

Corporate versus Public Interests: Community Responsibility to Defend Scientific Integrity

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In this issue, we include a report from the US Senate Committee on Finance (111th Congress) that addresses the role of ghostwriting in medical literature. The definition of ghostwriting has been discussed extensively.¹⁻³ Ghostwriting, or “medical ghostwriting,” is the intentional writing, drafting, and/or editing of an article by an outside source with the subsequent addition of an author who has little or no contribution to the paper’s development, but whose name lends credence to the paper’s content.³ The use of ghostwriting in medical literature is not new; high-profile journals (including the *Journal of the American Medical Association* [JAMA] and the *New England Journal of Medicine* [NEJM]) acknowledged the presence of ghostwriting more than a decade ago.⁴ In a study of articles appearing in peer-reviewed medical journals, Flanagin et al. found that “(19%) of [articles] had evidence of honorary authors (range, 11%–25% among journals); 93 articles (11%) had evidence of ghost authors (range, 7%–16% among journals); and 13 articles (2%) had evidence of both.”⁴ Mowatt et al. found that “One hundred forty-one Cochrane reviews (39%) had evidence of honorary authors, 32 (9%) had evidence of ghost authors (most commonly a member of the Cochrane editorial team), and 9 (2%) had evidence of both honorary and ghost authors.”⁵ In a review of Merck documents released as part of legal discovery, Ross et al. reported on Merck-sponsored ghostwriting, noting that external academic authors were listed as the first author of 16 out of 20 papers written by Merck personnel.⁶

Ghostwriting is a Part of Publication Planning

It is important to recognize that ghostwriting is not an isolated affair. It is usually part of a “publication planning” process wherein a pharmaceutical or device-manufacturing company may also manipulate data to enhance profits.⁷ Much of this work is subcontracted to companies that specialize in the creation of a plan to publish a series of articles to support a particular marketing objective. To share information, workers in this “industry” participate in a “professional organization” called the International Society of Medical Planning.⁷ Sismondo described their operating methods as involvement in “. . . all aspects of

the process, including: research design, the formulation of key messages intended to guide research, the tailoring and distribution of articles to particular audiences and journals, and the selection of potential authors for those articles.”⁸ Fugh-Berman and Dodgson graphically described the process (Figures 1 and 2).⁹

Ghostwriting within medical and scientific journals represents a serious and potentially dangerous expansion of corporate influence into medicine.⁸ The publication of ghostwritten articles is usually part of a corporate strategy designed to promote a product.⁹ These “endorsements” of papers by noncontributing authors mischaracterize the importance, and give a false

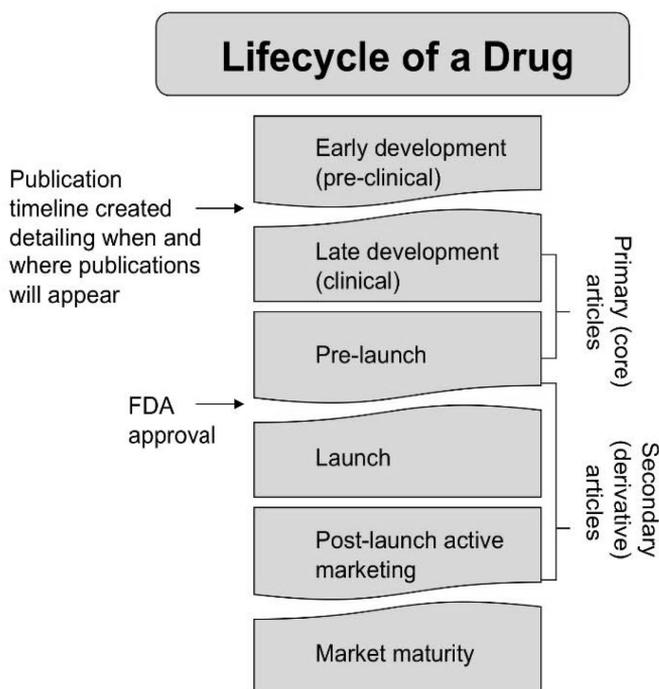


Figure 1—Lifecycle of Publication Planning and ghostwriting, Fugh-Berman AJ, Dodgson S. *Ethical considerations of publication planning in the pharmaceutical industry*. *Open Medicine*. 2008;2(4). Reprinted here with the permission of the author.

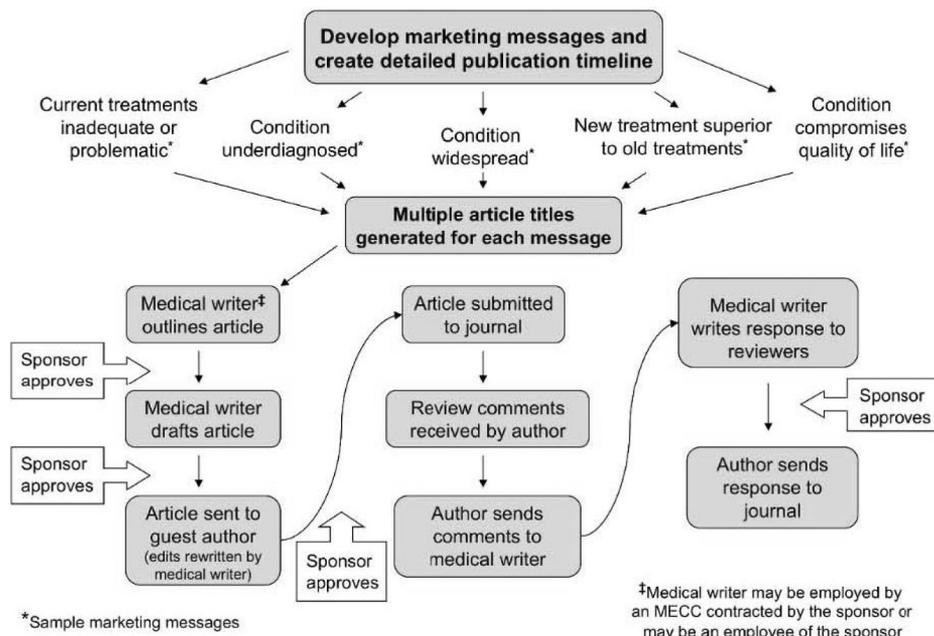


Figure 2—Publication Planning Process, Fugh-Berman AJ, Dodgson S. *Ethical considerations of publication planning in the pharmaceutical industry*. *Open Medicine*. 2008;2(4). Reprinted here with the permission of the author.

assurance of, the paper’s message.¹⁰ Ghostwriting corrupts the credibility of independently conducted research and publishing.¹¹

Medical Action Communications (MAC), a professional medical writing company, used graphics of a witches’ brew to illustrate its plan for enhancing Neurontin (gabapentin) sales in a presentation to Pfizer executives (Figure 3). Carey et al. describes the process through which Pfizer promoted the off-label use of Neurontin for mental illness as the creation of an “echo chamber.”¹² In this case, from 1998 to 2007 Pfizer organized the publication of 15 case series and six case reports that claimed Neurontin was effective for the treatment of bipolar disorder. In addition, nine letters to the editor mimicked these publications. To legitimize the off-label use of Neurontin, Pfizer manufactured the publication of review articles citing the case reports.¹³ These concluded that Neurontin was safe and effective for the treatment of bipolar depression. The bad news is that this drug has been found to increase the risk of suicide.¹⁴ The good news for Pfizer was that in just one state, from 1994 to 2002, Neurontin prescriptions

increased from 8/1000 Medicaid enrollees per quarter to a peak of 387/1000 enrollees.¹⁵ Neurontin was one of Pfizer’s most profitable drugs with sales peaking at 2.4 billion in 2003, 90% of which were for off-label use (Figure 4). Sales remain high despite its generic status and were over 387 million in 2008.¹⁶

The Response by Journals

Journals have begun to respond to claims of ghostwriting within the literature. Editors have not yet developed a procedure to identify ghost-written publications.¹⁷ Although no attempts have been made to quantitatively evaluate the problem since 1998, ghostwriting would seem to remain common practice.¹⁸ Journal editors have decried the practice, noting that ghostwriting threatens “the credibility of medical knowledge and medical journals.”^{19–21} Both the International Committee of Medical Journal Editors (ICMJE) and the World Association of Medical Editors (WAME) have made recommendations to prevent ghostwriting.^{22,23} Nevertheless, funding organizations such as the National Institute

of Health (NIH) have not addressed the problem.²⁴

Journals have failed to take steps to express concern publicly or make it known that publications were ghostwritten. Many journals have yet to implement rigorous methods capable of verifying the actual authors of submitted papers.¹ In some cases, journals ask whether the submitting author wrote the paper or if anyone else beyond those listed as authors had involvement in the paper.¹⁹ McHenry and Jureidini identified ghostwriting of a clinical trial of Paxil in the *Journal of the American Academy of Child and Adolescent Psychiatry*.²⁹ The journal has not retracted the article, nor publicly commented on the ghostwriting.³⁰ In addition, *Neuropsychopharmacology* has not commented on a ghost-written paper it published concerning Vioxx and Alzheimer’s disease, which was the subject of two articles in *JAMA*.^{6,31,32} One of these *JAMA* articles described intentional misrepresentation of data on drug-related MIs and other cardiovascular disease.³²

Some journals have recognized ghostwriting and taken action. The

Public Library of Science (PLOS) has taken direct legal action to determine authorship of papers.²¹ In another case, relating to clinical trials of Paxil, evidence of ghostwriting and professional medical writing became public as a result of discovery in a legal proceeding.²⁹ This ghostwritten article failed to report drug-related suicides and manipulated the outcome variables.³³

At least one journal has instituted a model response to ghostwriting. *Open Medicine's* policy not only retracts any article found to be ghostwritten but also bans any further contributions by the authors. Additionally, *Open Medicine* informs the authors' institutions of the breach and publishes a notice on the journal's website with the names of the responsible companies and authors.³⁴

Ghostwriting is dangerous to patient health

This combination of ghostwriting and data manipulation has occurred in other cases and contributed to drug use, which, in turn, resulted in the injury and even death of patients. Pfizer successfully used the ghostwritten Neurontin papers to increase use in patients with bipolar disease (Figure 4). Ironically, patients treated with Neurontin have an increased risk of committing suicide.³⁵ Other examples of the adverse impact of ghostwriting on patients include the failure to report evidence of suicides in patients on Paxil, the failure to report Vioxx-caused MIs and other adverse cardiovascular events, and the failure to report dose-dependent increase in Alzheimer's disease caused by Vioxx.^{6,26,36-39} In all of these cases, documents that revealed ghostwriting came to light because of litigation.^{6,21,29}

What can be done?

Plagiarism occurs when an individual takes credit for someone else's

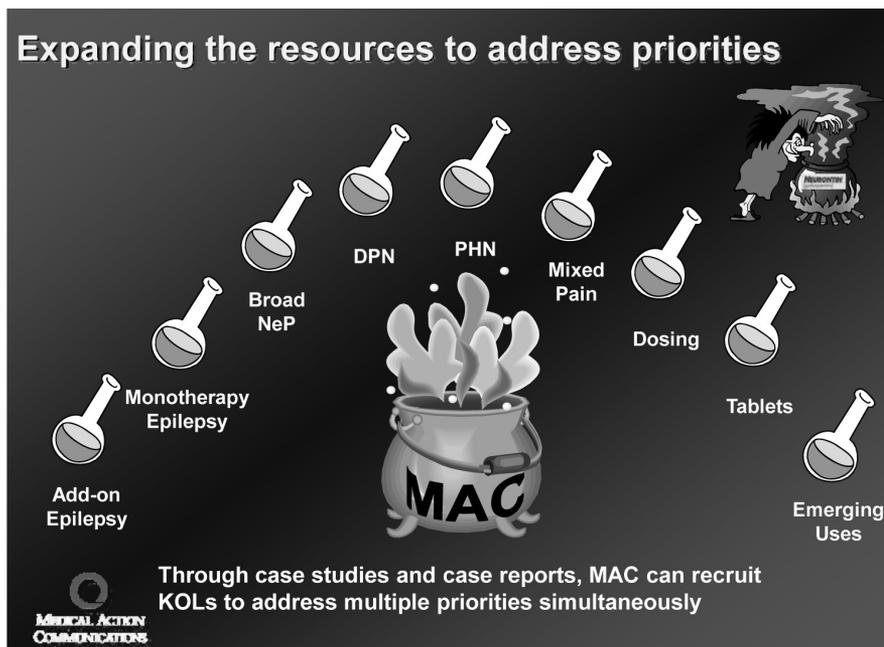


Figure 3—MAC used an image of Witches Brew to illustrate their strategy to enhance Neurontin sales. Available at <http://www.egilman.com/neurontin-docs/witches%20brew.ppt>

written work.² Authors who take credit for ghostwritten work have committed plagiarism. Plagiarism is considered unethical in the academic and scientific community whether or not the ghostwriter has authorized or been compensated for the work. Academic institutions punish students who commit plagiarism even if the work they take credit for was purchased or donated rather than stolen. Universities have policies that address plagiarism and ghost authorship is plagiarism. Student papers do not place patient lives at risk, whereas ghostwritten academic papers have resulted in patient deaths and injuries.^{37,38,40,41} We are not aware of any case where a university sanctioned—or even investigated—a faculty member for committing the same offense that brings disciplinary action against students, despite the fact that authors have admitted that they did not see all the data in papers where they were listed as authors.^{26,29,39} The lack of enforcement is not based on the fact that ghost authorship is rare.⁴

We believe that journals and universities must enforce their existing rules. Ethical standards are meaningless unless they are enforced. In fact, it is unethical to establish standards and not enforce them because the existence of standards contributes to the false impression that the scientific publication process is self-correcting.

Journal editors and publishers have a responsibility to ensure the legitimacy of the publication process.³⁰ Journals should institute processes that require disclosure of the role of all authors and institute audits of a subset of submitted articles.³⁰ A system of accountability used by journals must include the level of detail and scrutiny provided by lawsuits and internal investigations.¹ Journals should also be required to disclose financial information in the same way they require authors to do so, in order to improve transparency from both sides of publication.⁴² It has also been suggested the entire peer-review process be supplemented or “scrapped” in favor of an online open-source review of data.¹ In addi-

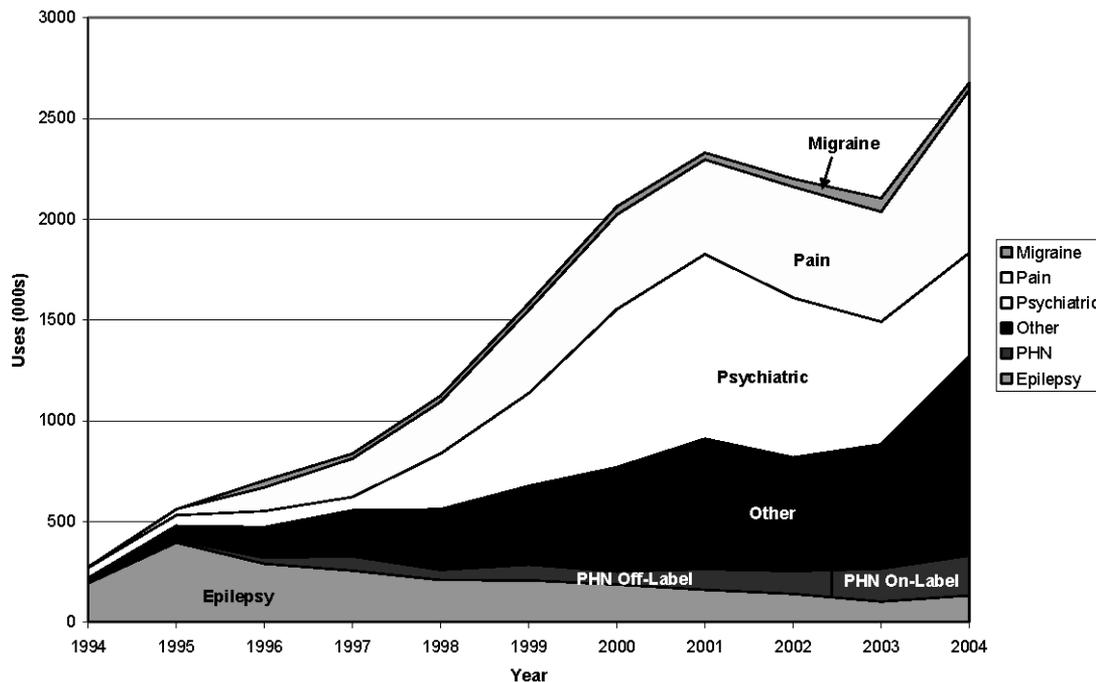


Figure 4—Neurontin Sales by year by diagnosis from Marketing Neurontin, Expert report of Charles King III in Neurontin Litigation 2007. Epilepsy and postherpetic neuralgia (PHN) were the only FDA-approved (“on-label”) uses of the drug. Available at [http://www.egilman.com/neurontindocs/2%20King%20B%20Report%20\(3\).pdf](http://www.egilman.com/neurontindocs/2%20King%20B%20Report%20(3).pdf)

tion, until authors and institutions are genuinely held accountable for ghostwriting, the practice will continue. Temporarily barring authors and/or pharmaceutical and medical device manufacturers who participate in ghostwriting from publishing in a consortium of prominent journals would be an effective deterrent.⁴³ Journals could require authors to disclose or report whether they have been disciplined for ghostwriting in the past.

Unfortunately, most evidence of ghostwriting has been revealed as a result of discovery in tort litigation.^{6,21,29,44} In contrast to Justice Brandeis’s admonition that “sunlight is the best disinfectant,” most judges have readily affirmed confidentiality agreements, which keep evidence of ghostwriting and other corporate misconduct out of the public eye.^{45,46} When plaintiffs’ lawyers have attempted to make these documents public, judges have often sided with the companies and refused to release documents—even when the documents

represented evidence of criminal conduct and substantiated that it increased mortality in the patients the drug was being marketed.⁴⁵ Illegal and unethical conduct of research is not a trade secret; many, if not most, pharmaceutical companies are repeat offenders.^{47–49} This continuing “crime spree” has indicated that “. . . drug companies don’t respect any boundaries of professionalism or the law.”⁴⁷ While the Sixth Amendment guarantees citizens the right to a public trial, it clearly reveals our founding fathers’ belief that public trials and the presentation of evidence were a good thing.⁴⁶ Judges must recognize that this applies to medical product manufacturers and they must stop sealing the evidence.

Like litigation, congressional investigations, such as the one published in this issue, open another window on corporate malfeasance. Continuing discussion and investigation such as this provide an opportunity to preserve the integrity of journal publication and

protect the health of the public. Further investigations that rely on corporate documents to determine the extent of ghostwriting are not only useful but also necessary to protect patients from harm. In addition, the posting of the original data to the Web would allow for independent review of publications, conclusions, and analysis.

This journal’s authorship policy can be found at <http://www.ijoe.com/index.php/ijoe/about/editorialPolicies#custom0>.

Disclosures: David Egilman has served as an expert witness in pharmaceutical litigation at the request of plaintiffs. Nicholas Druar has served as a research assistant to David Egilman in support of his pharmaceutical litigation work.

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