CASE AUTH/2172/10/08

BOEHRINGER INGELHEIM v BAYER SCHERING PHARMA

Promotion of Xarelto

Boehringer Ingelheim complained about Bayer Schering Pharma's promotion of its anticoagulant Xarelto (rivaroxaban). Boehringer Ingelheim supplied Pradaxa (dabigatron).

Given the dates of the activities in question the Panel decided to use the provisions of the 2006 Code using the 2008 Constitution and Procedure. The clauses at issue had not changed under the two Codes but some had been renumbered.

The detailed responses from Bayer Schering are given below.

Boehringer Ingelheim alleged that at the Irish Orthopaedic Association meeting, Belfast, in June 2008, Bayer Schering had an exhibition stand on venous thromboembolism which stated 'Great Clinical Need for New Anticoagulants…' and then described various desirable attributes. The stand was manned by sales representatives and marketing team members. Boehringer Ingelheim was concerned that having the stand would solicit questions on the availability of new anticoagulants and that questions would be answered by sales representatives, promoting the medicine prior to the receipt of the marketing authorization. The stand did not mention that the new anticoagulant Pradaxa (dabigatran) with this profile was available. Boehringer Ingelheim alleged that this was disparaging and misleading. Boehringer Ingelheim noted that Bayer Schering had distributed a leaflet entitled 'Thrombosis Adviser' and a two question quiz card on deep vein thrombosis and the characteristics of an ideal anticoagulant. The quiz offered entry into a draw to win a book voucher which Boehringer Ingelheim alleged was in breach of the Code.

The Panel noted that the material had been supplied by Bayer Schering's Irish affiliates. As the meeting took place in the UK, the UK Code applied.

The Panel noted that one of the exhibition panels at issue referred to VTE (venous thromboembolism) as a seriously underestimated killer. The second exhibition panel was headed 'Great Clinical Need for New Anticoagulants Providing: effective anticoagulation; low risk of bleeding; oral delivery; wide therapeutic window; fixed dosing; no monitoring; low risk of food and drug interactions and predictable pharmacology'. The Panel considered that the second exhibition panel, given the context in which it was used, ie a promotional exhibition space, in effect promoted Xarelto in June 2008 prior to the grant of its marketing authorization on 1 October 2008. The exhibition panel listed Xarelto's benefits; it would be clear to delegates that Bayer Schering had a commercial interest in an oral anticoagulant with the profile listed. A breach was ruled.

The Panel considered that the heading to the second exhibition panel 'Great Clinical Need for New Anticoagulants Providing:' ignored the fact that Boehringer Ingelheim's new anticoagulant (Pradaxa) was already available. The heading implied that no anticoagulant was available with the properties listed which was not so. The Panel noted Bayer Schering's submission that the unmet need referred to therapy areas other than preventing VTE following orthopaedic surgery. This was not made clear on the exhibition panel. The Panel considered that the exhibition panel was misleading and disparaging as alleged. Breaches of the Code were ruled.

The Panel noted that a leaflet distributed from the exhibition stand had asked delegates to 'Test your knowledge on VTE and enter a draw to win a book voucher .'. The supplementary information to Clause 18.2 of the 2006 Code stated 'The use of competitions, quizzes and suchlike, and the giving of prizes, are unacceptable methods of promotion'. A breach was ruled as alleged.

With regard to a supplement on rivaroxaban in the Journal of Bone and Joint Surgery (JBJS), Boehringer Ingelheim noted that the journal was available on 4 September 2008 prior to the grant of the marketing authorization for rivaroxaban.

The supplement was funded by Bayer Schering as stated in the acknowledgements of each article. However, there was no clear mention of the sponsor company at the outset.

Boehringer Ingelheim alleged that the statement 'An introduction to rivaroxaban: the first oral, once-daily, direct Factor Xa inhibitor for the prevention of venous thromboembolism' was misleading as it implied that rivaroxaban was available in September 2008 for prescription.

A statement, 'Rivaroxaban offers clinicians and their patients a novel orally active anticoagulant for extended thromboprophylaxis in the outpatient setting' was alleged to be misleading and promotion prior to the grant of the marketing authorization as 'offers' was in the present tense.

The claims 'Rivaroxaban will offer clinicians the opportunity….' and 'Importantly, unlike parenteral anticoagulants, rivaroxaban will enable an easy transition…' implied that rivaroxaban would work for all patients which was alleged to be

misleading and exaggerated. In addition, Boehringer Ingelheim considered that these claims implied that rivaroxaban would definitely be available which, given that rivaroxaban was not licensed at the time of publication, was in breach of the Code.

The graph 'Efficacy of *currently* available options for venous thromboprophylaxis' (emphasis added) did not include dabigatran which had a marketing authorization for primary prevention of venous thromboembolism events in adults following elective total hip or knee replacement surgery and was available in the UK. Boehringer Ingelheim alleged that the graph did not reflect up-to-date evidence and was misleading.

The Panel noted that the objective was to provide the proceedings of a symposium, sponsored by Bayer Schering at an international meeting, in the form of a journal supplement. The Panel considered that it would not always be possible to achieve this and comply with the requirements of the Code.

The Panel noted that the supplement had been initiated by Bayer Schering and its agency. The co-editors and first authors were those who had taken part in the company-sponsored symposium at EFORT 2008 and although they had not been paid to write the articles in question they had all received honoraria for other work they had done for Bayer. Professional writing support and editorial assistance was funded by Bayer HealthCare AG.

The Panel considered that Bayer Schering was inextricably linked to the production of the supplement. There was no arm's length arrangement between the provision of the sponsorship and the generation of the supplement. Circulation of the supplement was not limited to those who attended the meeting as it was circulated with the JBJS. Given the company's involvement and the content of the supplement, the Panel considered that the supplement was, in effect, promotional material for Xarelto. Further, the Panel noted that the supplement was not formally peer reviewed by the JBJS. The Panel considered that the material was a paid-for insert from Bayer Schering, not a supplement from the JBJS for which its editorial board would have been responsible. The back cover of the supplement stated:

> 'This supplement is provided free with the British Volume of JBJS. The contents have not been selected or edited by the Journal. All questions about scientific content should be addressed to the individual authors.'

The supplement was distributed with the September issue of the JBJS. Xarelto did not receive a UK marketing authorization until 1 October 2008. The Panel noted its comments above and considered that the supplement had promoted Xarelto to UK health professionals prior to the grant of the marketing authorization. A breach was ruled as acknowledged by Bayer Schering.

The Panel did not consider that the statement 'An introduction to rivaroxaban: the first oral, once daily, direct Factor Xa inhibitor for the prevention of venous thromboembolism' implied that the product was available for prescription in September 2008 as alleged. No breach was ruled. Similarly the Panel did not consider that the claim 'Rivaroxaban offers clinicians and their patients a novel orally active anticoagulant …' was misleading through the use of the present tense. No breach was ruled. Insomuch as the claim promoted Xarelto, however, the Panel considered that its ruling of a breach above covered this aspect.

The Panel did not consider that the statement 'Rivaroxaban will offer clinicians the opportunity to use a fixed dose, unmonitored, once-daily anticoagulant, given as a single 10mg tablet, for the prevention of VTE after major orthopaedic surgery. Importantly, unlike parental anticoagulant, Rivaroxaban will enable an easy transition from hospital to outpatient thromboprophylaxis, providing an opportunity to improve further the current standard of care in this high risk patient population' implied, as alleged, that Xarelto would work for all patients. In that regard the Panel did not consider that the statement was either misleading or exaggerated. No breach was ruled. Insomuch as the statement promoted Xarelto, the Panel considered that its ruling of a breach above covered this aspect.

The graph entitled 'Efficacy of currently available options for venous thromboembolism prophylaxis' was compiled from Geerts *et al* (2001). The data thus pre-dated the introduction of dabigatran onto the UK market. In that regard the data was not up-to-date and was misleading. Breaches were ruled.

The front cover of the supplement did not feature a statement acknowledging Bayer Schering's involvement thus a breach was ruled.

Boehringer Ingelheim was very concerned about the activities of Bayer Schering as detailed above and alleged that the company had undertaken pre-licence promotional activities. Boehringer Ingelheim was further concerned that, despite multiple discussions between the two companies regarding the need to comply with the Code, Bayer Schering had repeatedly undertaken activities in the sensitive pre-licence period which had not been through self-regulation review and approval processes according to the requirement of the Code. Taking all these activities into account Boehringer Ingelheim alleged that Bayer Schering's actions had brought the industry into disrepute in breach of Clause 2.

The Panel considered that the arrangements within Bayer Schering showed poor control. It appeared

that non UK parts of the business had little awareness of matters to be considered when conducting activities in the UK. It was the responsibility of the UK company to ensure compliance within the UK Code. A medicine had been promoted prior to the grant of its marketing authorization on more than one occasion. Taking all the circumstances into account the Panel considered that Bayer Schering had brought discredit upon and reduced confidence in the pharmaceutical industry and a breach of Clause 2 was ruled.

Boehringer Ingelheim Limited complained that Bayer Schering Pharma had promoted its anticoagulant Xarelto (rivaroxaban) prior to the grant of its marketing authorization (Clause 3) Xarelto received its marketing authorization on 1 October 2008.

Boehringer Ingelheim marketed the anticoagulant Pradaxa (dabigatran).

Given the dates of the activities in question the Panel decided to use the provisions of the 2006 Code using the 2008 Constitution and Procedure. The clauses at issue had not changed under the two Codes but some had been renumbered.

1 Meeting of the Irish Orthopaedic Association

COMPLAINT

Boehringer Ingelheim alleged that at the Irish Orthopaedic Association meeting, Belfast, 19-20 June 2008, Bayer Schering conducted a number of activities which were in breach of the Code. In particular Bayer Schering had an exhibition stand on venous thromboembolism which stated 'Great Clinical Need for New Anticoagulants…' and then described various desirable attributes. The stand was manned by sales representatives and marketing team members. Boehringer Ingelheim was concerned that having a stand on venous thromboembolism would solicit questions on the availability of such new anticoagulants thus breaching Clause 3.1. Boehringer Ingelheim was also concerned that any such questions would be answered by promotional sales representatives, thus breaching Clause 3.1.

The stand stated 'Great Clinical Need for New Anticoagulants…' but did not mention that the new anticoagulant Pradaxa (dabigatran) with this profile was already available. Boehringer Ingelheim alleged that this was disparaging and misleading in breach of Clauses 7.2 and 8.1.

Boehringer Ingelheim noted that Bayer Schering had distributed a leaflet entitled 'Thrombosis Adviser' and a two question quiz card on deep vein thrombosis and the characteristics of an ideal anticoagulant. The quiz offered entry into a draw to win a book voucher in breach of Clause 18.2.

RESPONSE

Bayer Schering explained that Bayer Schering in the UK only knew about this meeting after the event. Bayer Schering noted that this was a problem common to many international companies.

Bayer Schering refuted the claim 'Great Clinical Need for New Anticoagulants…' was in breach of Clause 3.1. The company's presence at the meeting was entirely educational, and none of the materials on the stand could lead any doctor to believe that the information was related to a specific medicine. Indeed, as Boehringer Ingelheim stated, the exhibition panel actually listed attributes that were met by dabigatran; thus, it seemed self-evident that this exhibition panel was not specific to a Bayer Schering product, hence not in breach of Clause 3.1.

Bayer Schering acknowledged that the stand was manned by sales and marketing personnel from its affiliate in the Republic of Ireland. Had this meeting been properly certified by the UK signatories, there would of course have been no sales or marketing personnel present at the stand.

Bayer Schering refuted the allegation that the claim disparaged or misled with regard to the availability of dabigatran. The stand did not refer to an *unmet* need for a new anticoagulant, but of great clinical need for new anticoagulants. Despite the arrival of new anticoagulants for the prevention of venous thromboembolism following major orthopaedic surgery of the lower limbs, there was still undoubtedly a great clinical need for new oral anticoagulants in other therapeutic areas.

Although dabigatran (and rivaroxaban) promised to meet many of the needs for new anticoagulants, there was still a long way to go before the full extent of clinical need, across multiple therapeutic areas, was actually met. It would be seriously misleading to suggest otherwise.

Bayer Schering disagreed with the allegation that the stand was in breach of Clauses 7.2 or 8.1.

Bayer Schering contended the allegation that the distribution of the leaflet 'Thrombosis Adviser' announcing the development of a new educational website for use by both health professionals and patients, constituted a breach of Clause 18.2. Bayer Schering could not find any connection between the leaflet and Clause 18.2 and was unsure as to the exact nature of the allegation.

The quiz card was a test of the delegates' knowledge of the subject matter. It was not a promotional item and therefore not in breach of the Code. However the offer of a prize was inappropriate, in breach of Clause 18.2. However this breach should be considered in the context in which it occurred. Bayer Schering understood that its Irish colleagues limited the quiz to health professionals from the Republic of Ireland but they accepted that the process used was not totally robust.

PANEL RULING

The Panel noted that the material used at the Belfast meeting had been supplied by Bayer Schering's Irish affiliates. It was an established principle under the Code that UK companies were responsible for the activities of overseas affiliates that came within the scope of the Code. As the meeting took place in the UK, both the UK Code and the Irish Code applied. Where the two codes differed the more stringent code would apply. The exhibition stand was manned by members of the sales and marketing team from the Republic of Ireland. The Panel noted that the supplementary information to Clause 1.7, 'Applicability of Codes', made it clear that at meetings held in the UK materials and activities had to comply with the UK Code. It also stated, *inter alia*, that 'All international events, that is to say events that take place outside the responsible pharmaceutical company's home country, must be notified in advance to any relevant local subsidiary or local advice taken'.

The Panel noted that one of the exhibition panels at issue referred to VTE (venous thromboembolism) as a seriously underestimated killer. The second exhibition panel was headed 'Great Clinical Need for New Anticoagulants Providing: effective anticoagulation; low risk of bleeding; oral delivery; wide therapeutic window; fixed dosing; no monitoring; low risk of food and drug interactions and predictable pharmacology'. The Panel considered that the second exhibition panel, given the context in which it was used, ie a promotional exhibition space, in effect promoted Xarelto in June 2008 prior to the grant of its marketing authorization on 1 October 2008. The exhibition panel listed Xarelto's benefits; it would be clear to delegates that Bayer Schering had a commercial interest in an oral anticoagulant with the profile listed. A breach of Clause 3.1 was ruled.

The Panel considered that the heading to the second exhibition panel 'Great Clinical Need for New Anticoagulants Providing:' ignored the fact that Boehringer Ingelheim's new anticoagulant (Pradaxa) was already available. The heading implied that no anticoagulant was available with the properties listed which was not so. The Panel noted that Bayer Schering's submission that the unmet need referred to therapy areas other than preventing VTE following orthopaedic surgery. This was not made clear on the exhibition panel. The Panel considered that the exhibition panel was misleading and disparaging as alleged. Breaches of Clauses 7.2 and 8.1 were ruled.

The Panel noted that a leaflet distributed from the exhibition stand had asked delegates to 'Test your knowledge on VTE and enter a draw to win a book voucher from …'. The supplementary information to Clause 18.2 of the 2006 Code stated 'The use of competitions, quizzes and suchlike, and the giving of prizes, are unacceptable methods of promotion'. The Panel considered it irrelevant that the quiz had been linked to those delegates from the Republic of Ireland. It had taken place in the UK with UK health professionals via a promotional stand. Bayer Schering had not complied with the supplementary information to Clause 18.2 and a breach of Clause 18.2 was ruled as alleged.

2 Supplements on rivaroxaban in the Journal of Bone and Joint Surgery (JBJS) September 2008.

COMPLAINT

Boehringer Ingelheim noted that the journal was available on 4 September 2008 when rivaroxaban was unlicensed. The supplement was published in the British volume of the journal and was circulated within the UK. As it was published prior to the grant of the marketing authorization for rivaroxaban, Boehringer Ingelheim alleged a breach of Clause 3.1.

The supplement was funded by Bayer Schering as stated in the acknowledgements of each article. However, there was no clear mention of the sponsor company at the outset; Boehringer Ingelheim alleged a breach of Clause 9.10.

Boehringer Ingelheim alleged that on the cover, page 1 and page 3, the statement 'An introduction to rivaroxaban: the first oral, once-daily, direct Factor Xa inhibitor for the prevention of venous thromboembolism' was misleading in breach of Clause 7.2 as it implied that rivaroxaban was available in September 2008 for prescription.

On page 22 under the conclusion of the article, 'Rivaroxaban: venous thromboembolism risk reduction after total hip arthroplasty' the statement, 'Rivaroxaban offers clinicians and their patients a novel orally active anticoagulant for extended thromboprophylaxis in the outpatient setting' was alleged to be misleading as 'offers' was in the present tense and thus was in breach of Clauses 7.2 and 3.1.

On page 28 under conclusions of the article, 'Rivaroxaban reduces symptomatic venous thromboembolism and has a potential positive economic impact after total knee arthroplasty', the claims 'Rivaroxaban will offer clinicians the opportunity….', and the statement, 'Importantly, unlike parenteral anticoagulants, rivaroxaban will enable an easy transition…' implied that rivaroxaban would work for all patients which was alleged to be misleading and exaggerated in breach of Clause 7.2 and 7.10. In addition, Boehringer Ingelheim considered that these claims implied that rivaroxaban would definitely be available which, given that rivaroxaban was not licensed at the time of publication, was in breach of Clause 3.1.

On page 30, the graph in figure 1, 'Efficacy of *currently* available options for venous thromboprophylaxis' (emphasis added) did not include dabigatran which had a marketing

authorization for primary prevention of venous thromboembolism events in adults following elective total hip or knee replacement surgery and was available in the UK. Boehringer Ingelheim alleged that the graph did not reflect up-to-date evidence and was misleading in breach of Clauses 7.2 and 7.3.

RESPONSE

Bayer Schering agreed that the supplement fell within the Code and was in breach of Clause 3. The supplement should have been certified in accordance with Clause 14.

An SOP was being developed to deal with the need identified under the supplementary information to Clause 19.1, for overseas affiliates to be reminded of their obligations under the Code, in relation to their meeting activities.

Finally, the therapeutic area head, thrombosis, Bayer Healthcare AG had confirmed by email that his Global Teams and Publications Agencies had been reminded to ensure that all global materials produced in the UK and/or intended for a UK audience must be submitted to Bayer plc for certification in accordance with the relevant UK SOP.

Notwithstanding the fact that the UK signatories were unaware of the entire supplement prior to its publication, Bayer Schering nonetheless argued against two of the specific concerns raised by Boehringer Ingelheim as to the content of the supplement.

Bayer plc understood Boehringer Ingelheim concerns in relation to the statement on pages 1, 3 and 22. However its concerns were based upon the tense of the wording relating to a non-licensed product, which referred to a breach of Clause 3 and not 7.2.

Boehringer Ingelheim had suggested that the statement on page 28 implied that rivaroxaban would work for all patients and was misleading. In Bayer Schering's view, the author had discussed the potential positive impacts following arthroplasty and the ease of transition from parenteral agents. The author did not comment that the potential benefits would be experienced by any specific group, or number, of patients. Bayer Schering did not believe that the statement referred to was in breach of either Clause 7.2 or 7.10.

With regard to the allegation that the graph on page 30 of the supplement disparaged dabigatran, Bayer Schering contended that it was taken from the most up-to-date reference; although dabigatran did not feature on the graph, it was discussed in the accompanying text of the article written by the author. Bayer Schering therefore refuted any breach of Clauses 7.2 and 7.3.

In summary, Bayer plc acknowledged a breach of Clause 3 caused by the Global affiliate, which was being addressed at the highest level. The company accepted that responsibility for this lay with it under the Code. Bayer Schering refuted the other allegations.

FURTHER RESPONSE

In response to a request for further information Bayer Schering submitted that the supplement had not been distributed in the UK or to UK health professionals other than by the Journal of Bone and Joint Surgery. Bayer Schering explained that it had discussed potential educational initiatives at and arising from the 9th EFORT Congress, Nice, France, 29 May-1 June 2008 with its medical education agency.

It was agreed that educational activities to be organized around EFORT 2008 would include a satellite symposium and an educational supplement involving renowned European experts in the field, including principal investigators and steering committee members of the RECORD clinical trial programme.

The satellite symposium and supplement were produced as non-promotional, educational communications adhering to Good Publication Practice for Pharmaceutical Companies and agreed publication operating procedures established between Bayer Schering and its agency. A flow chart showing the steps followed in the publication process was provided.

The satellite session had two co-chairmen who agreed to edit the journal supplement, such editing having been previously agreed by the journal editorial board. Bayer Schering provided details of the two co-chairman and of the other authors (the faculty) who contributed to the supplement.

The agency was responsible for contact and further discussion with the co-chairmen of the EFORT 2008 satellite symposium who were actively involved in generating the programme and proposing the faculty for the symposium; the faculty members were invited by the agency on behalf of the chairmen and Bayer Schering. All faculty members were subsequently involved in the generation of articles for the JBJS supplement.

The objective of the JBJS supplement was to provide a non-promotional, educational supplement generated by clinicians closely involved in the RECORD clinical trial programme for rivaroxaban to summarize clinical data that had not been presented to European orthopaedic surgeons, but had been presented previously at haematology congresses in the US in December 2007. Important new data, which was to be published in the New England Journal of Medicine and The Lancet, were to be incorporated to provide context for surgeons for these clinically important data. These objectives

were considered by the co-editors of the supplement to be an important educational requirement for surgeons attending the congress and for a wider audience reading orthopaedic journals.

The involvement of Bayer Schering in initiating the process was therefore to brief the agency on the broad educational objectives for the satellite meeting and the JBJS supplement.

Author selection for the supplement was based on the faculty speakers who participated at the Bayer Schering sponsored symposium entitled 'Improving patient outcomes after major orthopaedic surgery', which took place on Friday, 30 May 2008 during the 9th EFORT congress in Nice, France. The initial choice of faculty was based on their relevant clinical expertise and involvement in the RECORD clinical trial programme as either principal investigators or steering committee members, and was agreed in discussions between the agency, the co-chairmen and Bayer Schering. These discussions resulted in the agency being asked to invite the agreed faculty. The invitation to participate in both the satellite session and the subsequent supplement was issued by the agency on behalf of both the chairmen and Bayer Schering.

The co-chairmen of the symposium (and co-editors of the supplement) wrote the short introductory and concluding articles for the supplement entitled 'An introduction to rivaroxaban: the first oral, once-daily, direct Factor Xa inhibitor for the prevention of venous thromoembolism' and 'Anticoagulants after orthopaedic surgery: where are we now?' respectively. The other four articles included in the main body of the supplement were written by the four faculty members; one article was written by two other co-authors.

All faculty members of the EFORT 2008 satellite symposium were lead authors in the JBJS supplement. While faculty members were reimbursed for travel costs, accommodation, congress registration at EFORT and received an honorarium for their involvement with the symposium, no payment was made relating to development of articles within the subsequent JBJS supplement.

The objective was to provide the proceedings of the educational symposium at EFORT 2008 in the form of a supplement. All authors considered providing data on rivaroxaban was essential to ensure fair scientific balance, and was important in the education of their peers. All data included in the articles were referenced to peer reviewed publications and reflected the views of the authors.

Following author agreement to contribute articles to the supplement, the agency obtained author briefs from the faculty for the focus of the manuscripts for each article. Briefs from authors were taken by telephone and publications were progressed by the agency in line with this direction. Full author input was sought and provided at each subsequent stage as per the publication process document provided.

The JBJS did not conduct a formal peer-review procedure for supplements. In order to ensure fair balance and accurate presentation, it was considered important to include a review process for the supplement. The agency offered suggestions on a potential peer review process and, in line with this, the JBJS academic editor accepted the proposal that the co-chairmen of the symposium peer review and guest edit the supplement. Therefore, all draft manuscripts were submitted to the co-chairmen (co-editors of the supplement) for review, as agreed with JBJS.

Before final author review and approval of articles, draft manuscripts were submitted to Bayer Schering's global publication review team, to check the accuracy and validity of any rivaroxaban scientific and clinical trial data to be featured in the supplement. In accordance with Good Publication Practice for Pharmaceutical Companies, comments were provided directly to the authors for their consideration whereupon the authors made their final amendments, commenting where relevant, and gave their final approval of the submission drafts. The comments from Bayer Schering were marked up by the agency and forwarded to the authors for their review and decision on whether the comments be implemented. All authors had ultimate editorial control of their articles.

All authors were involved fully in directing the writing of their individual manuscript, from initial specification to final piece. This involved review and input of interim drafts, to final comment and approval of each submitted version. Professional writing support and editorial assistance was provided by the agency to authors at their request and under their direction, in the preparation of their manuscripts. This support was funded by Bayer HealthCare AG (part of the Bayer AG Group) and, in accordance with accepted Good Publication Practice, was fully acknowledged by the authors in their articles along with additional disclosure statements.

PANEL RULING

The Panel noted that it was acceptable for companies to sponsor material. It had previously been decided, in relation to material aimed at health professionals, that the content would be subject to the Code if it was promotional in nature or if the company had used the material for a promotional purpose. Even if neither of these applied, the company would be liable if it had been able to influence the content of the material in a manner favourable to its own interests. It was possible for a company to sponsor material which mentioned its own products and not be liable under the Code for its contents, but only if it had been a strictly arm's length arrangement with no input by the company and no use by the company of the material for

promotional purposes.

The Panel noted that the objective of the material in question, 'Improving Patient Outcomes After Major Orthopaedic Surgery', was to provide the proceedings of a symposium, sponsored by Bayer Schering at an international meeting, in the form of a journal supplement. The Panel considered that it would not always be possible to achieve this and comply with the requirements of the Code. Within the context of an international conference, attended by thought leaders, investigators and the like, it was possible for pharmaceutical companies to hold symposia about unlicensed products or indications as long as such activities were not otherwise promotional. The Code did not prohibit the legitimate exchange of medical and scientific information during the development of a medicine. The unsolicited distribution of symposia proceedings by a pharmaceutical company to health professionals who had not attended the meeting was not acceptable if the material promoted unlicensed medicines or did not otherwise comply with the Code.

The Panel noted that the supplement had been initiated by Bayer Schering and its agency. The co-editors and first authors were those who had taken part in the company-sponsored symposium at EFORT 2008 and although they had not been paid to write the articles in question they had all received honoraria for other work they had done for Bayer. Professional writing support and editorial assistance was funded by Bayer HealthCare AG.

The Panel considered that Bayer Schering was inextricably linked to the production of the supplement. There was no arm's length arrangement between the provision of the sponsorship and the generation of the supplement. Circulation of the supplement was not limited to those who attended the meeting as it was circulated with the JBJS. Given the company's involvement and the content of the supplement, the Panel considered that the supplement was, in effect, promotional material for Xarelto. Further, the Panel noted that the supplement was not formally peer reviewed by the JBJS. The Panel considered that the material was a paid-for insert from Bayer Schering, not a supplement from the JBJS for which its editorial board would have been responsible. The back cover of the supplement stated

> 'This supplement is provided free with the British Volume of JBJS. The contents have not been selected or edited by the Journal. All questions about scientific content should be addressed to the individual authors'.

The supplement was distributed with the September issue of the JBJS. Xarelto did not receive a UK marketing authorization until 1 October 2008. The Panel noted its comments above and considered that the supplement had promoted Xarelto to UK health professionals prior to the grant of the marketing authorization. A breach of Clause 3.1 was ruled as acknowledged by Bayer Schering.

The Panel did not consider that the statement 'An introduction to rivaroxaban: the first oral, once daily, direct Factor Xa inhibitor for the prevention of venous thromboembolism' implied that the product was available for prescription in September 2008 as alleged. No breach of Clause 7.2 was ruled. Similarly the Panel did not consider that the claim 'Rivaroxaban offers clinicians and their patients a novel orally active anticoagulant …' was misleading through the use of the present tense. No breach of Clause 7.2 was ruled. Insomuch as the claim promoted Xarelto, however, the Panel considered that its ruling of a breach of Clause 3.1 above covered this aspect.

The Panel did not consider that the statement 'Rivaroxaban will offer clinicians the opportunity to use a fixed dose, unmonitored, once-daily anticoagulant, given as a single 10mg tablet, for the prevention of VTE after major orthopaedic surgery. Importantly, unlike parental anticoagulant, Rivaroxaban will enable an easy transition from hospital to outpatient thromboprophylaxis, providing an opportunity to improve further the current standard of care in this high risk patient population' implied, as alleged, that Xarelto would work for all patients. In that regard the Panel did not consider that the statement was either misleading or exaggerated. No breach of Clauses 7.2 and 7.10 was ruled. Insomuch as the statement promoted Xarelto, the Panel considered that its ruling of a breach of Clause 3.1 above covered this aspect.

Page 30 of the supplement included a graph entitled 'Efficacy of currently available options for venous thromboembolism prophylaxis' the data for which was compiled from Geerts *et al* (2001). The data thus pre-dated the introduction of dabigatran onto the UK market. In that regard the data was not up-to-date and was misleading. Breaches of Clauses 7.2 and 7.3 were ruled.

Clause 9.10 required that material relating to medicines and their uses, whether promotional in nature or not, which was sponsored by a pharmaceutical company, must clearly indicate that it has been sponsored by that company. The front cover of the supplement did not feature a statement acknowledging Bayer Schering's involvement. Disclosures at the end of each article as to Bayer Schering's relationship with the author were not sufficient in this regard. A breach of Clause 9.10 was ruled.

3 Alleged breach of Clause 2

COMPLAINT

Boehringer Ingelheim was very concerned about the activities of Bayer Schering as detailed above and alleged that the company had undertaken pre-licence promotional activities. Boehringer

Ingelheim was further concerned that, despite multiple discussions between the two companies regarding the need to comply with the Code, Bayer Schering had repeatedly undertaken activities in the sensitive pre-licence period which had not been through self-regulation review and approval processes according to the requirement of the Code. Taking all these activities into account Boehringer Ingelheim alleged that Bayer Schering's actions had brought the industry into disrepute in breach of Clause 2.

RESPONSE

Bayer Schering strongly denied that its UK certification process was flawed. The company strongly refuted all of the claims made by Boehringer Ingelheim in relation to the Anticoagulation Congress in Birmingham.

Bayer Schering agreed that there were two related breaches of Clause 14 relating to the Irish Orthopaedic Association meeting and the JBJS supplement (which included other associated breaches). Having occurred very close together, Bayer Schering regarded these events as manifestations of the same international problem. This issue was already being addressed when both infractions occurred; in a large multi-national organisation, a certain amount of time was required for the finalisation and implementation of new processes. As explained above, this matter had been taken very seriously, and was actively being addressed at the highest level. Bayer Schering did not consider that its actions were such as to breach Clause 2.

PANEL RULING

The Panel considered that the arrangements within Bayer Schering showed poor control. It appeared that non UK parts of the business had little awareness of matters to be considered when conducting activities in the UK. It was the responsibility of the UK company to ensure compliance within the UK Code. A medicine had been promoted prior to the grant of its marketing authorization on more than one occasion. Taking all the circumstances into account the Panel considered that Bayer Schering had brought discredit upon and reduced confidence in the pharmaceutical industry and a breach of Clause 2 was ruled.

Complaint received **9 October 2008**

Case completed **23 December 2008**