Reviewer leaked Avandia study to drug firm

A peer reviewer for *The New England Journal of Medicine* (NEJM) broke confidentiality and leaked a damaging report about the blockbuster diabetes drug Avandia to the drug's manufacturer weeks ahead of publication, *Nature* has learned.

Avandia (rosiglitazone) came under heavy scrutiny after 21 May 2007, when the NEJM published online a meta-analysis¹ of other studies into the drug's efficacy and safety. The results showed that the drug increased the risk of heart attack by 43% in people who took it for at least 24 weeks. The report garnered wide-

spread media attention, prompted the Food and Drug Administration (FDA) to issue a safety alert, and cut the stock price of Avandia's manufacturer, GlaxoSmith-Kline (GSK), by 13%.

But 17 days earlier, the reviewer, diabetes researcher Steven Haffner of the University of Texas Health Science Center at San Antonio, had faxed his copy of the article to Alexander Cobitz, a GSK employee whom Haffner knew from working on an earlier clinical trial of the drug. "Why I sent it is a mystery," Haffner told *Nature*. "I don't really understand it. I wasn't feeling well. It was bad judgement," Haffner says that Cobitz did not ask to see the draft and was "probably a bystander".

Nancy Pekarek, a spokeswoman for GSK, says that the company did not offer any input to Haffner on the meta-analysis, and that she was not aware of anyone at GSK informing the NEJM of the confidentiality breach.

Haffner had earlier served on the steering committee of a GSK-sponsored clinical trial of Avandia. He says that he has given many talks for the company, although he declined to say how much he had earned from them. "I've got a considerable amount of money. I didn't do it to raise my income or anything like that," he says.

After publication of the meta-analysis, GSK

vigorously contested the study's methodology and "strongly disagreed" with its conclusions. Then on 5 June, again in the NEJM online, GSK-sponsored researchers published an interim analysis² of the company's RECORD trial of Avandia, a prospective study launched in 2001 to monitor adverse cardiac events. The June report referenced the May study and said that the new RECORD data "were insufficient" to determine whether Avandia increased the risk of a heart attack.

The interim RECORD analysis was published just 15 days after the damaging meta-

analysis. Pekarek says that the FDA had previously asked to see the RECORD data, but that the company's inside knowledge of the meta-analysis "added an additional sense of urgency" that drove the swift publication.

Karen Pederson, a spokeswoman for the NEJM, says that the journal's policy is not to discuss specific peer reviewers. But she adds that any reviewer who breaks confidentiality is banned from future reviewing and from contributing editorials and review articles. Last April, the journal imposed such penalties on a prominent cardiologist, Martin Leon of the Cardiovascular Research Foundation in New York, after he talked about an embargoed study at a meeting.

In November, after being ordered to do so by the FDA, GSK added a black-box warn-

ing on Avandia packaging. The lengthy warning describes the meta-analysis and its findings, but also says that "the available data on the risk of myocardial ischemia are inconclusive".

In the third quarter of 2007, sales of Avandia were down 38% from a year earlier worldwide and down 48% in the United States. ■

Brian Vastag

1. Nissen, S. E. & Wolski, K. *N. Engl. J. Med.* **356**, 2457-2471 (2007).
2. Home, P. D. et al. *N. Engl. J. Med.* **357**, 28-38 (2007).

Sales of diabetes drug Avandia have fallen sharply in the wake of health concerns.

"Why I sent it is a mystery. I don't really understand it. I wasn't feeling well. It was bad judgement."