

## Compromising the Medical Literature: The Hidden Influence of Industry-Biased Articles

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In a letter to the editor in this issue of *American Family Physician (AFP)*, Dr. Hyatt and colleagues note that documents revealed in litigation show that manufacturer-funded studies were selectively published and manipulated to exaggerate claims that gabapentin (Neurontin) was effective for the treatment of diabetic peripheral neuropathy.<sup>1</sup> The manufacturers of Neurontin paid medical education and communication companies up to \$18,000 per publication for developing articles, reviews, and letters aimed at promoting off-label use of gabapentin for neuropathic pain and bipolar disorder.<sup>2</sup> They also conducted “seeding trials,” which are clinical studies primarily designed for marketing rather than scientific purposes.<sup>3,4</sup>

This is not an isolated case. It is common for pharmaceutical manufacturers to suppress study results disadvantageous to marketing goals; to choose trial designs that favor a targeted drug; to report selected study outcomes; and to sponsor the publication of multiple reviews, commentaries, letters, and case reports to create the impression that a targeted drug is more effective or safer than the science supports.<sup>5</sup> Industry-paid physicians write these articles with the “editorial assistance” of industry-paid medical writers. The physicians and pharmacists whose names appeared on articles promoting off-label uses of Neurontin received \$1,000 honoraria.<sup>2</sup> Many internal company documents about these practices are available at <http://dida.library.ucsf.edu/>.

Extensive ghostwriting has also been documented for Prempro (conjugated equine estrogens/medroxyprogesterone), Paxil (paroxetine), Vioxx (rofecoxib), Seroquel (quetiapine), Effexor (venlafaxine), and Fenphen (phentermine/fenfluramine), among others.<sup>6</sup> The complete list of drugs is undoubtedly much longer.

Distorted information, once ensconced in the medical literature, is propagated by industry and by well-intentioned authors who unwittingly cite these studies. The medical literature is a permanent record that scientists and physicians rely on for decisions that ultimately affect patient care. Although the scientific process is never linear, the self-correcting process by which evidence is continually refined can be corrupted by the

infiltration of medical journals with research studies and review articles distorted by a hidden marketing agenda.

Although there is no foolproof way for readers to detect undue industry influence, readers should be alert for marketing messages that disparage older, generically available drugs or that position newer branded (or upcoming) drugs as more effective, more convenient, safer, or filling an unmet need. The last sentence of the abstract is typically where the marketing spin is inserted. Readers should alert medical journals to suspicious articles by writing letters to the editor.

Readers should also be familiar with the policies and procedures of the journals they consult. Some journals do not require disclosure of potential conflicts of interest, so the fact that an author is a paid consultant or speaker for a company may not be disclosed. Many journals do not ask authors whether or not they received “editorial assistance.” Such assistance, usually from a so-called medical education and communications company, strongly suggests that industry has helped craft the article. *AFP* is highly concerned about industry bias and requires authors to respond to a series of specific questions such as: “Did a pharmaceutical company, public relations firm, or any commercial entity sponsor the substance or creation of your article directly or indirectly?” and “Was any assistance provided by a medical communications company or professional writer or editor? If so, who provided this assistance and who paid for it?”

For decades, *AFP*'s policy has been to reject manuscripts written by any author who has financial ties to a commercial entity with an interest in the topic (not just to a specific drug or device).<sup>7</sup>

Litigation has resulted in public disclosure of direct payments to physicians from eight major pharmaceutical companies; ProPublica, a news organization, has created a searchable database at <http://projects.propublica.org/docdollars/> that identifies physicians provided with funding from these companies. Readers and medical journal editors can use this database to reveal undisclosed conflicts. In addition, *AFP* routinely checks for undisclosed conflicts by performing a Google search on authors of submitted manuscripts.

What should medical journals do when faced with proof that published articles were ghostwritten or otherwise compromised by undue industry influence? Options might depend on the degree of compromise. In cases in which the content was ghostwritten, but not ►

obviously distorted, the situation could be handled with a published notice of reprimand and a corrected disclosure statement.<sup>8</sup> In cases in which the science appears to be intentionally biased, the article can be retracted and tagged as such in electronic databases.<sup>9</sup>

Stealth marketing via journals threatens evidence-based practice, but eliminating ghostwriting does not guarantee the absence of undue bias. A further step to deter such practices is the retraction of articles for egregious instances of distortion. To leave obviously compromised articles in the medical literature is to accept that industry, rather than the medical profession, controls medical standards of care.

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