Drug company sues Spanish bulletin over fraud claim

Liza Gibson *London*

One of Spain's independent drug bulletins, *Bulletí Groc*, is being sued by Merck Sharp & Dohme for an article that claimed that the company committed scientific fraud in a trial of its cyclo-oxygenase-2 (COX 2) inhibitor rofecoxib (Vioxx). The case opened in Madrid last week.

The company wants the bulletin to retract its article on the Vioxx gastrointestinal outcomes research (VIGOR) trial and publish a new one reproducing text prepared by the company. However, Professor Joan-Ramon Laporte, the bulletin's editor, refuses to do so.

He said: "I feel this is an attack on independent information on drugs. The pharmaceutical industry has almost a monopoly on information on drugs and therapeutics." Professor Laporte claimed that the company's text was "mainly propaganda" for rofecoxib.

The article, entitled "The so called advantages of celecoxib and rofecoxib: scientific fraud," was published in the July-September 2002 issue of the bulletin (2002;15:13-5) but was not based on new material. It summarised earlier commentaries in the *Lancet* (2002;360:100-1) and the *BMJ* (2002;324:1287-8) on irregularities in the conduct and analysis of the VIGOR trial and the celecoxib long term arthritis safety study (CLASS). These large trials compared the gastrointestinal safety of two COX 2 inhibitors, rofecoxib and celecoxib (Celebrex), respectively, with traditional non-steroidal anti-inflammatory drugs.

In the VIGOR trial, which was published in the *New England Journal of Medicine* in November 2000 (343:1520-8), rofecoxib was found to be associated with significantly fewer upper gastrointestinal events than naproxen but with a higher incidence of myocardial infarction. The finding has been the subject of much debate in medical journals.

The bulletin said the results of the VIGOR trial generated doubts on the cardiovascular effects of rofecoxib. It referred to a *Lancet* commentary that had "raised the possibility that the company was already aware of

the likelihood of this adverse effect, and suggests that a selection bias may have been introduced which may have led to an underestimation of rofecoxib cardiovascular toxicity."

Merck Sharp & Dohme, however, disagrees with many aspects of the *Lancet* article.

The general conclusion of the bulletin's article, which referred to

tion of the results of the studies.

The company said it would not accept this "most serious accusation of fraud and data manipulation." It demanded "rectification" of the comments, which they claimed were defamatory, adding that such "rectification" was its constitutional right.

The company said that its legal action against Professor Laporte and the Catalan Institute of Pharmacology, the publisher of the bulletin, comes after unsuccessful discussions with the editor for more than a year.

It originally sought action in

Laporte believes that Pfizer felt that taking action would lead to worse results for the company.

The bulletin has received some 700 signatures of support—from countries in Latin America that use the bulletin and from European centres. One signatory is Professor Michael Rawlins, chairman of the National Institute for Clinical Excellence.

Professor Joe Collier, president of the International Society of Drug Bulletins, of which *Bulletí Groc* is a member, has also pledged support. He has written to the court saying that "large transnational pharmaceutical companies have a history of unjustified bullying of their critics" and that the bulletin accurately reflected the irregularities of the trials, noting that this had been described in various publications, including the society's newsletter in July 2002.

The matter has also become an issue for the World Health Organization, as the Catalan Institute of Pharmacology is a WHO collaborating centre. "Indirectly, this is an attack on the WHO," said Dr German Velasquez, coordinator of WHO's drug action programme. "It is a pity it is going to the courts, because they are not competent to debate technical issues. [It is best left] to scientific medical journals," he said.

This is the first time that a Spanish drug bulletin faces a court trial. A hearing took place on 16 January, and a decision is expected in the next two weeks.

The issue of the cardiovascular safety of rofecoxib has an EU-wide dimension. In November 2003 the European Agency for the Evaluation of Medicinal Products' scientific advisory body, the Committee for Proprietary Medicinal Products, concluded that the risk-benefit ratio of the two drugs remained positive. However, it recommended that warnings on the drugs should be added or strengthened, in particular for patients with underlying gastrointestinal and cardiovascular risks.

The European Commission has yet to issue a response to the committee's safety review, which was initiated by France in July 2002, around the time when the safety of the drugs was being debated.

A spokesman for Merck Sharp & Dohme said that on the basis of all available data it stands by the efficacy and safety profile of Vioxx. □

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both trials, said that the assessment and financing of the drugs was based on distorted information presented to the European regulatory body, the European Agency for the Evaluation of Medicinal Products—unlike the information that was available to the US Food and Drug Administration.

It said that the obvious commercial interests that led to the manipulation of the scientific results and the disregard of patients' health undermined trust in the scientific rigour of the published studies.

It also added that there were serious ethical transgressions in the design, analysis, and publica-

October 2002, but this was rejected by a lower court. The company then applied to a higher court, which overturned the earlier decision. The company says the lower court had not accepted the case because of a technicality.

Professor Laporte believes that the use of the words "scientific fraud" in the title of the article and its conclusion that the drug industry was more interested in profits than health could be part of the reason why the company was taking the journal to court. The manufacturer of celecoxib, Pfizer, unlike Merck Sharp & Dohme, did not take legal action against the bulletin. Professor