CASE AUTH/1851/6/06

ROCHE v NOVARTIS

Promotion of Myfortic

Roche complained about the promotion of Myfortic (mycophenolate sodium) by Novartis. Roche supplied CellCept (mycophenolate mofetil).

Roche was concerned that a review article (Budde *et al* 2004), which was freely available from the Novartis stand at a UK conference, referred to ongoing or planned clinical trials of Myfortic and Cellcept in which the products were used in ways which were not consistent with their summaries of product characteristics (SPCs). Roche alleged that as the article discussed off-licence indications for both products, its use in a promotional setting was in breach of the Code.

The Panel noted that as Budde *et al* had been available at the Novartis promotional stand and used proactively for a promotional purpose it had to comply with the Code. The supplementary information to the Code 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. The Panel considered that distribution of the paper from Novartis' promotional stand was not in accordance with this supplementary information; on balance the distribution of the paper from a promotional stand was inconsistent with the SPC. A breach of the Code was ruled.

The Panel considered there was a difference between proactive provision of a paper and a clinical trial register whereby information about clinical research could be accessed by interested parties from such a website.

Roche stated that an advertisement published in Transplant International was subject to the Code because the registered office for the publisher (Blackwell Publishing Ltd) was in the UK. The advertisement was alleged to contain a number of misleading claims for Myfortic, some of which had previously been withdrawn by Novartis following inter-company discussions.

The Panel noted that the supplementary information to the Code, Journals with an International Distribution, stated that the Code applied to the advertising of medicines in professional journals which were produced in the UK and/or intended for a UK audience. International journals produced in English in the UK were subject to the Code even if only a small proportion of their circulation was to a UK audience.

Transplant International was the journal of the European Society for Organ Transplantation and the European Liver and Intestine Transplant Association and was intended for an international readership. It was clearly an international journal with an editorial office, editor-in-chief and co-editor-in-chief all based in Vienna. It was published by Blackwell Munksgaard, Germany, it was printed in, and distributed from, Singapore.

The principal UK connection was that the head office of the publisher, Blackwell Publishing, was located in Oxford. The Panel noted that Blackwell Publishing had informed Novartis that, in legal terms, the journal must be considered as being produced in the UK.

The Panel, however, had to base its decision on the wording of the Code and its supplementary information. The Panel considered that in view of the locations in which the activities associated with the journal's publication took place, it could not be regarded as having been produced in the UK. The Panel's opinion was that the word 'produced' in the supplementary information related to factors such as where an international journal was compiled and edited and where it was physically produced etc, rather than the location of the publisher's head office. Further, the journal was not intended specifically for a UK audience but for an international one. It did not come within the scope of the UK Code. The Panel accordingly ruled that there could have been no breach of the Code.

Roche Products Limited complained about the promotion of Myfortic (mycophenolate sodium) by Novartis Pharmaceuticals UK Ltd. The items at issue were a review article and a journal advertisement (ref myf1001D). Roche supplied CellCept (mycophenolate mofetil).

1 Review article 'Review of the immunosuppressant enteric-coated mycophenolate sodium', Budde *et al*, 2004

COMPLAINT

Roche stated that this article was freely available from the Novartis trade display at the British Society for Transplantation meeting, held in Edinburgh on 29-31 March. Roche's specific concerns related to the section entitled 'Future directions' which provided details of ongoing or planned clinical trials investigating the following uses of Myfortic:

- withdrawal or avoidance of steroids;
- in combination with currently licensed immunosuppressants tacrolimus or sirolimus;
- in combination with the investigational compounds everolimus or FTY 720.

Furthermore, references were made to the use of mycophenolate mofetil (MMF) and tacrolimus in steroid-sparing or steroid-free regimens.

None of these uses were consistent with the recommendations in the respective summaries of product characteristics (SPCs) for Myfortic and CellCept. As the article discussed off-licence indications for both products, its use in a promotional setting such as a trade display was in breach of Clause 3.2 of the Code.

RESPONSE

Novartis noted that Roche had alleged that the inclusion of a brief description of the design of

Myfortic clinical trials at the end of an independent review article provided on the stand at the British Society for Transplantation meeting held in March of this year was in breach of Clause 3.2 of the Code. Novartis disagreed for two reasons. Firstly, the section of the article to which Roche referred was clearly entitled 'Future directions' and was distinctly separate from the section entitled 'Clinical safety and tolerability' and secondly, no claim for the efficacy, safety or tolerability of any unlicensed use was made in association with this listing.

The ABPI had made laudable efforts to increase the transparency of clinical trial activity, with the establishment of an ABPI Clinical Trial Register in 2003. Novartis was an early contributor to this register and the ABPI website currently contained links to Novartis trial listings. It was difficult to see how the bland listing of ongoing trials in an independent review paper breached Clause 3.2 of the Code when a similar listing on a public website was both encouraged and endorsed by the ABPI as part of a commitment to increased transparency regarding industry led research. With the greater availability of such information to prospective authors it was to be expected that many more would legitimately include summaries of ongoing and proposed research in their publications as Budde *et al* had done.

PANEL RULING

The Panel noted that Budde *et al* had been available at the Novartis promotional stand. It was being used proactively for a promotional purpose and thus had to comply with the Code. The Panel noted the supplementary information to Clause 3.1 of the Code 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 Panel considered that distribution of the paper from the Novartis' promotional stand was not in accordance with this supplementary information.

The Panel considered there was a difference between proactive provision of a paper and a clinical trial register whereby information about clinical research could be accessed by interested parties from such a website.

The Panel noted that the section at issue in Budde *et al* was headed 'Future directions' and referred to ongoing clinical studies. Reference was made to different patient populations and treatment regimes including withdrawal or avoidance of steroids. Some of the results were said to be expected in 2005. No outcomes were reported. The Panel considered that on balance the distribution of the paper from a promotional stand was inconsistent with the SPC. Thus a breach of Clause 3.2 of the Code was ruled.

2 Journal advertisement

COMPLAINT

Roche stated that an advertisement published in the May edition of Transplant International was subject to the Code because the registered office for the publisher (Blackwell Publishing Ltd) was in the UK.

The advertisement contained a number of misleading claims for Myfortic, some of which had previously been withdrawn by Novartis following inter-company discussions in September 2004 and January 2005. These included:

- 'advanced, enteric-coated formulation …'; this claim was alleged to be in breach of Clauses 7.2 and 7.4;
- 'designed to avoid MPA-related upper GI adverse events'; the claim 'designed to protect the upper GI tract' was alleged to be in breach of Clauses 7.2 and 7.4;
- 'The next step'; this claim was alleged to be in breach of Clauses 7.2 and 7.4.

The advertisement also contained a number of other claims that were alleged to be inappropriate and misleading:

- 'my protection' and subsequent 'patient quote'; this claim suggested clinical superiority of Myfortic in respect to CellCept: Roche stated that randomised head-to-head comparisons of CellCept and Myfortic had shown no statistically significant differences in terms of efficacy or safety or endpoints; therefore this claim was misleading and alleged to be in breach of Clause 7.3;
- '… designed to avoid MPA-related upper GI adverse events* with the goal of minimizing the need for dose reductions'; the presentation of this claim was misleading, as it was not made clear to the reader that there was no statistical difference in upper GI adverse events conferred by Myfortic. A breach of Clause 7.2 was alleged as the fact that there was no statistically significant difference in upper GI adverse events was qualified in a footnote, thereby breaching Clause 7 (general supplementary information).

RESPONSE

Novartis noted that the advertisement was not produced or placed in Transplant International by the UK company. The advertisement was designed for an international audience and had been placed in an international journal and, as such, Novartis did not believe that it was subject to the Code. The supplementary information to Clause 1.1 stated that 'The Code applies to the advertising of medicines in professional journals which are produced in the UK and/or intended for a UK audience'.

Transplant International was the journal of the European Society for Organ Transplantation and the European Liver and Intestine Transplant Association, and was intended for an international audience.

The editorial office, the editor-in-chief and co-editor-in-chief of the journal were all based in Vienna. The journal was published by Blackwell Munksgaard, Germany, and it was printed in and distributed from Singapore (communication from Blackwell publishing). It was not therefore produced in the UK or intended for a specifically UK audience.

It was possible that Roche had misinterpreted the statement 'Transplant International is published by Blackwell Publishing, 9600 Garsington Rd, Oxford, UK' to mean that the journal was produced in the UK and/or was intended for a UK audience. Blackwell Publishing was a global publisher, with its head office in Oxford. It published 805 journals worldwide and had offices in the US, UK, Australia, China, Denmark, Germany, Singapore and Japan.

Novartis did not believe that the listing of a UK head office representing a global publisher was an appropriate basis for defining production or intended readership. Many other Blackwell journals, for example the American Journal of Transplantation (AJT) could, by the same reasoning be classed as 'produced in the UK and/or intended for a UK audience' and therefore all advertisements carried would need to include UK prescribing information.

Following receipt of the response further comments were received from Novartis regarding new information received from Blackwell Publishing which appeared to contradict the information previously received from Blackwell's used as the basis for Novartis' original response.

Subsequent communication from Blackwell's confirmed the accuracy of the geographical information provided but it now suggested after consultation with its legal department that the journal in question, in legal terms, must be considered as being 'produced' in the UK.

Novartis continued to believe that applicability of the Code must relate to more than an individual publishers' legal definition of 'production' when by all practical criteria this was an international journal because of its intended auidence and geographical site of editing, production and distribution.

In practical terms, it would seem extremely problematic to define all 805 journals produced by Blackwell's, including titles such as the American Journal of Transplantation, as being produced in the UK. This would require them, by the wording of Clause 1.1, to adhere to the UK Code. Novartis suggested that to date international companies worked in good faith, and on the same assumption as Novartis, in placing non-UK advertisments in certain Blackwell Journals.

INITIAL CONSIDERATION BY PANEL

The Panel gave preliminary consideration to the matter and provisionally decided that the advertisement was published in a journal which was subject to the Code. As Novartis had thus far, only responded as to whether or not the advertisment was subject to the Code it now needed to respond to the specific allegations.

Novartis was asked to respond to the allegations.

FURTHER RESPONSE FROM NOVARTIS

Novartis was surprised and disappointed by the Panel's preliminary view that advertisments appearing in Transplant International were subject to the Code. Novartis continued to believe that the respective sites of publication, editing, printing and distribution of a journal, together with it purpose and readership, should be considered in addition to the location of the publisher's global head office when defining the location of 'production' of a journal.

With regard to the specific allegations made by Roche, the claims were not used in any promotional copy employed by the UK company and the advertisement in question was not placed in Transplant International by Novartis Pharmaceuticals UK Limited. The advertisements were placed by the parent company, Novartis Pharma AG, in the reasonable belief that this was an international publication with an international readership, not subject to the UK Code or having a specifically UK audience.

Novartis in the UK reached an intercompany agreement with Roche to stop using the claims detailed in Roche's letter of 19 June to Novartis. The two additional claims referred to in Roche's complaint, represented no more than an extension of the claims previously withdrawn in the UK.

Novartis had honoured its agreement with Roche and would continue to do so for UK materials. It did not seek to defend any specific allegations.

PANEL RULING

The Panel noted that the supplementary information to Clause 1.1 of the Code, Journals with an International Distribution, stated that the Code applied to the advertising of medicines in professional journals which were produced in the UK and/or intended for a UK audience. International journals produced in English in the UK were subject to the Code even if only a small proportion of their circulation was to a UK audience.

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The principal connection between the journal and the UK was that the head office of the publisher, Blackwell Publishing, was located in Oxford. The Panel noted that Blackwell Publishing had informed Novartis that, in legal terms, the journal must be considered as being produced in the UK.

The Panel, however, had to base its decisions on the wording of the Code and its supplementary information. The Panel considered that in view of the locations in which the activities associated with the journal's publication took place, it could not be regarded as having been produced in the UK. The Panel was of the opinion that the reference to 'produced' in the supplementary information related to factors such as where an international journal was compiled and edited and where it was physically produced etc, rather than the location of the publisher's head office. Further, the journal was not intended specifically for a UK audience but for an

international one. It did not come within the scope of the UK Code. The Panel accordingly ruled that there could have been no breach of the Code.

The advertisement in Transplant International would be covered by a code of practice and it was a question of which applied. As the advertisement had been placed by Novartis Switzerland, the Swiss, Austrian and German codes might apply.

Complaint received **22 June 2006**

Case completed **1 September 2006**