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Ghostwriters Used in Vioxx Studies, Article Says

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The drug maker Merck drafted dozens of research studies for a best-selling drug, then lined up prestigious doctors to put their names on the reports before publication, according to an article to be published Wednesday in a leading medical journal.

The article, based on documents unearthed in lawsuits over the pain drug Vioxx, provides a rare, detailed look in the industry practice of ghostwriting medical research studies that are then published in academic journals.

The article cited one draft of a Vioxx research study that was still in want of a big-name researcher, identifying the lead writer only as "External author?"

Vioxx was a best-selling drug before Merck pulled it from the market in 2004 over evidence linking it to heart attacks. Last fall the company agreed to a $4.85 billion settlement to resolve tens of thousands of lawsuits filed by former Vioxx patients or their families.

The lead author of Wednesday's article, Dr. Joseph S. Ross of the Mount Sinai School of Medicine in New York, said a close look at the Merck documents raised broad questions about the validity of much of the drug industry's published research, because the ghostwriting practice appears to be widespread.

"It almost calls into question all legitimate research that's been conducted by the pharmaceutical industry with the academic physician," Dr. Ross said, whose article, written with colleagues, was published Wednesday in JAMA, the journal of the American Medical Assocation.

Merck on Tuesday acknowledged that is sometimes hires outside medical writers to draft research reports before handing them over to the doctors whose names eventually appear on the publication. But the company disputed the article's conclusion that the authors do little of the actual research or analysis.

And at least one of the doctors whose published research was questioned in Wednesday's article, Dr. Steven H. Ferris, a New York University psychiatry professor, said the notion that the article bearing his name was ghostwritten was "simply false." He said it was "egregious" that Dr. Ross and his colleagues had done no research besides mining the Merck documents and reading the published medical journal articles.

In an editorial on Wednesday, the journal said the analysis showed that Merck had apparently manipulated dozens of publications to promote Vioxx.

"It is clear that at least some of the authors played little direct roles in the study of review, yet still allowed themselves to be named as authors," the editorial said.

The editorial called for immediate changes in the practice, calling upon medical journal editors to require each

author to report his or her specific contributions to articles.

JAMA itself published one of the Vioxx studies that was cited in Dr. Ross's article.

In that case, in 2002, a Merck scientist was listed at the lead author. But Dr. Catherine D. DeAngelis, the journal's editor, said in a telephone interview Tuesday that, even so, it was dishonest because the authors did not fully disclose the role of a ghostwriter.

"I consider that being scammed," Dr. DeAngelis said. "But is that as serious as allowing someone to have a review article written by a for-profit company and solicited and paid for by a for-profit company and asking you to put your name on it after it was all done?"

Although the role of pharmaceutical companies in influencing medical journal articles has been questioned before, the Merck documents provided the most comprehensive look at the magnitude of the practice, according to one of the study's four authors, Dr. David S. Egilman, a clinical associate medical professor at Brown University.

In the Vioxx lawsuits, millions of Merck documents were supplied to plaintiffs. Those documents were available to Dr. Egilman and Dr. Ross because they had served as consultants to plaintiffs' lawyers in some of those suits.

Dr. Ross said the concerns go beyond the authorship of drug research studies, raising questions about the validity of the clinical trials on which the research is based. "Who designed the trial? Who did the trial? Who did the analysis? Who interpreted the analysis?" Dr. Ross said.

Combing through the documents, Dr. Ross and his colleagues unearthed internal Merck e-mail messages and documents about 96 journal publications, which included review articles and reports of clinical studies. In some cases, Merck's marketing department was involved in developing plans for manuscripts, the article said.

The Ross team said it was not necessarily raising questions about all 96 articles. But for many of the papers their document searches found scant evidence that the recruited authors made substantive contributions.

For example, in 16 of 20 papers that reported on clinical trials, a Merck employee was designated as the author of the first draft of the manuscript. But an outside academic scientist was listed as the lead author when the study was published.

One paper involved a study of Vioxx as a possible deterrent to Alzheimer's progression.

The draft of the paper, dated August 2003 identified the lead writer as "External author?" But by the time the paper was published in 2005 in the journal Neuropsychopharmacology, the lead author was listed as Dr. Leon J. Thal, a well-known Alzheimer's researcher at the University of California, San Diego. Dr. Thal was killed in an airplane crash last year.

The second author listed on the published Alzheimer's paper, whose name had not been on the draft, was Dr. Ferris, the New York University professor. Dr. Ferris, reached by telephone Tuesday, said he had played an active role in the research and writing.

He said he reviewed data on hundreds of patients enrolled in the study to determine whether their mild cognitive

impairment had progressed to Alzheimer's. Later, he said, he was substantially involved in helping shape the final draft. "It's simply false that we didn't contribute to the final publication," Dr. Ferris said.

A third author, also not named on the initial draft, was Dr. Louis Kirby, currently the medical director for the company Provista Life Sciences. In an e-mail message Wednesday, Dr. Kirby said that as a clinical investigator for the study he had enrolled more patients, 109, than any of the other researchers. He also said he made revisions to the final document.

"The fact that the draft was written by a Merck employee for later discussion by all the authors does not in and of itself constitute ghostwriting," Dr. Kirby's e-mail said.

The current editor of the journal Neuropsychopharmacology, Dr. James H. Meador-Woodruff, said he was not editor in 2005 but planned to investigate the accusations. "Currently, we have in place prohibitions against this," said Dr. Meador-Woodruff, who is the chairman of psychiatry at the University of Alabama, Birmingham.

Merck said Tuesday that any outside authors named in its studies were involved in the research, as well as drafting and reviewing of the papers bearing their names.

While the company sometimes hires professional writers to formulate early drafts of scientific articles, the final work is the product of the doctor, the company said.

"Ultimately that doesn't change the fact that the work accurately reflects his or her opinion," a Merck lawyer, James C. Fitzpatrick, said.

The issue of JAMA published Wednesday also included another Vioxx-related paper that drew from the same cache of documents.

In that paper, Dr. Bruce Psaty and Dr. Richard A. Kronmal of the University of Washington concluded that in the years leading to the Vioxx recall, the company was not fully candid in submitting data to the Food and Drug Administration about the drug's heart attack risk.

Merck said that the Psaty and Kronmal analysis was misleading, saying the F.D.A. had been aware of concerns over cardiovascular risks associated with Vioxx and had been engaged in continuing discussions with the company.

The article about ghost-writing also reviewed the role of companies that engage in medical writing for hire. The paper included a copy of a 1999 memo from Scientific Therapeutics, a medical writing company in New York, which discussed the status of eight different reports the company was working on for Merck.

At least one of the Scientific Therapeutic papers was being aimed at The Journal of the American Medical Association, according to a letter in dated October 2000. The study was published in the association's journal in January 2002, with two academic physicians identified as co-principal investigators, but listing a Merck employee as the lead author. The article did not include a disclosure of the role of Scientific Therapeutics.

Wednesday's JAMA editorial noted, "Journal editors also bear some of the responsibility for enabling companies to manipulate publications."