information to Clause 3 provided additional details including a statement that the legitimate exchange of medical and scientific information during the development of a medicine was not prohibited provided that this did not constitute promotion which was prohibited by Clause 3 or any other clause. The PMCPA Guidance about Clause 3 further stated that companies must ensure that such activities constituted a genuine exchange of information and were not promotional. Documents must not have the appearance of promotional material. It should be borne in mind that it would be a breach of the Code if non-promotional information on products or indications that were not licensed was used for a promotional purpose.

The legitimate exchange of scientific information during the development of a medicine should involve debate that enhanced the current state of knowledge. To avoid being seen as promotional, it should not be a one way flow of information.

The Panel noted that the symposium started at 18:15 and consisted of two presentations on 'Leveraging IL-23 in psoriasis' and 'What next for IL-23 inhibition?' (from 18:20 until 18:50). Ten minutes were then set aside for Q&A and discussion and the seminar finished at 19:00. The Panel queried whether the agenda allowed for 'the exchange of information' given the very limited time for discussion and input from the audience.

The Panel noted that the first presentation (20 minutes) had a title slide of 'Selective blockade of IL-23 in psoriasis – A novel treatment concept'. Half of the 34 slides looked at selective IL-23 inhibition; risankizumab clinical trials featured on one slide, clinical trial results for tildrakizumab were discussed on 5 slides and data from guselkumab trials were on 8 slides.

The second presentation was entitled 'What next for IL-23 inhibition?'; the certificate for the material, however, described the item as 'Slide deck for 10 minute presentation titled 'What next for guselkumab?'. Focussing on how it could change clinical practice, what it would mean for patients and what trials are … [the text then became unreadable]'. Of the 19 slides, 12 were specifically about guselkumab clinical trials. The Panel noted the original title for the presentation had been changed. It queried whether such a product-specific slide deck would have been written by the speaker.

The Panel noted that the second presentation included prescribing information for Stelara which was referred to in the briefing notes as IL-12/23 so it appeared that there was a promotional element to the symposium.

The purpose of the symposium was set out in the briefing document for speakers as:

'This is an educational symposium, and the objectives for attendees are:

- To revisit the structure and role of IL-23, including differentiating between the p40 and p19 subunits, and how these can be targeted independently by psoriasis treatments.
- To develop an understanding of guselkumab and other IL-23 molecules clinical trial data.
- To relate understanding of the clinical trial data to the future of your clinical practice and patient outcomes.'

The Panel noted that there was no mention of the exchange of information and there was very limited time for such.

The evaluation form asked attendees to assess the session in terms of overall interest and fulfilment of learning objectives. Attendees were also asked to rate 'the relevance of the content i.e. could it change your clinical practice?'. The evaluation form also invited attendees to ask for 'further information on the topics discussed during this meeting'. In that regard, Janssen appeared to be soliciting questions about its unlicensed medicine.

It appeared from the Janssen staff briefing notes that the Janssen booth included a commercial section and that medical information staff would be present at certain times to provide assistance on a number of issues including off-label indications/uses, pipeline products and IIS.

In the Panel's view, it was reasonable to assume that, on the balance of probabilities, many of the booth visitors would ask about guselkumab. The briefing materials prepared staff for such questions and medical information staff were available to answer such questions.

The Panel considered that the symposium in July 2017 focussed on Janssen's product which was authorized by the FDA on 13 July. Although the term 'investigational' was not defined, the Panel queried whether a product for which a marketing authorization was applied for in the US and received just over a week after the symposium and was going through the EMEA process for a marketing authorization could be considered to be an 'investigational molecule' or being 'in development'. In the Panel's view, health professionals were likely to view guselkumab as a pre-licence product.

The Panel did not consider that the arrangements for the symposium would lead to an exchange of information. The limited time for discussion together with the balance of information presented being about Janssen's new product which would be likely

to receive a marketing authorization within a few months meant that the medicine had been promoted

prior to the grant of its marketing authorisation. A breach of Clause 3.1 was ruled.

The Panel considered that high standards had not been maintained. A breach of Clause 9.1 was ruled. Promotion of an unlicensed medicine brought discredit upon and reduced confidence in the pharmaceutical industry so a breach of Clause 2 was also ruled.

APPEAL BY JANSSEN

Janssen prided itself on being an ethical company and it did not agree with the Panel's rulings of breaches of Clause 2, 3.1 and 9.1 which it appealed.

Background

Janssen stated that the 97th Annual Meeting of the BAD that took place in Liverpool from 4-6 July 2017 was the largest dermatology meeting in the UK with over 1000 delegates attending a mixture of plenary sessions, keynote lecturers, special interest group sessions, hot topics and focus sessions, where scientific discussion and debate routinely took place, including at those sessions sponsored by pharmaceutical companies.

Janssen submitted that its activities at the congress included a Stelara only promotional stand in the main exhibition hall and the company-sponsored symposium in question.

In the spirit of transparency, Janssen pointed out that it had also held a hot topics session, covering registry data entitled 'Long-term management of psoriasis: applying learnings from registry data' and the slides were provided. The session was held within the exhibition hall, but separate to the stand and was an integral part of the congress program. This activity had not been subject to any complaint or alleged breach and was entirely unrelated to guselkumab or the symposium content.

Janssen submitted that its policy was to have clear separation between medical educational and commercial activities. Janssen reiterated this point to assert the fact that all activities pertaining to the symposium at the BAD congress were wholly owned and run by members of the UK Janssen Immunology Medical Affairs team, consisting of the medical education manager and the medical advisor working in collaboration with its retained medical communications agency. A brief description of these roles was provided.

Janssen submitted that both roles were entirely non-promotional in nature and reflected the fact the organisation of the symposium was in no way linked to commercial activities, such as the promotional stand at the congress. In line with Janssen's UK congress guidelines (ref TV-GDL-00753), which all Janssen employees at congress had to have completed prior to attendance, there were no Janssen sales personnel at the symposium and the symposium attendee list was not shared with them.

In addition, the symposium materials (invitations and slides) bore no resemblance to promotional materials, and this 45-minute symposium was the only Janssen organised activity at the BAD congress related to IL-23 or guselkumab. No follow-up activities were conducted with attendees.

Janssen noted that the Panel had queried whether the agenda allowed for 'the exchange of information' given the very limited time for discussion and input from the audience. The PMCPA's supplementary information with guidance on Clause 3 and specifically, wording directing companies to avoid being seen as disseminating data to expand the use of their products by ensuring that such activity must not be a 'one way flow of information'.

Janssen submitted that when the science, as it related to a new pathway or molecular target was new to the scientific community a certain amount of time needed to be devoted to the foundational knowledge, in order to facilitate a more informed debate. Janssen's assertion was that this was the balance it had sought to strike as it developed the content for the symposium. Whilst the Panel had examined the timings of the presentations, Janssen was not in agreement with the assessment of the proportion of time spent on the various elements of the symposium which would have afforded a true legitimate exchange.

Janssen submitted that it had examined audio recordings and raw transcripts of the symposium (provided) and when one excluded the welcome from the chair, house-keeping notes and speaker disclosures, twenty five percent (25%) of the rest of the symposium was devoted to questions and answers, which was an adequate proportion given the points discussed above.

Janssen submitted that there was no PMCPA guidance on the appropriate proportion of discussion time within such meetings, but stated that the amount of time at this meeting was aligned with Janssen policy of having at least 20% of the time being devoted to discussion. In order to facilitate this active discussion, questions could either be handed into the speakers by a card or asked directly from the floor. The discussion part of the symposium opened with the chair inviting questions from the audience with the words: 'We do have time for some questions. It would be nice if we could make this as interactive as possible'. The symposium only finished when all questions had been answered.

With regard to the Panel's note that 'the purpose of the symposium was set out in the briefing document …', Janssen submitted that this was an educational symposium, and the objectives for attendees were:

- To revisit the structure and role of IL-23, including differentiating between the p40 and p19 subunits, and how these could be targeted independently by psoriasis treatments.
- To develop an understanding of guselkumab and other IL-23 molecules clinical trial data.
- To relate understanding of the clinical trial data to the future of their clinical practice and patient outcomes.

Janssen confirmed that this was the first and only IL-23 symposium that it had held in the UK and that given this, reiterated the point that a certain amount of time needed to be spent on foundational knowledge of the pathophysiological elements of the IL-23 specific pathway to foster a more informed discussion. Janssen submitted that the breakdown of the symposium was as follows:

> Selective blockade of IL-23 in psoriasis – A novel treatment concept
> General psoriasis information ie pathogenesis, comorbidities etc (includes IL-17 inhibition information) – 19.67%
> IL-23 in general – 33.47%
> Guselkumab – 19.82%
> Risankizumab – 6.90%
> Tildrakizumab – 10.27%
>
> What next for IL-23 Inhibition?
> General psoriasis information ie pathogenesis, comorbidities etc – 0%
> IL-23 in general – 35.77%
> Guselkumab – 55.87%
> Risankizumab – 0%
> Tildrakizumab – 0%.

Janssen submitted that the balance of the data presented at the symposium was reflective of the disclosures in the public domain at the time of planning the symposium. A search of clinicaltrials.gov revealed that of the 18 studies evaluating IL-23 inhibitors in psoriasis, 8 were guselkumab trials, representing just under half of the combined investigational agents in this field. A thorough literature review was performed on selective IL-23 inhibitor development program (provided). The review was conducted by Janssen's medical communications agency and performed first in the week commencing 5 June 2017 and repeated in the week commencing 26 June (ie the week prior to the BAD congress) ensured that no new disclosures had been made in the intervening period. This document clearly demonstrated the greater number of guselkumab disclosures, owing to its more advanced development program and therefore reflected the balance of the data presented at the symposium.

Janssen pointed out that the late addition of recently published data (on risankizumab), which necessitated further rounds of review, also demonstrated its commitment to presenting a fair and balanced representation of the publicly up to date available data.

In response to the Panel's assessment of the second presenter's presentation, again, Janssen submitted that these were reflective of the ongoing program for the IL-23 inhibitors of which guselkumab was most advanced. These included further investigational indications such as psoriatic arthritis, inflammatory bowel disease and the possibility of disease modification with IL-23 inhibition. The data shown in relation to this were, from early phase trials, investigative in nature and in no way meant to promote the medicine for current clinical use. Rather, the aim was to inform the audience on the direction that clinical research on the IL-23 pathway in general was heading beyond only the psoriasis indication.

The symposium was 45 minutes attended by approximately 70 delegates, who were by definition, a self-selected audience and as previously stated, were invited to the symposium only through a flyer in the delegate bags. No invitations were made from the stand. Furthermore, there were no other Janssen activities including materials, posters or literature pertaining to IL-23 or guselkumab at the BAD meeting.

ith regard to the Panel's comment that '… the certificate for the material, however, described the item as "Slide deck for 10 minute presentation titled 'What next for guselkumab?"', Janssen submitted that the change of the original title from 'What next for IL-23 inhibition?' to 'What next for guselkumab?' was due to an unfortunate error by Janssen's agency which uploaded the job summary. As could be seen from Zinc from the first round of review, the document was always titled 'What next for IL 23 inhibition?'. Janssen referred to the briefing guide to the speaker as stated below and confirmed that no materials distributed to either speakers or delegates contained the title 'What next for guselkumab?.

Janssen noted that the Panel had queried 'whether such a product-specific slide deck would have been written by the speaker'. Janssen submitted that both speakers were eminent in their fields and as could be seen from their disclosures, conducted consultancy and research activities for numerous companies, including direct competitors in this therapy area. Specifically, the first presenter had been involved as an investigator in the development of all three IL-23 inhibitors, acted as a consultant in this field for several different pharmaceutical companies and had served as consultant and/or paid speaker for and/or participated in clinical trials. Details were provided.

Janssen submitted that its speaker briefings were also clear in its direction to its speakers: 'This meeting is non-promotional and aims to facilitate the exchange of scientific and medical information. We ask that speakers give a fair and balanced interpretation and analysis of data'. Janssen provided the email trail between its agency and the speakers requesting their slides to demonstrate that the slides were entirely the work of the speakers.

Janssen noted the Panel's comments about the evaluation form where attendees were also asked to rate 'the relevance of the content i.e. could it change your clinical practice?' and also invited to ask for 'further information on the topics discussed during this meeting'. In that regard, the Panel considered Janssen appeared to be soliciting questions about its unlicensed medicine. Janssen submitted that the evaluation form used was its standard template evaluation form, utilised at all medical educational events, completion of which was not compulsory. The primary use of the form was to collect feedback that allowed for continued improvement in the Janssen medical education programme. As previously stated, the symposium included topics covering the pathophysiology of psoriasis based on

the most current science. In particular, the newer IL-17 molecules, as well as discussions around co-morbidities such as uveitis and depression. Awareness of these might rightly have led clinicians to consider their practice and as such Janssen submitted that the section within the evaluation form about enquiring 'could it change your clinical practice' was appropriate in this setting. There was no inference that this was referring to prescribing habits and contrary to the Panel's suggestion neither was there any intention to solicit questions about Janssen's unlicensed medicine.

Rather, Janssen submitted that owing to fact that the symposium was short, Janssen chose to include in the form a section where the self-selected audience could ask any further scientific questions of its medical department should they not have had the opportunity in the symposium. This was to facilitate continued scientific exchange and any responses given would have been from the medical information team in response to the specific question asked. It also stipulated that the persons' email address/ phone number provided for the request would only be used for this purpose and no other follow up or promotional activity. Additionally, Janssen submitted that due to the fact the promotional stand at the BAD was a Stelara-only one and had no medical section/attendance, this was also included to ensure people did not seek out the promotional stand if they had any outstanding questions relating to the symposium. On examination of the evaluation forms Janssen identified a single request for information on IL-23.

Janssen submitted that its medical information department had reviewed all the guselkumab and IL-23 enquiries received over July 2017 and confirmed that no enquiries were logged during the BAD, and it had identified one delegate who attended the symposium and subsequently logged an enquiry via his account manager after the conference as follows:

> 'Dr X was at the BAD conference recently and he attended the guselkumab seminar. He is interested to understand more about this new molecule, especially around trials for 'disease modifying' capabilities. Please may I request an MSL visit? I explained as unlicensed I was unable to respond.'

Janssen submitted that the request had been processed through its medical information team.

Janssen noted that '… the Panel queried whether a product for which a marketing authorization was applied for in the US and received just over a week after the symposium and was going through the EMEA process for a marketing authorization could be considered to be an "investigational molecule" or being "in development". In the Panel's view, health professionals were likely to view guselkumab as a pre-licence product'. The Panel also noted that regulatory timelines for both the FDA and EMEA were close to the timing of the symposium and made the distinction between an investigational and pre-licence product. However, Janssen submitted that planning for the symposium commenced in March 2017 (email trail provided) and Janssen's internal working timelines for marketing authorisation from EMEA was in the first quarter of 2018. The EMEA timelines scenario planning (provided) demonstrated that Janssen's base case scenario for EC decision was 19 February 2018; eleven months ahead of when the planning began and seven months ahead of when the symposium was scheduled to occur. As it was, the EC decision arrived five to six months prior to when Janssen had anticipated and both at the time of planning and at the time the symposium occurred, Janssen could not have predicted this.

Janssen submitted that at the time this symposium was being planned and in the absence of prescriptive guidance on where the threshold between investigational and pre-licence product should lie, guselkumab could be considered an investigational product and was thus a legitimate candidate for a symposium at a learned congress where data were presented in a fair, balanced manner, reflective of the body of scientific disclosures in the public domain.

Janssen drew the Appeal Board's attention to the point made on the first presenter's first disclaimer slide to this effect, which stated 'This presentation contains information about products which are in development and are not licensed in the UK'.

Janssen noted that the Panel had noted that '… staff briefing notes that the Janssen booth included a commercial section and that medical information staff would be present at certain times to provide assistance on a number of issues including off-label indications …'. 'In the Panel's view, it was considered reasonable to assume that, on the balance of probabilities, many of the booth visitors would ask about guselkumab'. Janssen reiterated the clear separation between medical and commercial activities at the congress and it had also previously provided its briefing document to this end. Janssen again drew attention to the exact wording in the briefing, which stated that 'Medical Information (MI) Medical Education (who will be present at certain times) will provide assistance in the following situations upon request: – Off-label indications/ uses – Pipeline products – IIS – Additional in-depth information required – Adverse event (AE) reports – Product quality complaints (PQCs)'. Furthermore, there was no information about guselkumab or IL-23 at the booth ie no posters, papers, medical education materials, that any staff could have access to.

In addition, Janssen had a congress guideline which all staff were trained on which clearly delineated the role of medical and commercial at congresses (ref TVG-DL-00753 provided).

Janssen was, therefore, not in agreement with the Panel's view that there was, in any way, the intention to solicit off-licence questions about guselkumab. There were minor provisions made in the form of medical information request cards on the stand to capture any details of the requester and outline the questions that could then be followed up after the congress in a reactive manner. Janssen submitted that this was the provision of a responsible and legitimate medical information service. Contrary to the Panel's view regarding the balance of

probabilities, the number of guselkumab-related questions at the booth was zero.

With regard to the Panel's comments that the second presentation included prescribing information for Stelara … so it appeared there was a promotional element to the symposium', Janssen referred to previously stated rationale for inclusion of the Stelara prescribing information at the end of the presentations. The presentation included a trial which had Stelara as a comparator arm and although no promotional claims were made about Stelara, it submitted that provision of information such as contraindications, common and serious side effects and where to report adverse events for a licensed product would be of value to the audience. The decision to include the Stelara prescribing information at the symposium was so as not to drive delegates to the booth to seek prescribing information should they want it, and hence limit the traffic to the booth post the symposium. The use of the prescribing information was not intended to identify the symposium as being promotional, however, given historic cases, Janssen could see how this could be misconstrued by the Panel. Janssen's assertion was that the provision of prescribing information did not necessarily make an event promotional.

In conclusion, Janssen submitted that it had acted within the letter and the spirit of the Code. The limited amount of information shared about IL-23 inhibitors and guselkumab, which were all in development at the time of symposium had been demonstrated within the transcript of the symposium, as well as the opportunity for the audience members to participate in dialogue with the panel members for 25% of the time. Whilst guselkumab was being evaluated by the health authorities at the time of the symposium in July 2017, the licence had not yet been granted and therefore constituted a medicine in development. In fact, during the planning of the symposium the licence was not expected until Q1 2018, over 6 months from the time of the BAD meeting. No other activities related to IL-23 or guselkumab were conducted at the BAD by Janssen, and no materials were available. Usually the burden of proof sat with the complainant, however in this case it was an anonymous non-contactable one. Despite this, Janssen submitted that it had shown that this single symposium in the context of a learned society congress did not constitute pre-licence promotion, and hence denied breaches of Clauses 3.1, 9.1 and 2.

APPEAL BOARD RULING

The Appeal Board noted the supplementary information to Clause 3 stated that the legitimate exchange of medical and scientific information during the development of a medicine was not prohibited provided that any such information or activity did not constitute promotion which was prohibited under this or any other clause. The PMCPA Guidance about Clause 3 further stated that companies must ensure that such activities constituted a genuine exchange of information and were not promotional. Documents must not have the appearance of promotional material. It should be borne in mind that it would be a breach of the Code if non-promotional information on products or indications that were not licensed was used for a promotional purpose. The legitimate exchange of scientific information during the development of a medicine should involve debate that enhanced the current state of knowledge. To avoid being seen as promotional, it should not be a one way flow of information.

The Appeal Board noted that the symposium in question took place on 5 July 2017 and at that time although Janssen anticipated a CHMP opinion for guselkumab on 19 February 2018 it was in fact received on 15 September 2017. The marketing authorization was received in November 2017. Guselkumab was authorized by the FDA in the US on 13 July 2017.

With regard to the invitation flyer for the symposium, the Appeal Board considered that there was no evidence to show that this was available from the Janssen stand as alleged.

The Appeal Board noted that the symposium started at 18:15 and consisted of two presentations on 'Leveraging IL-23 in psoriasis' and 'What next for IL-23 inhibition?' (from 18:20 until 18:50). Ten minutes were then set aside for Q&A and discussion and the seminar finished at 19:00.

The Appeal Board noted that under the heading 'Meeting rationale and objectives' the briefing for the speakers and chairman made no mention that discussion and an exchange of scientific information were essential; the stated objectives implied that data was being presented. The general guidance for presentations stated that 'This meeting is non-promotional and aims to facilitate the exchange of scientific and medical information…' but did not make it clear that exchange of scientific information and discussion were critical.

The Appeal Board noted that Janssen provided guidance to the speakers about which topics should be discussed.

The Appeal Board noted that most of the available data for IL-23 inhibition related to guselkumab; there were two other selective IL-23 inhibitors in development for psoriasis; tildrakizumab and rizankizumab. There was no mention of tildrakizumab or rizankizumab data in the second presentation although this was included in the first presentation. The Appeal Board noted the trial data in the presentations which was discussed at the symposium; the transcript stated that these molecules presented a change in the treatment of psoriasis and that the chairman noted that '…it's important, obviously, for these companies to be first-to-market or have other differentiating data…'.

The Appeal Board noted Janssen's submission that the Zinc approval form (dated 4 July) for the second presentation was titled 'What next for guselkumab?' in error by its agency and that from the first round of the Zinc review the slide deck was always titled

'What's next for IL-23 inhibition?'. In that regard the Appeal Board noted that the Zinc approval dates were very close to the date of the symposium. The Appeal Board noted that of the 19 slides, 12 were specifically about guselkumab clinical trials. The Appeal Board noted from the Zinc approval form that the objective of the second presentation was to 'Develop an understanding of the guselkumab clinical trial data' and 'To relate understanding of the guselkumab clinical trial data to the future of your clinical practice and patient outcomes'. In that regard, the Appeal Board considered that the balance of the second presentation was specific to guselkumab.

The Appeal Board noted the information provided by Janssen regarding the time taken for the presentations and topics calculated from the transcript.

One of the symposium attendees had subsequently logged an enquiry via his/her Janssen account manager which had been referred to the medical information department. The account manager stated that 'Dr X was at the BAD conference recently and he attended the guselkumab seminar…'. It thus appeared that the perception of the symposium was that it was about guselkumab.

The Appeal Board considered that the inclusion of prescribing information for Jansen's product Stelara (which was licensed for the treatment of plaque psoriasis) on the second presentation added to the impression that the meeting was promotional.

The Appeal Board noted that the first (and main) presentation lasted for 20 minutes and was pre-recorded. The speaker was unavailable to answer questions at the meeting. The Appeal Board queried whether this format contributed to the low level of questions. After the presentations questions could either be handed into the speaker who was present or the chairman by a card, or asked directly from the floor.

The Appeal Board noted from the transcript of the meeting that there were only two questions from the audience despite encouragement from the chair. The Appeal Board considered this was surprising given the data and the potential impact of a different treatment approach. The Appeal Board considered that the company should have done much more to engage the audience and to stimulate debate to enable two-way discussion and an exchange of medical and scientific information. There were a number of simple practical ways of stimulating debate and yet these were absent.

The Appeal Board considered that there was very little evidence of any legitimate scientific exchange. The Appeal Board did not consider whether the medicine was still in development; this had not been raised by the complainant. The Appeal Board considered that the balance of information presented in the second presentation was about Janssen's new product which would be likely to receive a marketing authorization within a few months and that this in conjunction with the points mentioned above meant that the medicine had been promoted prior to the grant of its marketing authorisation. The Appeal Board upheld the Panel's ruling of a breach of Clause 3.1. The appeal on this point was unsuccessful.

The Appeal Board considered that high standards had not been maintained. The Appeal Board upheld the Panel's ruling of a breach of breach of Clause 9.1. Promotion of an unlicensed medicine brought discredit upon and reduced confidence in the pharmaceutical industry therefore the Appeal Board upheld the Panel's ruling of a breach of breach of Clause 2. The appeals on both points were unsuccessful.

Complaint received **25 September 2017**

Case completed **29 January 2018**