ABBVIE v BRISTOL-MYERS SQUIBB

Alleged off-licence promotion disguised as a medical symposium

AbbVie alleged that a medical symposium at the British Society of Rheumatology (BSR) 2015, sponsored by Bristol-Myers Squibb, was promotional and encouraged the use of abatacept (Orencia) which was inconsistent with its marketing authorization.

Orencia, in combination with methotrexate (MTX), was indicated for the treatment of moderate-to-severe active rheumatoid arthritis (RA) in adults who had responded inadequately to previous therapy with one or more disease-modifying anti-rheumatic drugs.

AbbVie alleged that although the symposium was presented as being medically led, it was a promotional event in that: it was sponsored by Bristol-Myers Squibb; no new scientific data was presented; abatacept was proactively and prominently discussed and its benefits were emphasised and there were several presentations during the 90 minute symposium, which did not allow for significant two-way exchange with the approximately 100 strong audience.

AbbVie further alleged that the symposium encouraged the use of abatacept inconsistent with its marketing authorization, for example in undifferentiated inflammatory arthritis. Interactive patient case studies used a poll to measure the change in the audience's intention to prescribe with an unlicensed dose.

AbbVie alleged the content of the symposium went beyond what was acceptable for legitimate scientific exchange.

The detailed response from Bristol-Myers Squibb is given below.

The Panel noted that pharmaceutical companies could sponsor symposia at third party meetings. The symposium in question had clearly been characterised as 'A Bristol-Myers Squibb Medical Symposium'; potential attendees would know that it was a pharmaceutical company sponsored event. The material used to advertise the symposium did not include any direct or indirect reference to Orencia. The Panel further noted that the BSR organising committee considered that the symposium topic 'Rheumatoid Arthritis: Is There a Path to Drug-Free Remission' was suitable for discussion at its conference and had included the event in its conference programme and advertised it as such. Invitations had only been distributed in delegate bags of registered attendees. The symposium had not been advertised on a promotional stand and members of Bristol Myers-Squibb's sales force who had attended the conference had been instructed not to discuss the symposium with delegates or invite/direct them to attend. Bristol-Myers Squibb appeared to have no control over who attended the symposium. The Panel noted Bristol-Myers Squibb's submission that the symposium discussed, *inter alia*, new trials which would potentially advance the understanding of the immunological basis of rheumatoid arthritis. The Panel further noted that Bristol-Myers Squibb had emphasised that only its medical department had been involved in organising, reviewing, approving or funding the arrangements and/or materials for the symposium and that there was no commercial input. In that regard the Panel noted that it was immaterial as to which department organised, reviewed, approved or funded the event; it was the content and arrangements which determined whether it was promotional or could be considered the legitimate exchange of medical and scientific information.

The Panel noted that the symposium, which lasted 90 minutes, consisted of three presentations. The programme allowed half an hour for questions and answers and throughout the presentations delegates could use mobile devices to send comments/questions directly to the faculty and speakers. This was in contrast to AbbVie's submission that there were several presentations which did not allow for significant two way exchange with the audience. Feedback from the symposium indicated a high level of audience satisfaction with regard to the discussion session and the opportunity to ask questions.

The first presentation was entitled 'The "at-risk" individual – definition and prospects for therapy'. The presentation included information about APIPPRA and AARIA, investigator initiated abatacept studies. The APIPPRA study set out to investigate Arthritis Prevention In the Pre-clinical Phase of RA with Abatacept and the AARIA study set out to see if abatacept could prevent inflammatory lesions in at-risk patients. Neither use of abatacept was licensed. One of the slides detailing the APIPPRA study was headed 'Why should we try abatacept?' and in this regard the Panel noted Bristol Myers Squibb's submission that the slide set out the rationale for investigating abatacept in the prevention of rheumatoid arthritis. In the Panel's view it was possible that the audience might translate the heading to mean 'Why should I try abatacept [for disease prevention]?', however it was clearly stated in one slide that the APIPPRA study was now recruiting across the UK and the Netherlands. Two of the speaker's earlier slides referred to the PRAIRI study (also an investigator initiated study) which explored disease prevention with rituximab. The Panel noted, that Bristol-Myers Squibb described preventative rheumatoid arthritis studies as new and ground breaking. The first speaker's summary slide stated that clinical trials to date had not identified an intervention proven

to delay or prevent the onset of clinically apparent synovitis and that exploration of the impact of targeted therapies in the at-risk population was still ongoing. In the Panel's view this slide summarised the direction that current research was taking but neither the summary slide nor the presentation was likely to encourage delegates to use Orencia in at-risk patients to prevent rheumatoid arthritis.

The second presentation was entitled 'Biomarkers – a road map for individualized treatment?'. Only six of the 49 slides variously referred to abatacept; many of the other slides referred to other medicines such as methotrexate, rituximab, and tocilizumab. The concluding statement read 'Individualized medicine approaches are anticipated to transform future management of [rheumatoid arthritis] – but we're not there yet!'

The final presentation, entitled 'Early treatment – is this the pathway to drug-free remission?', presented some case studies including audience polls and discussed, *inter alia*, the withdrawal or de-escalation of abatacept. Other medicines were also discussed.

Overall, the Panel considered that the presentations stimulated new ways of thinking with regard to treating and or preventing rheumatoid arthritis. Two of the three current studies examining prevention used abatacept (APIPPRA and AARIA) however the Panel did not consider that the tone or content of the presentations would encourage the audience to use abatacept outside its marketing authorization for disease prevention. The Panel did not consider that the presentations emphasised the benefits of abatacept as alleged; in its view there was no greater prominence given to abatacept than any other medicine.

Overall, the Panel did not consider that AbbVie had, on the balance of probabilities, proven its complaint that the symposium constituted the disguised promotion of abatacept for an unlicensed indication. No breaches of the Code were ruled. Given its view that the symposium did not constitute the promotion of abatacept, the Panel did not consider that delegates needed to be given the prescribing information or the statement regarding reporting adverse events. No breaches of the Code were ruled.

The Panel noted its rulings above and considered that there was no evidence that high standards had not been maintained. No breach of Code was ruled. Given its rulings of no breach of the Code, the Panel consequently ruled no breach of Clause 2.

AbbVie Ltd complained about the content of a medical symposium at the British Society of Rheumatology (BSR) 2015 sponsored by Bristol-Myers Squibb. AbbVie alleged that the symposium was promotional and encouraged the use of abatacept (Orencia) which was inconsistent with its marketing authorization. The symposium ran from 17:45-19:15 on 29 April.

Orencia, in combination with methotrexate (MTX), was indicated for the treatment of moderate-to-severe active rheumatoid arthritis (RA) in adults who had responded inadequately to previous therapy with one or more disease-modifying anti-rheumatic drugs (DMARDs) including methotrexate (MTX) or a tumour necrosis factor (TNF)-alpha inhibitor.

COMPLAINT

AbbVie alleged that although the symposium was presented to health professionals as being medically led, it was a promotional event in that: it was sponsored by Bristol-Myers Squibb; no new scientific data was presented; abatacept was proactively and prominently discussed and its benefits emphasised and there were several presentations during the 90 minute symposium, which did not allow for significant two-way exchange with the audience of approximately 100 attendees.

AbbVie further alleged that the symposium encouraged the use of abatacept inconsistent with its marketing authorization, for example in undifferentiated inflammatory arthritis. Interactive patient case studies used a poll to measure the change in the audience's intention to prescribe with an unlicensed dose.

AbbVie alleged the following breaches of the Code: disguised promotion (Clause 12.1) and absence of prescribing information and adverse event reporting (Clauses 4.1 and 4.10); promotion inconsistent with the marketing authorization (Clause 3.2) and discredit to and reduction of confidence in, the industry (Clauses 2 and 9.1). AbbVie alleged the content of the symposium went beyond what was acceptable for legitimate scientific exchange.

RESPONSE

Bristol-Myers Squibb noted that the complaint related to its sponsored symposium at the BSR conference. AbbVie had made a series of non-specific allegations that differed from those which it raised in inter-company dialogue and those specified in its letter to the PMCPA. As AbbVie had not provided the PMCPA (or Bristol-Myers Squibb) with a detailed explanation of why it considered that the sponsored symposium had breached the specified clauses of the Code, it had been difficult to respond in detail to the allegations. Thus, unless otherwise stated, Bristol-Myers Squibb had responded to the most recent allegations – ie those set out above.

Bristol-Myers Squibb noted that in its initial exchange with AbbVie, it proposed that it should ask the members of the faculty for their opinion on the matters about which AbbVie had concern. Bristol-Myers Squibb had not received any response from AbbVie to this suggestion. However, following the escalation of this complaint to the PMCPA, Bristol-Myers Squibb had shared the details of AbbVie's complaint with the three health professionals who delivered the presentations at the symposium together with the Bristol-Myers Squibb response. All three health professionals verbally agreed with the content of the Bristol-Myers Squibb response.

When asked if they wished to comment on the complaint one health professional voluntarily wrote a letter describing the circumstances surrounding the symposium. Bristol-Myers Squibb stated that

whilst the speaker was not an expert on the Code, his letter provided important evidence because he was a truly independent and eminent rheumatologist who acted as a witness on the context and arrangements of the symposium. The speaker's letter was significant because it provided strong evidence to support Bristol-Myers Squibb's rebuttal of AbbVie's allegations about the facts surrounding the symposium. The speaker agreed with Bristol-Myers Squibb that his presentation topic was of high scientific importance to the attendees, that significant medical and scientific exchange did take place and that AbbVie's complaint was based on inaccurate information. It also provided evidence that the BSR conference was a learned society meeting.

Background

Bristol-Myers Squibb submitted that the sponsorship arrangements of this medically led symposium complied with the Code; all of the arrangements were appropriate for a non-promotional symposium.

Bristol-Myers Squibb submitted that its sponsorship was prominently declared on all of the delegates' materials, where the Code required an appropriately worded declaration of the company's involvement. No branding colours, brand names, clusters or logos were used.

The symposium consisted of the following presentations in addition to dedicated time for audience surveys and questions and answers:

Welcome and Introduction; 'The "at-risk" individual – definition and prospects for therapy'; 'Biomarkers – a road map for individualised treatment?' and 'Early treatment – is this the pathway to drug-free remission?'.

Full details of the agenda and copies of the relevant slides were provided.

The only members of Bristol-Myers Squibb UK who had been involved in organising, reviewing, approving or funding the arrangements and/or materials for this symposium were from the company's medical department.

The symposium was not advertised at any promotional booths and the sales force did not distribute invitations or flyers. Invitations were only distributed in the delegate bags of registered conference attendees. Additionally there was a symposium advertisement in the BSR programme, one plasma screen advertisement and two banners.

Bristol-Myers Squibb submitted that it tried to ensure that only attendees sporting full delegate badges attended the symposium. Sales employees were specifically forbidden to attend as per the company briefing of 24 April 2015 which informed the sales team that the company was sponsoring a non-promotional symposium which the sales force should not discuss with BSR delegates nor invite/direct them to attend it. The details of the symposium were not given to members of the sales force and if they received any questions they were to direct the enquirer to the medical information stand.

When Bristol-Myers Squibb received the attendee list from the BSR after the congress, it realised that one of its overseas sales colleagues had attended without making his presence known to the Bristol-Myers Squibb medical team. If the medical team had known of his sales role (albeit from a territory outside the scope of the Code) he would not have been allowed to attend.

Sponsorship by Bristol-Myers Squibb

Bristol-Myers Squibb submitted that it was entirely appropriate for pharmaceutical companies to sponsor a wide range of meetings. The supplementary information to Clause 22.1 stated:

> 'Pharmaceutical companies may appropriately hold or sponsor a wide range of meetings. These range from small lunchtime audio-visual presentations in a group practice, hospital meetings and meetings at postgraduate education centers, advisory board meetings, visits to research and manufacturing facilities, planning, training and investigator meetings for clinical trials and non-interventional studies, launch meetings for new products, management training courses, patient support group meetings and **satellite symposia through to large international meetings organised by independent bodies with sponsorship from pharmaceutical companies.'** (emphasis added).

Bristol-Myers Squibb stated that in addition, its sponsorship was prominently declared on all materials that the delegates would have seen as required by Clause 22.4. The company submitted that sponsorship *per se* did not turn the event into a promotional activity and so it rejected this aspect of the complaint.

No new scientific data was presented

The title of the symposium was 'Rheumatoid Arthritis: Is There a Path to Drug-Free Remission?'. This topic was of great scientific and clinical interest and currently much discussed by rheumatologists. The topic was discussed with each speaker at great length and they agreed with the proposed scientific exchange. Additionally, the BSR organising committee approved it as a suitable topic for scientific discussion at its conference. The BSR 2015 Annual Meeting was advertised by the society as a world-class conference for all health professionals interested in musculoskeletal conditions.

Bristol-Myers Squibb submitted that the speaker agreed with the company that his presentation topic was of high scientific importance to the attendees, that significant scientific exchange did take place and that AbbVie's complaint was based on inaccurate information.

AbbVie's assertion that the symposium was promotional because no new scientific data was presented had not been raised during inter-company dialogue and was incorrect; new data were presented (see below), therefore, Bristol-Myers Squibb rejected this aspect of the complaint.

Whilst legitimate exchange of medical and scientific information was not solely defined by the presentation of new scientific data, the symposium detailed new and current data which reflected advances in rheumatologic medicine. Bristol-Myers Squibb submitted that its symposium included discussion of new data as well as new clinical trial designs, which would potentially advance the understanding of the immunological basis of rheumatoid arthritis. This included the clinical trial designs for the recently completed PRAIRI (rituximab) study as well as the recently initiated APIPPRA and AARIA (abatacept) studies. There were also discussions on data from the following recently published or presented studies; ACT-RAY (tocilizumab), AVERT (abatacept), DRESS (adalimumab and etanercept), HONOR (adalimumab) and the Cochrane review of de-escalation and withdrawal of anti-TNF treatment strategies.

Abatacept was proactively and prominently discussed and its benefits emphasised

Bristol-Myers Squibb acknowledged that the event included data about many agents used to treat rheumatoid arthritis, including abatacept, all of which were proactively discussed in the interest of an open and balanced scientific exchange. It was unreasonable of AbbVie to expect a company-sponsored symposium at a learned society event, addressing issues relating to the management of rheumatoid arthritis, not to mention particular medicines. Bristol-Myers Squibb noted that AbbVie had not explained why it considered abatacept had been prominently discussed.

All presentations presented data on abatacept, as well as many other rheumatoid arthritis treatments. Medicines used in the treatment of rheumatoid arthritis were frequently mentioned by non-proprietary names and over the three presentations of 126 slides, they appeared on or were discussed as follows; abatacept 23 slides, anti-TNFs (adalimumab, certolizumab pegol, etanercept and infliximab) 42 slides, rituximab 9 slides, corticosteroids and synthetic DMARDS on 20 slides and tocilizumab on 3 slides. In addition, no claims for any products, including abatacept, were made.

Bristol-Myers Squibb did not believe that abatacept was given greater prominence than any of the other rheumatoid arthritis medicines. The use of the word abatacept was fair and balanced when considering the use of the medicine name in line with the content and context of each data presentation and within the overall symposium itself.

Biologic DMARDs with different modes of action were discussed. Abatacept was a T-cell co-stimulatory modulator. Four of the other medicines discussed were of the same mode of action ie anti-tumour necrosis factor (anti-TNFs); adalimumab, certolizumab pegol, etanercept and infliximab. Rituximab was an anti-CD20 and tocilizumab was an anti-Interleukin 6 (anti-IL6) biologic DMARD.

Preventative rheumatoid arthritis studies were new and ground breaking within rheumatology. There was a hypothesis that rituximab and abatacept might help to prevent rheumatoid arthritis as they worked earlier in the rheumatoid arthritis inflammatory cascade by targeting B-cells and T-cells respectively. In rheumatoid arthritis, activation of T-cells led to activation of B-cells, antibody production and the subsequent production of several immune mediators which led to the clinical manifestations of rheumatoid arthritis. The first presentation of the symposium detailed three investigator initiated studies, PRAIRI (rituximab), APIPPRA and AARIA (abatacept) as these were the only studies known to the speaker and Bristol-Myers Squibb, which were currently investigating the prevention of rheumatoid arthritis using current rheumatoid arthritis therapies. Therefore abatacept and rituximab were the only two biologic DMARDs that were discussed in this presentation. Additionally steroids and synthetic DMARDs were also discussed as part of this presentation.

Bristol-Myers Squibb submitted that the discussion of abatacept in the symposium, when placed within its proper context of the legitimate exchange of scientific, medical and clinical information, was accurate, balanced, up-to-date, appropriate and non-promotional. Bristol-Myers Squibb thus rejected AbbVie's allegation that abatacept had been proactively and prominently discussed.

Bristol-Myers Squibb noted that AbbVie did not detail how it considered that the presentations had emphasised the benefits of abatacept. The definition of a benefit was 'an advantage or profit gained from something' or in a more commercial setting a 'desirable attribute of a product'. Bristol-Myers Squibb reiterated its comments above regarding the references to abatacept as well as the many other rheumatoid treatments, across all of the presentations.

The subject of the symposium was 'Is There a Path to Drug-Free Remission?' and its three presentations were entitled: 'The "at-risk" individual – definition and prospects for therapy'; 'Biomarkers – a road map for individualised treatment?' and 'Early treatment – is this the pathway to drug-free remission?'. This encompassed the idea that intensive targeted therapies in early or established rheumatoid arthritis might subsequently lead to extended periods of medicine-free remission in a subset of patients. Including the rationale that if the pre-clinical phase of disease could be accurately defined, targeting therapy to those at highest risk of developing the more severe form of disease would potentially prevent or at least delay the onset of rheumatoid arthritis. It would therefore be unrealistic to expect participants to have a proper informed discussion without being able to discuss how any of the current therapeutic options might be used. This did not constitute emphasis of the benefits of abatacept.

Due to a lack of detail and clarity in AbbVie's complaint about what in the presentations it considered had emphasised the benefits of abatacept, Bristol-Myers Squibb addressed AbbVie's concerns about one sentence in one slide of the speaker's presentation. AbbVie mentioned this in its

original letter to Bristol-Myers Squibb. The speaker included one slide containing the text 'Why should we try abatacept?' to explain why the medicine was investigated in the APIPPRA study. In this instance 'try' equated to 'investigate using'. When read within the context of the sequence of the slides presented, Bristol-Myers Squibb submitted that the meaning was appropriate and non-promotional.

Bristol-Myers Squibb strongly refuted the allegations that the benefits of abatacept were discussed let alone emphasised during the symposium; it therefore rejected this aspect of the complaint.

There were several presentations which … did not allow for significant two way exchange

As stated above, the symposium consisted of three presentations and Bristol-Myers Squibb submitted that it had made substantial efforts to ensure that the event was highly interactive in order to facilitate significant two way exchange with the audience. This was achieved by both a dedicated question and answer session of about half an hour as well as by the use of keypads. Bristol-Myers Squibb noted that devices such as telephones and tablets were not simply used to indicate answers to questions posed by the panel, but could be used to send comments or questions to the faculty and speakers during the presentation so that questions could be answered immediately, as well as at the end of the session – thus the keypads enabled delegates to ask questions throughout the symposium. The outputs from the keypads were provided.

The third lecture was specifically designed to encourage delegate participation before and after the lecture and, contrary to AbbVie's allegation, a lively discussion took place with delegates. In addition, discussion on the symposium continued well after the symposium ended as acknowledged by the speaker. Bristol-Myers Squibb noted that the speaker stated that AbbVie was incorrect to allege that there was no significant exchange with the audience and that the symposium 'fostered discussion and debate both during and after the event' as true medical and scientific exchange should. Bristol Myers-Squibb noted that 90% of respondents of the anonymous returned feedback forms stated that they were 'satisfied', 'very satisfied' or 'completely satisfied' with the opportunity to ask questions during the symposium.

Given that delegates had considerable opportunities to ask questions throughout the symposium and that a lively discussion took place, Bristol-Myers Squibb rejected this aspect of the complaint.

The symposium encouraged the use of abatacept inconsistent with its marketing authorization, for example in undifferentiated inflammatory arthritis

Bristol-Myers Squibb noted that AbbVie had not detailed why it considered that delegates had been encouraged to use abatacept in a manner inconsistent with its marketing authorization. Thus, Bristol-Myers Squibb addressed AbbVie's concerns mentioned in its original letter to Bristol-Myers Squibb.

- Prevention of rheumatoid arthritis in patients with ACPA (anti-citrullinated protein antibody) positive arthralgia (APIPPRA study) and delay of progression in patients with undifferentiated inflammatory arthritis (ADJUST study):

Bristol-Myers Squibb noted that preventative rheumatoid arthritis studies were new and ground breaking within rheumatology. This was not currently a licensed indication anywhere in the world for any disease-modifying drug. The supplementary information to Clause 3 allowed the legitimate exchange of medical and scientific information which was outside of the current label for a medicine.

There was a hypothesis that rituximab and abatacept might help to prevent rheumatoid arthritis as they worked earlier in the rheumatoid arthritis inflammatory cascade by targeting B-cells and T-cells respectively. In rheumatoid arthritis, activation of T-cells led to activation of B-cells, antibody production and the subsequent production of several immune mediators which led to the clinical manifestations of rheumatoid arthritis.

Data suggested that individuals with high levels of ACPA were at high risk of developing rheumatoid arthritis. Rituximab affected the production of antibodies by specifically targeting B-cells. Abatacept inhibited T-cell activation, T-cell antibody dependent responses and T-cell dependent B-cell proliferation and thus indirectly impacted antibody production.

The three investigator initiated studies discussed at the symposium, PRAIRI (rituximab study), APIPPRA and AARIA (abatacept studies) were the only studies known to the speaker and Bristol-Myers Squibb which were currently investigating the prevention of rheumatoid arthritis using current rheumatoid arthritis therapies. It was clearly stated during the presentation that the studies were either recruiting or had recently finished recruiting. The speaker's presentation also focussed on the scientific rationale and design of other relevant studies including PROMPT (methotrexate), SAVE and STIVEA (corticosteroids), as well as ADJUST (abatacept). The aim was to discuss studies that had investigated prevention of progression of undifferentiated inflammatory arthritis to rheumatoid arthritis. Discussion of these studies unavoidably meant that the medicines being investigated were mentioned; to have omitted any of these studies would not have been fair or balanced.

As previously stated, the speaker included one slide containing the question 'Why should we try abatacept?' to explain why the medicine was investigated in the APIPPRA study. In this instance, 'try' equated to 'investigate using'. When read within the context of the sequence of the slides presented, the meaning was appropriate and non-promotional. This was not an encouragement to use abatacept in a manner inconsistent with its marketing authorization.

- Use of abatacept in MTX-naïve rheumatoid arthritis (AGREE study) and dose de-escalation of abatacept (AGREE study).

The subject of the third lecture presented by a second speaker ('Early treatment – is this the pathway to drug-free remission?') discussed the concept of how early rheumatoid arthritis treatment might lead to sustained medicine-free remission and if dose reduction was possible to maintain disease remission.

This lecture discussed studies on rheumatoid arthritis therapies that had investigated the prospects of sustained medicine-free remission including synthetic DMARDS, anti-TNF biologic DMARDS (adalimumab, certolizumab, etanercept and infliximab), anti-IL6 biologic DMARD (tocilizumab) and T-cell co-stimulation modulator (abatacept). The objective of this session was to discuss which subsets of patients in remission might be considered for DMARD dose reduction or treatment withdrawal, for example patients with established rheumatoid arthritis vs patients with early rheumatoid arthritis. Discussion of abatacept within the context of the slides presented and data discussed was appropriate and non-promotional.

In its complaint AbbVie referred to the use of interactive patient case studies. Bristol-Myers Squibb noted that AbbVie did not raise its concerns about the use of the interactive poll during the symposium in inter-company dialogue. Bristol-Myers Squibb noted that, contrary to the inference in AbbVie's complaint, only one of the cases presented in the second speaker's presentation referred to abatacept, whilst the other cases referred to other medicines. These cases were presented so as to allow the audience to discuss how a patient who had achieved remission from rheumatoid arthritis might be managed. Cases were presented for three different types of DMARDs including a synthetic DMARD (methotrexate), an anti-TNF biologic DMARD (etanercept) and a T-cell co-stimulatory modulator (abatacept). The same questions were asked following presentation of each case to determine if current treatment should be continued, modified or stopped. The question of how to manage patients who no longer had active rheumatoid arthritis was a valid subject for rheumatologists and discussion on this particular issue was appropriate within the context of a purely scientific meeting. When read within the context of the sequence of slides presented, the questions were appropriate and non-promotional. Bristol-Myers Squibb submitted that the case studies discussed were entirely hypothetical and designed to illustrate some of the points made in the presentations and to stimulate debate amongst the audience and faculty. Bristol-Myers Squibb strongly refuted the allegation that they were intended to encourage off-label use of abatacept or any other DMARD.

As this was a legitimate scientific and medical exchange, Bristol-Myers Squibb rejected this aspect of the complaint.

Summary of symposium

Bristol-Myers Squibb submitted that the symposium was a standalone legitimate scientific and medical exchange organised by its medical department in conjunction with an eminent and independent external faculty. Bristol-Myers Squibb did not intend to repeat the meeting or use the data or information presented or discussed in any way other than to stimulate and encourage legitimate scientific, medical and clinical debate during the symposium.

For the reasons set out above, Bristol-Myers Squibb was satisfied that all of the symposium arrangements and materials met the requirements for a legitimate exchange of scientific clinical information.

Specific clauses

Bristol-Myers Squibb noted that AbbVie's complaint concluded with a list of alleged breaches which appeared to be linked to its overall allegation that the symposium was promotional. Bristol-Myers Squibb thus rejected every alleged breach as it strongly believed it had shown that the event was an appropriate scientific symposium. Nevertheless, for completeness, a response to each specific clause cited was given below, even though it was incredibly difficult to link some aspects to specific allegations as the construct of the complaint was unclear.

Bristol-Myers Squibb submitted that all of the alleged breaches were based on AbbVie's false allegation that the symposium was promotional. Bristol-Myers Squibb refuted this allegation, and all of the associated breaches of the Code in the strongest possible terms.

12.1 – Disguised promotion

Bristol-Myers Squibb had described why, in its view, the symposium complied with the Code and was non-promotional and therefore was not disguised promotion. Company sponsorship was clearly stated and all medicines were appropriately discussed, including Bristol-Myers Squibb's. As previously stated, the topic discussed was of great scientific and clinical interest and was currently the subject of much discussion amongst rheumatologists. The topic for the symposium was discussed with each of the speakers at great length and they agreed with the proposed scientific exchange. Additionally, the BSR organising committee approved the topic as a suitable for scientific discussion at its congress.

The symposium was a standalone, legitimate scientific and medical exchange. Bristol-Myers Squibb considered that the sponsorship arrangements for the symposium complied with the Code and could not be considered disguised promotion.

4.1 – Lack of prescribing information and
4.10 – Lack of adverse event reporting statement

Bristol-Myers Squibb submitted that as this was a non-promotional meeting, the Code did not require either prescribing information or an adverse event reporting statement to be included.

3.2 – Promotion inconsistent with marketing authorization

Bristol-Myers Squibb noted that the symposium was a non-promotional meeting involving medical and scientific exchange as discussed in some detail above. There was no promotion at this event and therefore promotion inconsistent with the marketing authorization did not occur. Preventative rheumatoid arthritis studies discussed were new and ground breaking within rheumatology. This was not currently a licensed indication anywhere in the world for any disease-modifying medicine. Additionally, as described above, the question of how to manage patients who no longer had active rheumatoid arthritis was a valid question for rheumatologists and discussion on this particular issue was appropriate within the context of a purely scientific meeting. The supplementary information to Clause 3 allowed for the legitimate exchange of medical and scientific information which was outside of the current label for a medicine. Promotion inconsistent with the marketing authorization did not occur.

2 – Discredit to and reduction of confidence in, the industry and
9.1 – Maintaining high standards

Bristol-Myers Squibb stated that it had described above and in its letter to AbbVie why the meeting should be considered as legitimate exchange of medical and scientific information. It had gone to great lengths to ensure the symposium complied with the Code and therefore the company submitted that it had maintained high standards and had not engaged in any activity which should be the subject of censure by the PMCPA.

PMCPA Questions

The PMCPA had requested some specific additional information regarding the criteria used to select the faculty, details of how the topic was agreed with the faculty and the number of delegates attending:

The three eminent rheumatologists who comprised the faculty were selected by Bristol-Myers Squibb medical personnel based on their expertise; details were provided.

The subject matter of the symposium was identified by Bristol-Myers Squibb medical personnel, based on interest in this topic at international congresses in recent years, as well as general conversations with UK rheumatologists. In addition, it was approved by the BSR. The overall concept of the symposium was supported by the faculty as being of genuine interest to UK rheumatologists.

The specific topic of 'The "at-risk" individual – definition and prospects for therapy' approved by the BSR was suggested by one of the speakers as the next frontier in rheumatology research.

The rheumatology community's interest in the subject of medicine-free remission was further supported by the volume of data presented at the European League Against Rheumatism (EULAR) Congress, June 2015 in Rome, on the subject of biologic dose modification when remission was achieved. Pharmaceutical companies had organised symposia on these topics including AbbVie which sponsored a non-promotional symposium at EULAR 2015 on managing patients in remission entitled 'Dose tapering after achieving sustained remission - Can we predict disease progression?'.

The content of each presentation of the symposium at issue was developed at the discretion of each speaker following an initial brief from Bristol-Myers Squibb. Further contributions from Bristol-Myers Squibb were made when requested by the speakers and also to ensure the presentations reflected the latest available scientific evidence. Additionally, Bristol-Myers Squibb reviewed the presentations to ensure compliance with the Code. The faculty briefing documents made it very clear that the meeting was to be non-promotional and the content should represent a balanced view of the latest evidence on all relevant therapies. Any mention of abatacept within the speaker presentations were presented within the context of the topic discussed and were done so at the discretion of the faculty.

Bristol-Myers Squibb submitted that correspondence between it, the faculty and the third party agency showed the company's genuine intention to engage in legitimate scientific exchange. The design of the programme had input from the faculty and the final agenda and programme structure were based on comments from the faculty.

Before presenting, the speakers were briefed to deliver non-promotional, fair, balanced, up-to-date and clinically relevant presentations to enhance the audience's scientific knowledge. They were asked to provide an unbiased view of the topics discussed. To keep true with the spirit of scientific exchange and Code requirements, speakers were asked to ensure all data presented was accurate, balanced, fair, objective, unambiguous, based on an up-to-date evaluation of all the evidence, not misleading, capable of substantiation and not disparaging or disrespectful to competitor companies or products.

A list of the 158 attendees was provided.

This event was a standalone legitimate scientific and medical exchange organised solely by the Bristol-Myers Squibb medical department in conjunction with an eminent and independent external faculty. Bristol-Myers Squibb stated that it would not be repeating the meeting or using the data or information presented or discussed in any way other than to stimulate and encourage legitimate scientific and clinical debate at this particular meeting.

As the symposium was non-promotional and did not otherwise meet the requirements for certification as described in Clause 14.3, materials were not certified but they were examined to ensure compliance with the Code.

Bristol-Myers Squibb submitted that throughout this matter it had complied with the spirit and letter of the Code. The symposium was conducted to the highest

standards, in line with the Code, and the company had been fully transparent in demonstrating this.

PANEL RULING

The Panel noted that Clause 3 prohibited the promotion of a medicine prior to the grant of its marketing authorization. It also required that promotion must be in accordance with the marketing authorization and not be inconsistent with the summary of product characteristics (SPC). The supplementary information to Clause 3 provided additional details, including a clear 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 in the Code. 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.

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 AbbVie had the burden of proving its complaint on the balance of probabilities. The company's complaint was broad in its scope and almost no detail had been provided as to why it alleged that breaches of the Code had occurred.

The Panel noted that it was well accepted that pharmaceutical companies could sponsor symposia at third party meetings. The symposium in question had clearly been characterised as 'A Bristol-Myers Squibb Medical Symposium'; potential attendees would be well aware that they would be attending a pharmaceutical company sponsored event. The material used to advertise the symposium did not include any direct or indirect reference to Orencia (abatacept); brand colours or logos were not used. The Panel further noted that the BSR organising committee considered that the symposium topic 'Rheumatoid Arthritis: Is There a Path to Drug-Free Remission' was suitable for discussion at its conference and had included the event in its conference programme and advertised it as such. Invitations had only been distributed in delegate bags of registered attendees. The symposium had not been advertised on a promotional stand and members of Bristol Myers-Squibb's sales force who had attended the conference had been instructed not to discuss the symposium with delegates or invite/direct them to attend. Bristol-Myers Squibb appeared to have no control over who attended the symposium. The Panel noted Bristol-Myers Squibb's submission that the symposium discussed, *inter alia*, new trials which would potentially advance the understanding of the immunological basis of rheumatoid arthritis. The Panel further noted that Bristol-Myers Squibb had emphasised that only its medical department had been involved in organising, reviewing, approving or funding the arrangements and/or materials for the symposium and that there was no commercial input. In that regard the Panel noted that given the broad definition of promotion in Clause 1.2, it was immaterial as to which department organised, reviewed, approved or funded the event; it was the content and arrangements which determined whether an event was promotional or could be considered the legitimate exchange of medical and scientific information.

The Panel noted that the symposium, which lasted an hour and a half, consisted of three presentations. The programme allowed half an hour for questions and answers and throughout the presentations delegates could use mobile devices to send comments/questions directly to the faculty and speakers. This was in contrast to AbbVie's submission that there were several presentations which did not allow for significant two way exchange with the audience. Feedback from the symposium indicated a high level of audience satisfaction with regard to the discussion session and the opportunity to ask questions. The audience included rheumatologists, nurse specialists, hospital doctors as well as a number of staff from pharmaceutical companies.

The first presentation was entitled 'The "at-risk" individual – definition and prospects for therapy'. The presentation included information about the APIPPRA and AARIA studies both of which were investigator initiated abatacept studies. The APIPPRA study set out to investigate **A**rthritis **P**revention **I**n the **P**re-clinical **P**hase of **R**A with **A**batacept and the AARIA study set out to see if abatacept could prevent inflammatory lesions in at-risk patients. Neither use of abatacept was licensed. One of the slides detailing the APIPPRA study was headed 'Why should we try abatacept?' and in this regard the Panel noted Bristol Myers Squibb's submission that the slide set out the rationale for investigating abatacept in the prevention of rheumatoid arthritis. In the Panel's view it was possible that the audience might translate the heading to mean 'Why should I try abatacept [for disease prevention]?', however it was clearly stated in one slide that the APIPPRA study was now recruiting across the UK and the Netherlands. Two of the speaker's earlier slides referred to the PRAIRI study (also an investigator initiated study) which explored disease prevention with rituximab. The Panel noted, that Bristol-Myers Squibb described preventative rheumatoid arthritis studies as new and ground breaking. The first speaker's summary slide stated that clinical trials to date had not identified an intervention proven to delay or prevent the onset of clinically apparent synovitis and that exploration of the impact of targeted therapies in the at-risk population was still ongoing. In the Panel's view this slide summarised the direction that current research was taking but neither the summary slide nor the presentation was likely to encourage delegates to use Orencia in at-risk patients to prevent rheumatoid arthritis.

The second presentation was entitled 'Biomarkers – a road map for individualized treatment?'. Only six of the 49 slides variously referred to abatacept; many of the other slides referred to other medicines such as methotrexate, rituximab, and tocilizumab. The concluding statement read 'Individualized medicine approaches are anticipated to transform future management of [rheumatoid arthritis] – but we're not there yet!'

The final presentation, entitled 'Early treatment – is this the pathway to drug-free remission?', presented some case studies including audience polls and discussed, *inter alia*, the withdrawal or de-escalation of abatacept. Other medicines were also discussed.

Overall, the Panel considered that the presentations stimulated new ways of thinking with regard to treating and or preventing rheumatoid arthritis. Two of the three current studies examining prevention used abatacept (APIPPRA and AARIA) however the Panel did not consider that the tone or content of the presentations would encourage the audience to use abatacept outside its marketing authorization for disease prevention. The Panel did not consider that the presentations emphasised the benefits of abatacept as alleged; in its view there was no greater prominence given to abatacept than any other medicine. Although feedback on the symposium included one comment, 'Machiavellian strategy to use more abatacept', the Panel noted that it had no information as to which delegate had made that comment; it was not echoed by other feedback comments recorded. The Panel noted that a number of the audience were from other pharmaceutical companies and so it was possible that such a comment could have been made by one of them.

Overall, the Panel did not consider that AbbVie had, on the balance of probabilities, proven its complaint that the symposium constituted the disguised promotion of abatacept for an unlicensed indication. No breach of Clauses 12.1 and 3.2 were ruled respectively. Given its view that the symposium did not constitute the promotion of abatacept, the Panel did not consider that delegates needed to be given the prescribing information or the statement regarding reporting adverse events. No breaches of Clauses 4.1 and 4.10 were ruled accordingly.

The Panel noted its rulings above and considered that there was no evidence that high standards had not been maintained. No breach of Clause 9.1 was ruled. Given its rulings of no breach of the Code, the Panel consequently ruled no breach of Clause 2.

Complaint received **9 July 2015**

Case completed **6 October 2015**