

Who You Gonna Call? Journal Editors Flounder In Addressing Medical Literature's Dirty Little Secret

By Johnathan Fish, J.D., LL.M. Candidate (Health Law)
jcfish@central.uh.edu

Concern over medical ghostwriting – typically involving a prominent physician taking credit for a scientific paper written primarily by a representative of a drug company to promote a product – is nothing new. However, recent revelations have rekindled debate as to whether it is a problem and, if so, how best to deal with the pharmaceutical industry's influence on scientific literature.

Background

In its most controversial form, medical ghostwriting involves a drug company initiating and funding a public relations campaign that uses medical journals to promote the sales of a top-selling drug.¹ The drug company begins by hiring a medical communication company that, in turn, hires ghostwriters to draft a scientific manuscript favorable to a particular drug product. After a draft is completed, the medical communication company finds a prominent and/or academically affiliated physician who agrees to lend his or her name as the author despite little or no contribution to the manuscript. The article is then published in a well-respected medical journal without disclosing the roles of either the ghostwriters or the drug company. This arrangement benefits both the ostensible author, who receives payment in addition to credit as the author, and the drug company, which promotes its product under the guise of legitimate, objective science.

Recently, ghostwriting has been primarily associated with reviews of previously published medical literature.² Review articles are opinion pieces that do not contain original data. Rather, an author picks from published studies to support a clinical recommendation for the use of a drug, procedure, or diagnostic test. A writer may bias the review by selectively omitting studies from consideration, such as those critical of a particular drug. Ghostwriting is considered particularly dangerous in review articles because they influence medical practice and the direction of new investigation.³

The Debate

While most agree that ghostwriting has a legitimate place in medical literature, critics claim the practice has gone far beyond openly acknowledged editorial assistance.⁴ Evidence suggests that drug companies hire ghostwriters under explicit agreements to emphasize the benefits and downplay the risks of a given treatment, and many ostensible

¹ See Sheldon Krinsky, *When Conflict-of-Interest Is a Factor in Scientific Misconduct*, 26 MED. & L. 447, 450 (2007).

² Jerome P. Kassirer, *Ghostwriters and Ghostbusters*, TRIAL, Sept. 2007, at 38.

³ Natasha Singer & Duff Wilson, *Medical Editors Push for Ghostwriting Crackdown*, N.Y. TIMES, Sept. 18, 2009, at B1.

⁴ E.g., Kassirer, *supra* note 2, at 41.

authors make few if any changes to ghostwritten manuscripts prior to publication. As such, the practice contaminates medical literature with commercial bias and reduces objective science to mere advertising. Since practicing physicians rely on journals to publish objective scientific studies, and ghostwritten articles do not acknowledge industry's involvement in writing the article, this practice may improperly influence the prescribing practices of physicians. Senator Charles Grassley, ranking member of the Senate Finance Committee, fears that ghostwriting may "mislead doctors to prescribe drugs that may not work or cause harm to patients," thereby increasing the cost of healthcare and undermining the public trust in medicine.⁵

On the other hand, proponents claim that these risks are exaggerated.⁶ Medical literature is the product of scientific, rather than literary, intellect, and the value of medical literature lies in its contribution to scientific knowledge. Therefore, ghostwriters' literary contributions are merely incidental to the production of scientific knowledge. Further, authors ensure against improper bias by retaining the final authority over the content of articles. From a practical perspective, many physicians and academics are not skilled writers and need assistance expressing their ideas in a clear and concise manner.⁷ Some researchers are also notoriously slow to produce manuscripts, so ghostwriting enables drug companies to expedite the publication of important scientific knowledge.⁸ Thus, proponents claim that a crackdown on ghostwriting could slow scientific advancement.⁹

Scope of the Problem

The true scope of ghostwriting is unclear.¹⁰ Fifteen years ago, researchers began going public with accounts of unsolicited offers to author prepared manuscripts.¹¹ Subsequent revelations suggest that the practice is prevalent, particularly in articles concerning top-selling drugs. Industry-sponsored ghostwriting has surfaced in connection with diet-drug combo fen-phen, painkiller Vioxx, epilepsy drug Neurontin, antidepressant Zoloft, and high blood pressure drug nebivolol. In 2009, reports connected ghostwriting with antipsychotic Zyprexa, antidepressant Paxil, and menopause drug Prempro.

⁵ See *Wyeth in US Senate Ghostwriting Probe*, PHARMA MARKETLETTER (UK), Dec. 22, 2008, available at 2008 WLNR 25943527.

⁶ See Singer & Wilson, *supra* note 3.

⁷ Kassirer, *supra* note 2, at 41.

⁸ Bruce F. Mackler, *Update on Evolving Regulatory Guidance*, GENETIC ENG'G & BIOTECHNOLOGY NEWS, Oct. 15, 2009, available at <http://www.genengnews.com/articles/chitem.aspx?aid=3064>.

⁹ Singer & Wilson, *supra* note 3 (quoting a representative of the Pharmaceutical Research and Manufacturers of America as claiming a crackdown on ghostwriting could "chill research and chill support for research").

¹⁰ Singer & Wilson, *supra* note 3.

¹¹ Lawrence K. Altman, *The Doctor's World; Some Authors in Medical Journals May Be Paid by 'Spin Doctors'*, N.Y. TIMES, Oct. 4, 1994, at C3, available at 1994 WLNR 3568773. For instance, a physician at Georgetown University alleged that she refused a drug company's offer of an honorarium in exchange for her agreeing to be listed as the author of a ghostwritten editorial. She later went public after being asked to review a modified version of the same article under a different author's name. Adriane Fugh-Berman, *The Corporate Coauthor*, 20 J. GEN. INTERNAL MED. 546 (2005).

A 2009 study released by the editors of *The Journal of the American Medical Association* (JAMA) found that, out of 630 articles published in six journals in 2008, 7.8 percent of the authors acknowledged contributions by people who should have been listed as authors.¹² *The New England Journal of Medicine* (NEJM) had the highest ghostwriting rate at 10.9 percent. Although some claim the study overstated the prevalence of ghostwriting by including assistance not financed by industry, experts suggest that the actual rates may be much higher because the surveyed authors may have been reluctant to admit the involvement of ghostwriters.

Wyeth and Hormone Replacement Therapy

The most significant of the recent revelations involved a ghostwriting campaign initiated by drug manufacturer Wyeth to support its top-selling Premarin family of drugs. In the late 1990s, Wyeth's hormone replacement therapy (HRT) products, including Premarin and Prempro, were the most-prescribed drugs in the United States, with sales approaching \$2 billion by 2001.¹³ In 1997, as evidence linking HRT to breast cancer mounted, Wyeth hired DesignWrite, a medical communication company, to launch a public relations campaign designed to accentuate the benefits, and "diminish negative perceptions," of HRT among physicians.¹⁴ DesignWrite proposed targeting medical journals to "position the product appropriately to influence prescribers."¹⁵ DesignWrite's role was to analyze research data, write manuscripts favorable to Wyeth's HRT drugs, recruit prominent researchers to sign on as authors, and submit the manuscripts to medical journals. The involvement of authors in producing the final article varied, but many authors contributed little if at all to the published articles. However, most of the published articles failed to explicitly disclose the roles of either Wyeth or DesignWrite, although individual medical writers were sometimes credited for "editorial assistance."¹⁶

All told, twenty-six ghostwritten papers – mostly review articles – favorable to Wyeth's HRT products were published in eighteen medical journals.¹⁷ The papers – mostly review articles – were published from 1998 until 2005, three years after researchers halted a federal study after finding a link between HRT use by menopausal women and increased risk of breast cancer, heart disease, and stroke. Because of these findings, Wyeth's sales of Prempro ultimately fell by 60 percent.¹⁸ Although the articles were scientifically sound and the ostensible authors were not paid, the reaction was harsh, with one bioethicist calling some authors' conduct the "prostitution of their own academic standing" and an academic physician likening the resulting uncertainty to that caused by

¹² Duff Wilson & Natasha Singer, *Ghostwriting Is Called Rife in Medical Journals*, N.Y. TIMES, Sept. 11, 2009, at B5.

¹³ Kris Hundley, *Do Drug Authors Write, or Sign Off?*, ST. PETERSBURG TIMES, Sept. 20, 2009, at 1A, available at <http://www.tampabay.com/news/business/when-stories-extol-drugs-maker-may-be-behind-it/1037331>.

¹⁴ *Id.*

¹⁵ *Id.*

¹⁶ *Id.*

¹⁷ *Id.*

¹⁸ Stuart Laidlaw, *Ghostwriting for Medical Journals Amounts to Bad Medicine; Lawsuit Exposes World of Academic Publishing*, TORONTO STAR, Aug. 15, 2009, at L01.

steroids in baseball – “You don’t know who was using and who wasn’t; you don’t know which articles are tainted and which aren’t.”¹⁹

Ghostbusting and Journal Policies

Because editors are in a superior position to detect industry-financed ghostwriting, many feel that medical journals have a duty to deal with industry’s surreptitious involvement in medical literature – so called “ghostbusting.”²⁰ The primary means by which journals can deal with ghostwriting is through their editorial policies, which generally permit industry-financed assistance provided that it is properly disclosed and the contributions of all parties are properly acknowledged.²¹

Most journals require that authors attest to their own contribution to an article. Several journals, including *JAMA* and *NEJM*, follow the International Committee of Medical Journal Editors (ICMJE) by expressly defining the criteria necessary for authorship.²² Under the ICMJE guidelines, an author is anyone who: (1) makes “substantial contributions” to designing the study or analyzing its data; (2) drafts the article or revises it “for important intellectual content;” and (3) has “final approval of the version to be published.”²³ Those satisfying all three criteria are listed as authors, while all non-author contributors are listed in the acknowledgments.

Even though such policies require that authors play a substantial role in producing a manuscript, the primary concern is the involvement of a party who is *not* acknowledged or whose role is inappropriately minimized. In this respect, journals differ as to the obligation to disclose the involvement of other contributors. Some journals require the disclosure of any assistance, including those adopting ICMJE’s requirement that authors acknowledge the identity and funding source of anyone contributing to “study design, data collection, data analysis, or manuscript preparation.”²⁴ Other journals, however, do not have such explicit requirements. At the time of the *JAMA* study, some required incomplete information about contributors, allowing authors to acknowledge industry-financed assistance without disclosing its primary role in creating the manuscript.²⁵ Moreover, *NEJM* did not require authors to list other contributors, leaving the decision to the author’s discretion. Other journals did not have a specific ghostwriting policy in place.

¹⁹ Laidlaw, *supra* note 18.

²⁰ Singer & Wilson, *supra* note 3.

²¹ Michael O’Roirdan, *Senator Grassley Asks Medical Journals About Ghostwriting*, HEARTWIRE, July 8, 2009, available at <http://www.theheart.org/article/984881.do>.

²² Singer & Wilson, *supra* note 3.

²³ Kassirer, *supra* note 2, at 41. Moreover, many editors are members of the World Association of Medical Editors (WAME), which calls on editors to require authors to describe their own role in preparing the manuscript and the role of all coauthors of the paper.

²⁴ INT’L COMM. OF MED. JOURNAL EDITORS, UNIFORM REQUIREMENTS FOR MANUSCRIPTS SUBMITTED TO BIOMEDICAL JOURNALS: ETHICAL CONSIDERATIONS IN THE CONDUCT AND REPORTING OF RESEARCH: AUTHORSHIP AND CONTRIBUTORSHIP (2009), available at http://www.icmje.org/ethical_1author.html.

²⁵ Singer & Wilson, *supra* note 3.

The Unwilling Ghostbusters

Unfortunately, impotent policies may not be the only reason for the prevalence of ghostwriting. The *JAMA* study indicates that even journals with strict disclosure policies publish many ghostwritten articles each year.²⁶ Although journal editors portray themselves as victims of dishonest authors and conniving drug companies, the authors known to have published ghostwritten articles have done so with impunity. In July 2009, Senator Grassley sent letters to eight medical journals asking about ghostwriting policies and any related disciplinary action taken against authors since 2004.²⁷ Although the consequences for violations of disclosure policies vary, no journal reported taking any action against an author for ghostwriting.²⁸

Sources within medical literature suggest that editors' reluctance to address ghostwriting stems from ties to industry. For example, the editors at *The Public Library of Science Medicine* (PLoS) accuse journal editors of having lost their way:

[T]he medical publishing and pharmaceutical industries and the medical academic community have become locked into a cycle of mutual dependency, in which truth and lack of bias have come to be seen as optional extras. Medical journal editors need to decide whether they want to roll over and just join the marketing departments of pharmaceutical companies.²⁹

Others contend that journals are compromised by financial conflicts of interest. Editors play the lead role in detecting ghostwriting and enforcing related policies, yet studies show that less than half of journals have a policy on editor conflicts of interest and less than a third of these require editors reporting a conflict to recuse themselves.³⁰ While little is known about editors' conflicts, ghostwritten articles can generate substantial revenue for journals.³¹ Federal law generally prohibits drug manufacturers from directly marketing off-label uses of approved drugs to physicians.³² However, the FDA permits drug companies to distribute peer-reviewed articles on off-label uses to physicians under certain circumstances.³³ Consequently, drug companies have an incentive to invest in

²⁶ Singer & Wilson, *supra* note 3 (stating that both *JAMA* and *PLoS Medicine* had rates exceeding seven percent).

²⁷ *Id.*

²⁸ *Id.*

²⁹ The *PLoS Medicine* Editors, *Ghostwriting: The Dirty Little Secret of Medical Publishing That Just Got Bigger*, *PLOS MED.*, Sept. 8, 2009.

³⁰ Joel Lexchin, *The Secret Things Belong Unto the Lord Our God: Secrecy in the Pharmaceutical Arena*, 26 *MED. & L.* 417, 427 (2007).

³¹ O'Riordan, *supra* note 21.

³² See 21 C.F.R. § 202.1(e)(4)(i)(a) (2008).

³³ FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: GOOD REPRINT PRACTICES FOR THE DISTRIBUTION OF MEDICAL JOURNAL ARTICLES AND MEDICAL OR SCIENTIFIC REFERENCE PUBLICATIONS ON UNAPPROVED NEW USES OF APPROVED DRUGS AND APPROVED OR CLEARED MEDICAL DEVICES 4 (2009), available at <http://www.fda.gov/OHRMS/DOCKETS/98fr/FDA-2008-D-0053-gdl.pdf> (warning against distributing articles "edited or significantly influenced by a drug or device manufacturer or any individuals having a financial relationship with the manufacturer.").

ghostwritten articles to promote off-label uses of their drugs. To do so, drug companies purchase large numbers of reprinted articles from journals for distribution to physicians across the country. As such, a crackdown by journals would jeopardize future revenue generated by ghostwritten articles.³⁴

Conclusion

Whatever one thinks of the risks of ghostwriting, it is clear that the practice threatens public confidence in medicine whether or not it ultimately produces scientifically sound medical literature. Perhaps unrealistically, the public holds the medical community to high standards and expects, at a minimum, honesty. There may be a legitimate role for ghostwriting in medical literature, but authors who deliberately conceal the primary role of industry-financed assistance are rightfully perceived as dishonest. Journals have also failed to fulfill their responsibilities as purveyors of unbiased scientific knowledge. While ghostwriting is difficult to detect prior to publication, journals and their editors refuse to adopt and enforce effective policies. Most troubling, this unwillingness may be linked to the journals' own conflicts of interest.

Disclosure policies do not address the scientific quality of journal articles, and strict compliance will not rid medical literature of industry bias. Rather, disclosures allow readers to evaluate the accuracy and completeness of the research.³⁵ If journals decide to get serious about encouraging transparency, they should follow the advice of editors at *PLoS*, who suggest journals adopt more explicit ghostwriting policies.³⁶ Journals should require academic authors to submit statements disclosing the involvement of "any company whose products are mentioned (positively or negatively, directly or indirectly) in the commissioning of a third party to provide editorial assistance, manuscript preparation, or submission of the paper."³⁷ Moreover, policies should include serious consequences for violations. For instance, a journal finding that an author failed to report anything about the involvement of an industry-financed medical writer should immediately retract the paper, ban the author from further publication, and report the misconduct to the author's institution.³⁸

Health Law Perspectives (December 2009)

Health Law & Policy Institute

University of Houston Law Center

<http://www.law.uh.edu/healthlaw/perspectives/homepage.asp>

³⁴ O'Riordan, *supra* note 21.

³⁵ Brendan Borrell, *Using Forensics to Reveal Medical Ghostwriting*, REUTERS HEALTH, Sept. 11, 2009, <http://www.reuters.com/article/idUSTRE58A3BC20090911>.

³⁶ The *PLoS Medicine* Editors, *supra* note 29.

³⁷ *Id.*

³⁸ *Id.*