JAMA articles say Merck used Vioxx ghostwriters

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Merck & Co. Inc. hid the true peril of its now-withdrawn pain reliever Vioxx as its employees were ghostwriting papers praising the drug and giving author credit to leading professors who did little work, assert two articles appearing today in the Journal of the American Medical Association.

The JAMA authors said Vioxx was a case study of how a company could manipulate research and plant favorable articles to buff up a drug's image.

The journal's editor, Catherine D. DeAngelis, said her journal had been duped by a ghostwritten manuscript in 2002 that compared Vioxx with two competitors' drugs for knee pain, and she acknowledged that editors bore some responsibility.

One of the professors, however, yesterday disputed the JAMA articles as misrepresenting his role. And Merck released two statements saying that the articles contained numerous errors and that they merely reprised arguments made by plaintiffs' attorneys in lawsuits involving Vioxx. The company stressed it had shared all safety data with the Food and Drug Administration, which monitors drug safety.

Several of the JAMA authors had consulted for plaintiffs' attorneys, and none asked the company for comment before publication.

Vioxx, used to quell pain in arthritis and other ailments, was a blockbuster drug that rang up more than $11.2 billion in sales for Merck from 1999 to 2004, company reports show.

The firm, which employs roughly 12,000 people at extensive operations around West Point, Montgomery County, voluntarily took Vioxx from the market Sept. 30, 2004, amid concerns over heart attacks. The company announced a $4.85 billion deal in November 2007 that is on pace to settle most suits, said James Fitzpatrick, a New York lawyer representing the firm.

One JAMA article was highly critical of Merck's handling of research data. Bruce M. Psaty and Richard A. Kronmal, both of the University of Washington, wrote that two trials on whether Vioxx could delay the onset of Alzheimer's disease showed a significantly higher risk in mortality for those taking the drug.

When the FDA asked about those extra deaths, Merck called the findings "small numeric differences . . . most consistent with chance," the researchers wrote.

But Psaty, who has not consulted with Vioxx plaintiffs' attorneys, said the combined trials found a three-times-higher mortality rate in those taking Vioxx.

Psaty said he was disturbed that, while the trials were mostly finished in 2001, the complete results were not published until 2005, after Vioxx had been withdrawn from the market.

One trial also lacked an independent safety-monitoring board, he said.

"Our study raises questions about the wisdom of allowing the sponsor to control the data and the analysis," Psaty said. "I don't think the companies have the ability to weigh the risks and benefits of their drugs."

In an accompanying editorial, JAMA editor DeAngelis echoed those concerns, saying that independent investigators should be involved in collecting and analyzing trials funded by for-profit firms.

Fitzpatrick, the Merck attorney, said Merck had used outside scientists to monitor late-stage trials since 2006. The company told the FDA in July 2001 that more deaths had occurred among patients taking Vioxx. But he said they were due to factors unrelated to the drug.

In a second article, JAMA authors found documents indicating that Merck employees had written papers or hired ghostwriting firms to do so.

DeAngelis, in an interview, lambasted medical ghostwriters, calling their work "a terrible form of prostitution" and said it was another sign of how physicians and researchers had succumbed to drug firms' influence.

"We've given up the profession," DeAngelis said, "and we've got to get it back."

The first draft of a 2002 Vioxx article published in JAMA was written by staff of Scientific Therapeutics in Springfield, N.J., according to the JAMA article.

Scientific Therapeutics' president, John Romankiewicz, did not respond to requests by phone and e-mail for comment.

Lead author of the JAMA article, Joseph S. Ross, a geriatrician at Mt. Sinai School of Medicine in New York, said ghostwriting had been used for other drugs, including the anticonvulsive drug Neurontin.

"Our suspicion is that it's quite common," said Ross, who has consulted for Vioxx plaintiffs' attorneys. "It taints all the potential legitimate research that is being done by the pharmaceutical industry."

Ross and his colleagues cited an Alzheimer's study that initially listed Merck scientists as authors and came to show three outside researchers in the top spots.

The first author was Leon J. Thal, of the University of California-San Diego. His co-author, Steven H. Ferris of New York University, said yesterday that Thal, who died in a plane crash last year, played a key role in designing the study for Merck.

Ferris said he himself was paid to serve on a committee that checked whether patients had developed Alzheimer's disease, the subject of the study. And Louis Kirby, the third author, ran one of the largest clinical-trial sites, Ferris said.

"I personally find it somewhat scandalous," Ferris said of the JAMA piece. "Our names were not simply stuck on at the last minute."

Paul Aisen, a professor in neurosciences at UCSD who worked with Thal, voiced similar concerns.

"The article is irresponsible and false," Aisen said. He said Thal was well-known as the father of Alzheimer's disease drugs and was heavily involved in the study.

"The fact that there was no effort," Aisen said, "to get a statement from the authors named is irresponsible on the part of the journal."