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Drug Maker Said to Pay Ghostwriters for Journal Articles

By DUFF WILSON

Wyeth, the pharmaceutical company, paid ghostwriters to produce medical journal articles favorable to its female hormone replacement therapy Prempro, according to Congressional letters seeking more information about the company's involvement in medical ghostwriting. At least one article was published even after a federal study found the drug raised the risk of breast cancer.

The letters, sent electronically Friday by Senator Charles E. Grassley, ask Wyeth and DesignWrite, a medical writing firm, to disclose payments related to the preparation of journal articles and the activities of doctors who were recruited to put their names on them for publication.

The letters are part of a continuing investigation by Mr. Grassley, a member of the Senate Finance Committee, into drug industry influence on doctors.

"Any attempt to manipulate the scientific literature, that can in turn mislead doctors to prescribe drugs that may not work and/or cause harm to their patients, is very troubling," Mr. Grassley, an Iowa Republican, wrote Friday to Wyeth's chairman and chief executive, Bernard J. Poussot.

Phone calls and e-mail messages to Wyeth and DesignWrite were not immediately returned.

Mr. Grassley's staff on the Senate Finance Committee released dozens of pages of internal corporate documents gathered from lawsuits showing the central, previously undisclosed role of Wyeth and DesignWrite in creating articles promoting hormone therapy for menopausal women as far back as 1997.

One article was published as an "Editors' Choice" feature in May 2003 in The American Journal of Obstetrics and Gynecology, more than a year after a big federal study called the Women's Health Initiative linked Wyeth's Prempro, a combination of estrogen and progesterin, to breast cancer. The May 2003 article said there was "no definitive evidence" that progestins cause breast cancer and added that hormone users had a better chance of surviving cancer.

At the peak of hormone therapy, in 2001, more than 126 million prescriptions for such drugs were written for women in the United States. Sales that year, primarily by Wyeth, were \$3 billion. But after the federal finding, sales of the hormone drugs plummeted.

The drugs, which contain cancer warnings on the label, are still approved to treat severe symptoms of menopause, but their use is advised at only the lowest possible doses.

The documents show company executives came up with ideas for medical journal articles, titled them, drafted outlines, paid writers to draft the manuscripts, recruited academic authors and identified publications to run the articles — all without disclosing the companies' roles to journal editors or readers.

The issue of ghostwriting for medical journals has been raised in the past, involving various companies and drugs, including the Merck painkiller Vioxx, which was withdrawn in 2004 after it was linked to heart problems, and Wyeth's diet pills, Redux and Pomdimin, withdrawn in 1997 after being linked to heart and lung problems.

But the documents Mr. Grassley released Friday provide a detailed look at the practice — from the conception of ideas for journal articles through the distribution of reprints.

The articles all involve reviews of clinical studies and other research. While such reviews are common in medical publishing, what Mr. Grassley contends happened with the Wyeth-commissioned articles is that that expert authors whose names appear on the articles became involved only after outlines or drafts of the articles were already written.

When accusations of ghostwriting have cropped up in patient lawsuits over its hormone drugs, Wyeth executives to date have insisted that their publication practices were legitimate and that the listed authors played significant roles in journal articles.

But the documents released Friday include a “publication plan tracking report” by Wyeth showing 10 articles in which manuscripts were completed by the company before they were sent to the putative author for review. Any revisions were subject to final approval from the company, according to the tracking report.

Such activities would seem to run afoul of medical journal guidelines. The International Committee of Medical Journal Editors says authorship means “substantive intellectual contributions” including conception or analysis of the subject and drafting or critical revision of the document. The World Association of Medical Editors says ghost authorship — which it defines as a substantial contribution not mentioned in the manuscript — is “dishonest and unacceptable.”

Congressional investigators were given the documents about a month ago by James F. Szaller, a personal injury lawyer in Cleveland who has sued drug makers. Mr. Szaller collected the documents from court filings and made reference to some in an article he wrote last year for a law magazine, *Trial*.

“For the last three years, I’ve looked at ghostwriting at Wyeth,” Mr. Szaller said in a telephone interview. “There is a mammoth amount of material. The problem is that almost all of it is still under seal.”

In Friday’s letter, Mr. Grassley asked Wyeth to list all scientific reports prepared for the company by DesignWrite since Jan. 1, 1995, to describe the named authors’ “extent of involvement” and to disclose fees paid to DesignWrite, authors and others. He also requested “all internal and external correspondence, communications and meeting minutes regarding each of the DesignWrite-prepared studies.”

The letter to DesignWrite requested all manuscripts prepared for Wyeth since 1995, along with information on related payments and a description of the author’s involvement.

The May 2003 article supporting Prempro was signed by Dr. John Eden, an associate professor at the University of New South Wales and director of the Sydney Menopause Center in Australia. Wyeth executives suggested that Dr. Eden write such a paper in 2000, according to the documents, and had the outline and draft manuscript written for him. The Archives of Internal Medicine rejected the paper before it was published in *The American Journal of Obstetrics and Gynecology* — with no mention of Wyeth or DesignWrite connections.

Dr. Eden did not respond to an e-mail request for comment.

In another case, documents show, Dr. Lila E. Nachtigall, a New York University professor and director of its Women’s Wellness Center, was recruited by Wyeth as author of a 1999 journal article extolling hormone treatment after the manuscript had already been drafted.

Dr. Nachtigall, reached by telephone Friday afternoon, said she had written all of the approximately 1,000 articles and three books she has had published. Asked about the Wyeth documents, she said, “If they came up with the idea or gave me an outline or something, I don’t remember that at all.” Dr. Nachtigall, who is still practicing at age 75, added: “It kind of makes me laugh that with what goes on in the Senate, the senator’s worried that something’s ghostwritten. I mean, give me a break.”

Two months before the negative findings of the federal study were released, a May 2002 memo to DesignWrite employees said that Michael S. Dey, who was president of Wyeth’s Women’s Healthcare Business unit, asked a committee to increase the number of positive journal articles related to another of its hormone replacement drugs, Premarin. “Mike would like us to publish at least 1 study per month,” the memo said.

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