

Conflicts of Interest, Authorship, and Disclosures in Industry-Related Scientific Publications: The Tort Bar and Editorial Oversight of Medical Journals

LAURENCE J. HIRSCH, MD

In recent years, *Mayo Clinic Proceedings* has published a variety of articles dealing with important, broad-reaching matters of societal interest that impact medicine and patient care. Topics included ideal physician behaviors, gender and medical career mentoring, advance directives and end-of-life issues, physician involvement in capital punishment, and, germane to this article, institutional conflicts of interest (COIs), as well as the journal's approach to publication of industry-sponsored clinical research.¹⁻¹⁵ Equally important to the well-being of patients and of medicine is the legitimacy of interactions between industry sponsors of research and investigator-authors who communicate the information and the journals/editors who review and ultimately determine publication of the material. In this age of transparency, disclosure of COIs has assumed great prominence in medical journals. However, transparency is not always clear, disclosure policies are varied, and their implementation (by journals and medical societies) is asymmetric and biased. This commentary examines some prominent recent actions by consultants to plaintiffs' attorneys and a series of publications in 3 top-tier general medical journals that illustrate selective and incomplete disclosure of conflicts—both financial and otherwise. In my view, these events call into question actions by a medical specialty society with one of the consultants and, more broadly, the editorial practices at the journals concerning COIs. Specific recommendations are offered to address the latter.

In April 2008, the *Journal of the American Medical Association (JAMA)* published a "research" article by Ross, Hill, Egilman, and Krumholz¹⁶ that was based on materials obtained through legal discovery; the authors claimed that Merck & Co, Inc (Whitehouse Station, NJ) previously hired professional writers (termed *ghostwriters*) to draft papers concerning clinical trials of rofecoxib (Vioxx) and invited academic physicians to accept authorship of them (without acknowledgment of the compensated writing) to increase their credibility. These guest authors supposedly made little contribution to the research, analysis, or interpretation of the data, an unacceptable practice. Many of the articles were from the mid- to late 1990s. *JAMA* issued press releases and an accompanying editorial¹⁷ that berated medical product companies broadly for manipulating clinical research, with resulting widespread media coverage. Some other journals opposed *JAMA*'s posture.¹⁸ Several direct responses to *JAMA*

by authors of publications listed in the article pointed out lapses in the report by Ross et al and mistaken inclusion of their publications in the analysis, with predictable rejoinders by the authors and editors.¹⁹⁻²⁵ One letter²³ suggested that "an author's declaration of financial dealings with industry is only meaningful if the monetary value received from each company over a preceding period (perhaps the past 2 years) is clearly stated," a point to which I will return.

I have worked in both academia and industry, including more than 17 years through 2006 at Merck, primarily in clinical drug development. From 2001 to 2006, this included management of a department of medical writers, support staff, and statisticians who worked with Merck scientists and external investigators to publish many (although not all) articles related to mid- and late-phase clinical trials sponsored by Merck. We adhered to the authorship criteria of the ICMJE (International Committee of Medical Journal Editors) and acknowledged lesser contributions to manuscripts by persons who did not meet those criteria. (The ICMJE states that, "Authorship credit should be based on (1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be published. Authors should meet conditions 1,

For editorial comment, see page 771

Dr Hirsch was an employee at Merck & Co from 1988-2006 and managed the Medical Communications Department for clinical research publications from late 2001 to mid-2006. He currently is employed at a medical device and technology company that has no financial interest in any matters related to rofecoxib or the resulting tort litigation involving Merck & Co. Dr Hirsch owns mutual funds with stock from a variety of pharmaceutical and device companies, including Merck, and some shares of Merck and other medical product companies. He is a founding member and prior president of ISMPP (International Society for Medical Publication Professionals), a nonprofit 501(c)6 organization (www.ismpp.org). The views in this article are those of Dr Hirsch alone. The article was not reviewed or edited by individuals at any of the aforementioned organizations.

This work was presented in part at the Annual Meeting of the Council of Science Editors, May 3, 2009, Pittsburgh, PA, and at the Charter Meeting of the Association of Clinical Researchers and Educators (ACRE), July 23, 2009, Boston, MA.

This article is freely available on publication, because the author has chosen the immediate access option.

Individual reprints of this article are not available. Address correspondence to Laurence J. Hirsch, MD, at hirschla3@gmail.com.

© 2009 Mayo Foundation for Medical Education and Research

2, and 3.”)²⁶ These criteria are widely used in biomedical research, although by no means universally. Speaking only for myself, and in no way as a spokesperson, this is *not* a defense of Merck or of actions related to Vioxx. However, readers may have a different perspective concerning the report of supposed authorship misconduct by Merck when they learn what was *not* disclosed by Ross et al or by *JAMA*. That article¹⁶ (and the others discussed subsequently) illustrates the far-reaching influence of the American tort bar,²⁷ now impacting the content of important medical journals to further its litigation interests, abetted by journal editors who appear biased against industry.

COI AND THE CURRENT ENVIRONMENT

Consider today’s environment. There is a politically correct herd mentality that ascribes to the concept that objectivity is forsaken by medical companies that seek profit (and by their employees) because of “conflict of interest.” A COI has been defined as “a set of conditions in which professional judgment concerning a primary interest (such as a patient’s welfare or the validity of research) tends to be unduly influenced by a secondary interest (such as financial gain).”²⁸ Previously, the president of the Association of American Medical Colleges emphasized that the term indicates a state of affairs and not a behavior, that COIs are ubiquitous, and that despite their inaccurate portrayal by the media, COIs do *not* indicate the occurrence of any improper behavior, much less scientific misconduct, analogous to a state of potential energy.²⁹ The editors of *JAMA* also wrote, “Conflicts of interest represent the potential for biased judgment, but are *not* [emphasis added] an indicator of the likelihood or certainty that such judgments or compromises will occur.”³⁰ Indeed, in its recently published report on COI in medical research, education, and practice, the Institute of Medicine defined COI as “A set of circumstances that creates a *risk* [emphasis added] that professional judgment or actions regarding a primary interest will be unduly influenced by a secondary interest.”³¹ Editors at *The Lancet* and the *British Medical Journal (BMJ)* similarly noted that finance is only one of many issues that can lead to COI; other factors such as publication pressure, prestige, scientific reputation, career advancement, and even religion can be more potent than dollars in potentially biasing a researcher.^{32,33} Yet today there is a McCarthyesque reaction to the term, *conflict of interest*, with an unstated presumption of guilt until proven innocent.

What led to this? The reputation of the pharmaceutical industry, once among the highest ranked by the public, has plummeted and is now similar to that of financial and insurance companies and lower than that of the automotive industry.³⁴ A small number of highly publicized incidents occurred in the mid-1990s and early 2000s that involved frankly egregious attempts to manipulate publication of

clinical research in ways that would favor the sponsor’s product. These included blocking publication by contractual means,^{35,36} withholding study data from a principal investigator,³⁷ and reporting a 12-month study as a 6-month trial that provided a misleadingly favorable profile of the drug without explanation of the changed reporting period.^{38,39} In 2001, the ICMJE published a policy/editorial, “Sponsorship, Authorship, and Accountability,” that specified principles for investigators working with industry to ensure investigator access to study data and control of the decision to publish study results.⁴⁰ Less than 3 years later, reports appeared of a sponsor allegedly suppressing publication of placebo-controlled clinical studies that failed to demonstrate efficacy of a selective serotonin reuptake inhibitor antidepressant in adolescents; the studies also raised questions (difficult to quantify) about possible adverse effects of the drug/drug class on suicidal ideation.^{41,42}

These events led to the ICMJE’s initial call for mandatory clinical trial registration in September 2004.⁴³ Merck voluntarily withdrew Vioxx from the market later that month; although close in timing, the 2 events were unrelated. On December 8, 2005, an “Expression of Concern” was published online by *The New England Journal of Medicine (NEJM)*, suggesting incomplete reporting of serious adverse cardiovascular events in a gastrointestinal safety outcome study of rofecoxib originally published in 2000,⁴⁴ although the validity of those concerns as well as circumstances and timing of the *NEJM* statement have been challenged.⁴⁵⁻⁴⁷ All these events doubtless contributed to passage of Title VIII (Section 801) of the Food and Drug Administration Act of 2007, known as FDAAA,^{48,49} making it federal law to register most interventional clinical trials at outset *and* to disclose trial results (for marketed products) by 12 months after study completion, on www.clinicaltrials.gov.

Other studies have reported that industry sponsorship of clinical research is related to a higher frequency of positive outcomes that favor the sponsor’s intervention^{50,51} or positive conclusions,⁵² although it is difficult to see how the latter can be assessed in a neutral manner. Publication bias (preferential publication of studies with positive outcomes vs trials with negative, neutral, or ambiguous outcomes) has been reported for more than 2 decades,⁵³ and industry is frequently criticized for contributing to this phenomenon. However, one analysis showed that large randomized trials with pharmaceutical sponsorship that were presented at a major oncology meeting were published *sooner* than those sponsored by cooperative groups or those in which sponsorship was not indicated⁵⁴; publication bias clearly extends to government- and nonprofit-funded research.^{55,56} A different type of publication bias, whereby only selected outcomes within study protocols are reported in the published article (ie, positive outcomes are elevated and negative or border-

line results demoted or neglected), has been described.⁵⁷ This analysis also failed to show any relationship between funding source and reporting of biased results.⁵⁷ Nevertheless, it is not difficult to understand a degree of extra scrutiny of industry-sponsored research by reviewers and editors, but the extent and the method of doing so are important to ensure that work deserving publication is not censored.

VARIATIONS IN JOURNAL DISCLOSURE AND ENFORCEMENT POLICIES

About 4 years ago, *JAMA* started requiring that *only* for papers describing industry-sponsored studies that were analyzed by a company statistician, the sponsor had to provide the raw data to an “independent” academic biostatistician (paid by the sponsor of course) to confirm the analyses, before it would consider the paper for publication.⁵⁸ Reaction to this policy was almost uniform: statistical societies and industry organizations alike protested the unspoken but clear demeaning of industry scientists’ integrity,^{59,60} with no change by *JAMA*.⁶¹ Prominent editors and biostatisticians strongly criticized the policy.⁶²

A number of companies stopped submitting manuscripts to *JAMA* because of the policy. In an editorial revealingly titled, “The Influence of Money on Medical Science,”⁶³ the *JAMA* editor stated that any company doing so “... risks not only the perception that the company may have something to hide, but the reputation of any researcher willing to accede to such a company demand.” The pejorative implications of this policy rationalization were clear. At Merck, the situation was discussed with investigators, who per company guidelines had final authority over manuscript submission decisions, and they fully supported pursuing publication of some major clinical trials elsewhere than *JAMA*—there were no company “demands.” Colleagues at other companies reported identical experiences (personal communications). In the end, *JAMA*’s policy is a clear example of bias in manuscript review and provides no real benefit to its readers.

Medical journals today differ widely in their approach to disclosures of COI. Requests for uniform COI disclosure policies have been made,^{64,65} without noticeable impact. *JAMA* is one of the most stringent in enacting its policy for disclosure of financial COI, which appears to apply especially to any type of paid relationship with industry. For example, in 2006 *JAMA* published an important National Institutes of Health (NIH) observational study that showed benefits of continued antidepressant use in pregnant women.⁶⁶ After news reports that *JAMA*’s COI disclosure rules had not been followed, *JAMA* forced public apologies and corrected disclosures from the authors regarding their financial relationships with multiple manufacturers of antidepressants (which the authors thought irrelevant because of the NIH sponsorship and observational nature of the study).⁶⁷ *JAMA* also requested what it called corrective

actions by deans of the authors’ medical schools.^{68,69} Yet, *JAMA*’s editor simultaneously affirmed that the publication was still valid because it had passed peer review,⁶³ raising questions about the intense reaction to the supposed “in-fractions.”

In March 2009, a similar situation ensued. According to multiple reports in the *Wall Street Journal*, 2 editors of *JAMA* allegedly threatened and intimidated a neuroanatomist at a small university medical center and the dean of the school because the professor posted a letter on the Web site of *BMJ*⁷⁰ that raised questions about the reporting of a trial’s results and about undisclosed financial COI by authors of the article originally published in *JAMA*, 5 months after bringing this to the attention of the *JAMA* editor.⁷¹ *JAMA* demanded that the author retract the letter in *BMJ*.⁷² Nonprofit groups normally critical of industry called for investigations of the editors, and *JAMA*’s editorial oversight committee was reportedly doing so.^{73,74} The cause of the uproar? Modest honoraria (about \$3000) that had been accepted 4 years previously for 2 talks, apparently forgotten by the lead author,⁷⁵ from the company that markets the drug studied (the company had no role in the design, conduct, or analysis of the NIH-funded study). *JAMA* responded by issuing online a new policy on COI disclosures, requiring whistle-blowers to essentially agree to be gagged until *JAMA* completes its investigation of alleged COI.⁷⁶ Other editors criticized this approach, one calling the new policy “a dangerous position.”⁷² In July 2009, *JAMA* updated its policy on addressing unreported COI, saying that it will “explain” to the person raising such allegations the value of maintaining confidentiality while *JAMA*’s investigation is under way,⁷⁷ as opposed to requiring it. According to the *Wall Street Journal*, the change came about after the *JAMA* editorial oversight committee presented recommendations to the board of the AMA (American Medical Association).⁷⁸ Both *JAMA* and the AMA declined to comment; the AMA said “...it is an internal matter...”⁷⁸ In any case, this is far from the supposed mission of medical journals to communicate scientific information and educate their readers on new advances in biomedical research, while providing informed commentary on such developments.

JAMA issued a strident editorial in 2008 that accompanied the rofecoxib-related ghostwriting article by Ross et al¹⁶ (and a second article in the same issue, also based on materials from legal discovery, that concluded that Merck had failed to properly report mortality data to the Food and Drug Administration [FDA] in certain rofecoxib clinical trials⁷⁹). *JAMA* declared “...all journals *must* disclose all pertinent relationships of all authors with any for-profit companies”..., “*must* seriously consider funding sources and authors’ disclosed financial conflicts of interest and financial relationships when deciding whether to publish a study

or review,” [emphasis added] and, “For-profit companies... should not be solely or primarily involved in collecting and monitoring of data, in conducting the data analysis, and in preparing the manuscript reporting study results.”¹⁷ The latter proviso is prejudiced and untenable for any company that is developing a new drug, biologic, or device because the company must reach *a priori* agreement with the FDA on all aspects of study design, conduct, data collection, end point adjudication (if applicable), data analysis, and reporting. In other words, companies need close involvement in all these important clinical trial functions for preregistration studies. Sponsor function in postregistration trials varies; it may be minimal for some investigator-initiated studies or substantial for other company-initiated research. Blanket mandates regarding sponsor involvement in clinical trials are not useful.

SELECTIVE DISCLOSURES: DIFFERENCES BASED ON SOURCE OF FUNDING

JAMA's implementation of its rigorous financial disclosure policy appears inconsistent and selective. For the 2008 article that was critical of Merck's authorship practices by Ross, Hill, Egilman and Krumholz,¹⁶ the entire disclosure statement was, “All of the authors have been compensated for their work as consultants at the request of plaintiffs in litigation against Merck & Co, Inc, related to rofecoxib.” Only in the middle of the Comment (Discussion) portion of the article was it mentioned that the authors had served as paid expert witnesses for plaintiffs' attorneys in rofecoxib litigation. The terse disclosure statement seems at odds with *JAMA*'s stated policy in its Instructions for Authors that financial COI disclosure must be *complete*.⁸⁰ Regardless, the information provided hardly conveyed that, as of January 2007, Krumholz had received more than \$300,000 for his consulting from plaintiffs' attorney Mark Lanier (no relationship to *Mayo Clinic Proceedings* Editor-in-Chief William L. Lanier, MD), which only became public in a letter to the editor of *BMJ* that responded to a *previous* article critical of Merck by Krumholz et al.^{81,82} To put this in context, in 2008 the FDA revised its policies on COI for Advisory Committee participation to not allow anyone on these bodies if they or their immediate family have more than \$50,000 in “disqualifying financial interests.”⁸³ It should also be contrasted with the disclosure and lengthy disclaimer in the other article on mortality reporting in certain rofecoxib trials for authors Psaty and Kronmal,⁷⁹ which goes to great length to explain the authors' independence despite extensive interactions with plaintiffs' attorneys who reviewed and commented on the authors' own reports on rofecoxib documents obtained in litigation proceedings against Merck.

Krumholz' remuneration seems substantial until it is compared to that of another coauthor of the *JAMA* authorship report,¹⁶ David Egilman. Egilman has testified for

Mr Lanier and other attorneys in more than 100 tort cases (nearly always for plaintiffs) for approximately 2 decades and, by his own estimate, has earned \$20 to \$25 million for such testimony.⁸⁴ Besides dollars, Egilman's objectivity is questionable on other grounds. In 2007, he signed an admission that “there was another side to the story”⁸⁵ and was fined \$100,000 by an outraged federal judge for actively facilitating the leak (through a third party) to a *New York Times* reporter (exclusively) of court-sealed documents in litigation involving Eli Lilly (Indianapolis, IN) and olanzapine (*Zyprexa*).^{86,87} (The judge subsequently agreed to make the documents public since they had been circulating on the Internet for months.) Surely, disclosure of these facts about the authors was relevant for *JAMA* readers, the media, and the public to assess their portrayal of Merck's handling of rofecoxib publications (many dating back 8-10 years). Yet, the editors of *JAMA* published the “case study” with only the aforementioned nonspecific disclosure. It strains credulity that such consultants can be objective in depicting the behavior of the defendant they are being paid to help plaintiffs' attorneys sue. The editors of *JAMA* will doubtless argue that the paper by Ross, Hill, Egilman and Krumholz¹⁶ on authorship practices at Merck was peer-reviewed and that the source documents are posted on the Internet for public access; however, those peer reviewers were chosen by the editors, and how many persons will take the time to read the voluminous materials resulting from legal discovery? The lasting impressions from these publications are those of the article titles, editorials, press releases, and resulting media coverage.

The first article published by Krumholz et al⁸¹ concerning rofecoxib appeared in *BMJ* in January 2007 and was entitled “What have we learnt from Vioxx?” The disclosure statement with that article is even *less* informative than the one in *JAMA*; it says only that all the authors “... have been consultants at the request of plaintiffs” involved in rofecoxib litigation, with no mention of their compensation. That article reads remarkably like the opening arguments used by attorney Lanier in court proceedings against Merck⁸⁸ and includes a picture of him before a jury in New Jersey in March 2006 titled “Vioxx in the dock.”⁸¹ Apparently, neither the authors nor the editors of *BMJ* thought it relevant to mention that plaintiffs lost that case. This “Feature” resembles tabloid journalism in the guise of medical publication, and the subheading under the article title that “...researchers and journals can still benefit from this case if they learn from the mistakes”⁸¹ is sensationalistic, not responsible medical communication. Richard Smith, former editor of *BMJ*, has argued that today's medical journals are mere extensions of pharmaceutical marketing.⁸⁹ The same might be said for some journals about their relationship with the tort bar.

The disclosures in rofecoxib-related articles in both *JAMA* and *BMJ* were inadequate and indeed misleading.^{16,81} Enormous sums received by several of the authors were not divulged in *JAMA*, and compensation was not even mentioned in the *BMJ* disclosure.⁸¹ Another article by the same authors regarding a rofecoxib study appeared subsequently in the *Annals of Internal Medicine* with a similarly uninformative disclosure statement.⁹⁰ Did the editors ask about these matters, and if so, why was the information not forthcoming at the time of publication? Implementation of COI disclosures by these journals appears inequitable, seemingly dependent on the source of the authors' compensation.

SERIOUS COIs NOT RELATED TO THE PHARMACEUTICAL INDUSTRY

Most major medical journals today restrict publication of commentaries, opinions, reviews, and editorials by individuals with any ties to the pharmaceutical-biotech-medical device industry. However, the role of experts who have significant COI *not* related to industry has not been explored. Expert witnesses are qualified by lawyers and judges, not by medical peers or professional societies. Egilman reports having testified for plaintiffs in legal cases involving asbestosis, occupational lung disease, beryllium poisoning, silicone breast implants and connective tissue disease (characterized as the epitome of junk science⁹¹), selective serotonin reuptake inhibitor and suicide risk, atypical antipsychotics and metabolic changes, and selective COX-2 inhibitors and cardiovascular disease, an amazing breadth of medical expertise.

Meanwhile, Krumholz' interactions with Merck have not been limited to rofecoxib. Two weeks before publication of the *JAMA* article that he coauthored,¹⁶ he chaired the panel at the 2008 American College of Cardiology annual meeting that was asked to review the controversial ENHANCE (Ezetimibe and Simvastatin in Hypercholesterolemia Enhances Atherosclerosis Regression) study evaluating the effect of ezetimibe plus simvastatin (Vytorin, Merck-Schering Plough) vs simvastatin alone, on carotid intima-medial thickness (CIMT) progression in patients with heterozygous familial hypercholesterolemia.⁹² The trial did not achieve its primary end point; a likely explanation relates to the study's flawed design, in which more than 80% of patients enrolled had been treated aggressively with high-dose statins for years so their baseline CIMT was normal ("floor effect"). In both study groups, CIMT progression was much less than expected in an untreated population with familial hypercholesterolemia, suggesting that both therapies were effective.⁹³ The study certainly did not refute the massive body of evidence that both primary and secondary cardiovascular disease event risk reduction are directly related to lowering low-density lipoprotein cholesterol, nor the conclusion based on several statin trials that

"lower is better" in terms of clinical benefit from reduction in low-density lipoprotein cholesterol.⁹⁴

ENHANCE was not a negative study, but in his remarks Krumholz⁹⁵ called it exactly that and likened Vytorin to "an expensive placebo." Media coverage was sensational—the findings often reported (inaccurately) as the drug that fails to prevent heart attacks and strokes⁹⁶—with major repercussions for patients, prescribing physicians, and employees of Merck-Schering Plough. It will be a number of years before the 18,000-patient clinical outcome study with ezetimibe and simvastatin is completed.^{93,94} All this leads to 2 basic conclusions: (1) There are numerous physicians with expertise in cardiovascular medicine and surrogate outcome trials whom the American College of Cardiology could have consulted without such substantial COI *and* involvement in litigation against Merck. (2) Krumholz should have simply recused himself from participating in this exercise.

AUTHORSHIP, GHOST AUTHORSHIP, AND MEDICAL WRITING

What about the allegations of authorship misdeeds in the article by Ross et al?¹⁶ Merck personnel did develop initial drafts of some manuscripts, including (in 2003) one for the Vioxx Alzheimer's Disease prevention study, protocol 078, mentioned in the article by Ross et al. The non-Merck authors had a substantial role in the design of this study, acquisition of data, and interpretation of the results; had previously spoken with Merck personnel about manuscript concepts; reviewed and edited the manuscript; and gave final approval to its content but did not write the first draft. Several external authors voiced their strong disagreement in *JAMA* with the conclusion that they were guest authors²² for the article. Coauthor S. Ferris called it "egregious" that Ross et al had done no research besides mining the Merck documents and reading the published journal articles; the idea that he and the others were guest authors was "simply false."⁹⁷ (Lead author Leon Thal could not comment because he is deceased.)

Ross et al¹⁶ neglect other facts that they surely learned in their research of documents obtained through legal discovery. Merck adopted publication guidelines in 2003 (posted online in January 2004⁹⁸) that committed to publication of its hypothesis-testing trials regardless of outcome and addressed the role of medical writers and disclosure of their contribution (if applicable) as well as criteria for authorship, essentially the same as those of the ICMJE.²⁶ The guidelines also indicated Merck's willingness to share study protocols with journal editors at the time of manuscript submission, well before any journal adopted such a policy. Shortly thereafter, the guidelines were commented on favorably by the then-editor of the *Canadian Medical Association Journal*⁹⁹ and elsewhere more recently.¹⁸ The guidelines (and internal resource materials) clearly stipu-

lated that external authors would have full access to study data, including the electronic database by mutually agreeable methods, and ultimate control of the content of a paper to be submitted for publication. The guidelines could not alter how some papers had been developed years earlier but led to major changes in authorship of manuscripts in parts of the company outside the Medical Communications Department, directly influenced other companies to develop their own guidelines as well as PhRMA (Pharmaceutical Research and Manufacturers Association) to develop its Principles for the Conduct and Disclosure of Results of Clinical Trials.¹⁰⁰ Describing violations of today's standards in events that (in some cases) took place a decade earlier is hardly balanced reporting and essentially old news.

Furthermore, determining authorship is as much art as science. It is a subjective judgment that someone has made a "substantive intellectual contribution" warranting authorship vs a lesser effort that may or may not be acknowledged, regardless of funding source for the work. The article by Ross et al¹⁶ ignored such nuance. For academia, publication is the "coin of the realm," and authorship highly sought and valued (unless questions of integrity later arise, when suddenly authors' contributions to the work become minor, etc).^{101,102} As trials have increased in size and complexity, so has the average number of authors per paper, making it sometimes difficult to determine precise roles.¹⁰³ Editors have increasingly requested detailed descriptions of each author's contributions to manuscripts,¹⁰⁴ but authorship decisions are often contentious. In a published survey of an English academic medical center, two-thirds of faculty reported authorship problems, and half claimed they had been wrongly excluded, events described politely as "memorable and upsetting."¹⁰⁵ Guest or honorary authorship has been detected after publication in major medical journals in 20% to 50% of authors who do not meet all 3 ICMJE authorship criteria.¹⁰⁶ Honorary and ghost authoring were even reported in 39% and 9%, respectively, of Cochrane reviews,¹⁰⁷ far removed from industry. A recent article critical of purported industry influence on publications states, "Ghost writing and honorary authorship are not in and of themselves scientific problems..." and then explains, "Some honorary authors are senior professors and chairs of departments, who are added to articles because of local academic politics rather than at the request of drug companies."¹⁰⁸ Apparently, acceptable authorship practices differ in industry and academia, particularly regarding guest authoring.

One journal has taken a different approach to preventing ghostwriting and guest authoring. *Neurology* announced in 2008 a new policy wherein anyone who writes the first draft of a manuscript accepted for publication will be a named author.¹⁰⁹ Although seemingly unambiguous as policy, a first

draft of a manuscript may be extensively revised such that the final paper barely resembles the initial version. Usually, a medical writer would not be asked to approve the final manuscript version submitted for peer-reviewed publication. In either case, the writer would not merit authorship per ICMJE criteria.²⁶ Furthermore, a medical writer not involved in original literature review, study design, and/or data analysis might not be able to defend content of the manuscript in response to reviews or criticism, a critical role of a true author. In my view, authorship is 2-faceted: it provides credit and recognition for work done before publication, and it assigns responsibility to explain and defend the work after publication. Authorship decisions in many cases are shades of gray, not black-and-white. Regardless, *Neurology* now follows a different (some might say, less-rigorous) definition of authorship than that of the ICMJE. The impact and/or benefit of this approach remains to be seen.

Despite the intense debate and accusations about ghostwriting and guest authoring, there is consistent agreement among many organizations on 2 issues: (1) Medical writing is a valuable, accepted function that can assist in the timely, well-organized, clear communication of scientific studies. (2) Medical writing or editorial assistance that does not merit named authorship should be acknowledged, along with the source of funding support for such work. The American Medical Writers' Association (AMWA), European Medical Writers' Association (EMWA), World Association of Medical Editors (WAME), Council of Science Editors (CSE), PhRMA, and ICMJE *all* have similar positions on medical writing.¹¹⁰ The Association of American Medical Colleges clearly states, "Transparent writing collaboration with attribution between academic and industry investigators, medical writers, and/or technical experts is not ghostwriting."¹¹¹

Ironically, it has not been uncommon for industry sponsors to either demote one or more of their own deserving scientists from byline authorship to acknowledgment or to remove them entirely from the manuscript. This has been done to avoid the appearance of excess company influence because of fears that such papers would be less-favorably received by editors, reviewers, and journal readers. One small study, although not without flaws, supports this concern.¹¹² In fact, these behaviors by sponsors perpetuate unfounded suspicions of industry scientists, are intellectually dishonest and demotivating, and result in yet-another form of ghost authoring.

Change may be coming: a recent controlled clinical study published in *The Lancet* has first and corresponding authors from Merck, with a clear majority of Merck authors overall. A letter to the editor deemed the article "an advertorial," questioned who could vouch for the integrity of the data, and declared, "Employees of the study sponsor... have no conflict of interest—their one interest is the wel-

fare of the company and its stock price.”¹¹³ The academic and Merck authors replied independently, and the former characterized the letter as “...a shocking, simplistic, arrogant and rather disappointing view on life and science.”¹¹⁴ They further noted that rather than using ghostwriters and “fake” first authors, the authorship was open and honest, fairly representing the scientific contributions of all authors in compliance with authorship guidelines.¹¹⁴ This exchange sadly demonstrates the current distrustful state of interactions between academia and industry.

MEDICAL JOURNALS’ POLICIES FOR PUBLISHING INDUSTRY-SPONSORED RESEARCH

Other journals approach industry-sponsored research and medical writer–assisted manuscript submissions differently (even with full disclosures): they simply reject them. A recent manuscript submitted to the *Journal of Family Practice* clearly stated in both the cover letter and the acknowledgments the role of a medical writer and the writer’s compensation in developing the paper, consistent with ICMJE recommendations.²⁶ The editor’s response is perplexing, almost Orwellian: “...After initial review, I regret that we will be unable to further consider your manuscript. Recently, we have made the decision to not consider any articles that have been sponsored by industry or written in conjunction with a medical education intermediary. While...this might eliminate useful articles and authors, we believe this policy is consistent with recent trends in transparency [sic] and measures to assure fair balance” (Gene Snyder, MBA, written communication, March 2, 2009). Censorship based on affiliation does not equate to transparency and is the antithesis of supposed fair balance.

Nearly all major medical journals will consider primary reports of industry-sponsored controlled trials (as noted previously, *JAMA* requires independent validation of the statistical analysis⁵⁸). However, reviews (even commissioned), perspectives, and commentaries from authors with financial COI are treated differently. *JAMA* and *The Lancet* will generally not even consider them^{80,115}; *NEJM* will consider such manuscripts but only if the author has received less than \$10,000 from a company whose product may be affected by the review, a stance adopted because of the difficulty of finding experts with no associations with for-profit sponsors.¹¹⁶ *Annals of Internal Medicine* takes a somewhat more reasoned, individualized approach, acknowledging “...we would be taking the quest too far if we adopted a policy in which we discounted expert opinion solely because of a potential conflict of interest.”¹¹⁷

Another influential medical journal disinvited a tenured academic researcher from writing a review (initially requested by that journal) in their area of expertise solely because of the “perception” of a COI. The “problem” was that

the professor had received partial research support from 1 or more pharmaceutical companies (even though all findings from the funded research were stipulated to be placed in the public domain, with no patenting) (Tom Stossel, MD, written communication, March 2, 2009). In a 1993 commentary published in *JAMA*, Rothman¹¹⁸ warned of censoring scientific discourse (which he presciently termed *the new McCarthyism in science*) if authors’ affiliations and/or funding, irrespective of a paper’s scientific merit, become the basis for editors’ publication decisions. In her penultimate editorial as Acting Editor of the *NEJM* in 2000, Angell¹¹⁹ posed the question, “The pharmaceutical industry: to whom is it accountable?” The same question might be raised today, but for editors of some medical journals.

These overt restrictions on researcher communications in today’s climate of political correctness on COI are causing more than policy debates among various stakeholders: they are beginning to affect the willingness of prominent researchers to interact with industry in any manner that involves even minimal compensation for their time and efforts. In a revealing *New York Times* article¹²⁰ the day before the Ross et al¹⁶ article on supposed ghostwriting at Merck appeared, 3 prominent researchers, 1 at Yale and 2 at Harvard, described how they stopped accepting any reimbursement from medical product companies when consulting or serving on advisory boards, essentially for appearance’s sake. One of them, Eric Winer, Professor at Harvard and Director of the Breast Oncology Center at the Dana Farber Cancer Institute, poignantly commented, “I am responding to a societal pressure....And in truth, it has made my life simpler.” Yet, Winer further noted, “My willingness to go to an advisory board meeting has gone down.... This is a complicated arena. And on some level, I resent the fact that I had to make this decision.”¹²⁰ There are serious negative implications for the future of medical product development if top academic researchers are shamed into ceasing any type of compensated interactions with industry.

LEGAL DISCOVERY AND PEER-REVIEWED PUBLICATION

Documents obtained in legal discovery proceedings may be suitable for the courtroom but are much more questionable for medical “research” articles, at least as they have been presented to date. Such articles take only one side of complex legal proceedings and legitimize the interests of the tort bar through publication in major medical journals. Bedrock principles of our legal system are that the accused be informed about the charges against them *and* the evidence that will be used. The accused may depose and face their accuser(s) in court, may cross-examine them, and present his or her version of events before a judge and/or jury. Only then is there deliberation to reach a verdict. It seems paradoxical that top-tier peer-reviewed medical

journals, supposedly the bastion of objectivity and disinterested communication, publish articles based on a unilateral presentation of legal discovery proceedings without allowing a real-time response from the accused. Merck was never invited to respond to these articles by the editors, leaving only press release and subsequent short letters to the editor as responses.

Several weeks after *JAMA*'s 2008 publications and editorial denunciations of industry, 2 early rofecoxib verdicts against Merck were overturned, including the first case won by attorney Lanier in which the jury returned a total verdict against the company for \$253 million (reduced to \$26 million by Texas state law). A Texas appeals court ruled that there was no compelling evidence to support the finding that rofecoxib had caused the heart attack of the plaintiff's husband.¹²¹ Beyond these events, if Merck's conduct was anywhere near as egregious as depicted by these authors,^{16,79,81,90} how do they explain that as of May 2008, according to the *New York Times*, plaintiffs had won only 3 of the nearly 20 cases that had gone to decision?¹²¹

Although general disclosure statements that an author has received compensation (and the source for it) have been considered adequate, I believe editors have an additional responsibility to inform their readers of the explicit role(s) played by and the extent of compensation received by authors in publications arising from legal proceedings. I recommend that for these specific papers only, companies that are named be offered adequate time and space to address the accusations made in the forthcoming article(s) in the *same* journal issue. Let readers have the opportunity to see both sides of a story and pass judgment about the actions of the company or individual, much as in a court of law. Editors might request an uninvolved third party (if one can be found) to review the article and the company response and write a commentary. Some may protest that this would provide "special" treatment for one stakeholder, for-profit industry. I respectfully disagree; if material from legal discovery is to be the subject of medical journal publication, I am suggesting a balanced approach to its presentation before the "jury"—the journal readership, public, and media. I am *not* recommending this approach for any other type of publication.

CONCLUDING COMMENTS: INDUSTRY, PUBLICATIONS, AND PUBLIC TRUST

The developments discussed herein are symptoms of the underlying lack of trust in industry-sponsored research. There are frequent calls for greater "transparency" on the part of industry, which seem to ignore the major changes that have occurred in the past decade. Even before the FDAAA, companies were registering clinical trials in response to ICMJE policies and posting detailed study result summaries for any marketed products on [\[studyresults.org\]\(http://studyresults.org\), after voluntary positions taken by PhRMA and international pharmaceutical trade group associations in 2004 and 2005.^{122,123} PhRMA recently extended its policy to go beyond the current FDAAA requirements, calling on its members to register and disclose results of all studies involving patients \(not healthy volunteers\) for all products marketed and those investigational products whose development has been discontinued, effective October 2009.¹²⁴](http://www.clinical-</p>
</div>
<div data-bbox=)

Calls for posting raw data online from all clinical research trials tend to discount the complexities of analysis of such databases, which can lead to mistaken findings,⁴⁹ and of the real potential for misuse of such data for analyses of outcomes unrelated to the initial studies' design (hypothesis-generation, not proof of causality) and/or by persons with other agendas.¹²⁵⁻¹²⁷ Reflecting on the rosiglitazone cardiovascular event meta-analyses of 2007, a recent commentary by senior academic physicians and biostatisticians with decades of experience in design and monitoring of major clinical trials said, "To do more good than harm, a ceasefire from academicians, prestigious medical journals, regulatory and other government officials who should report but not make the news seems prudent."¹²⁸

Industry can do its part by collaborating with academics to design credible clinical trials (especially comparative studies); by providing investigators with full access to study data, including, if requested, the aggregate or electronic database in a manner that is mutually acceptable and protects the sponsor's proprietary information and intellectual property; by allowing external investigators to control publication decisions; by providing study protocols to journals if requested at the time of manuscript submission; and, importantly, by respecting authorship criteria. The last-mentioned item means that deserving industry scientists should not only be named authors but also act as corresponding author and/or guarantor of study integrity, when appropriate.¹¹⁴

Primary reports of randomized trials are more formulaic and less prone to manipulation than are reviews and commentaries. Companies should avoid attempts to develop the latter as marketing pieces, particularly through ghostwriting and guest authoring; if published, such articles are often received negatively by physicians and scientists already suspicious of industry because of previous episodes of publication misconduct. Peer reviewers and editors, for their part, should evaluate manuscripts based on merit, not by the affiliation of 1 or more authors, and should not apply a presumption of "guilty until proven innocent." If a manuscript is valid, balanced, and credible, it will withstand even an extra degree of scrutiny in the review process.

When all is said about COI and its supposed adverse effects on the biomedical literature, readers should consider the widely divergent definitions of COI^{28,29,31,83,115-117} and the uneven approaches to disclosure^{30,32,33,64,65,80} and ask

themselves if they are “helped” by page-long columns of disclosures for authors today¹²⁸ or by postpublication corrections for authors’ failures to mention modest commercial interactions in previous years.¹²⁹ In contrast are the tangible benefits of academic-industry collaborations over the past several decades. Nearly all modern medical therapies that are taken for granted today have resulted from applied research and development by industry (often building on mechanistic basic research funded by government), done largely in collaboration with academic physicians.¹³⁰

Conflicts of interest are widespread and represent a state of affairs, not a behavior or misconduct. They should be managed, rather than vainly attempting their elimination. If disclosure is the method of management, it should be implemented consistently. The Center for Science in the Public Interest concluded its prepared remarks before the Institute of Medicine Committee on Conflicts of Interest in March 2008, “Where there is total financial independence, there can be no questions about objectivity.”¹³¹ This assertion is political in nature, not scientific, and merely rehearses the age-old dogma that money is the root of all evil. Such pronouncements ignore both the plethora of other influences that can bias research^{32,33,120} and, more directly, the worst cases of research misconduct—fraud and fabrication—that have occurred almost entirely in government and foundation-sponsored research.^{102,132,133}

Finally, despite the rhetoric of organizations such as the Center for Science in the Public Interest and Public Citizen, when the latter analyzed voting patterns at more than 220 FDA drug advisory committee meetings from 2001 to 2004, they could not find a statistically significant relationship between COI (defined several ways) and member voting patterns. Furthermore, exclusion of “conflicted” advisory committee members would not have changed the overall vote outcome at any meeting they studied.¹³⁴ These findings confirm that physicians and medical scientists can provide objective, evidence-based reasoning even if supported by industry. At least in some cases, the same cannot be said when the tort bar, consultants to plaintiffs’ attorneys, and medical publication mix.

REFERENCES

- Menaker R, Bahn RS. How perceived physician leadership behavior affects physician satisfaction [published correction appears in *Mayo Clin Proc*. 2008;83(12):1414]. *Mayo Clin Proc*. 2008;83(9):983-988.
- Lanier WL, Rose SH. The contemporary medical community: leadership, mentorship, and career choices [editorial]. *Mayo Clin Proc*. 2008;83(9):974-977.
- Mayer AP, Files JA, Ko MG, Blair JE. Academic advancement of women in medicine: do socialized gender differences have a role in mentoring? *Mayo Clin Proc*. 2008;83(2):204-207.
- Sherazi S, Daubert JP, Block RC, et al. Physicians’ preferences and attitudes about end-of-life care in patients with an implantable cardioverter-defibrillator. *Mayo Clin Proc*. 2008;83(10):1139-1141.
- Cohen NH. Advance directives: know what you want, get what you need [editorial]. *Mayo Clin Proc*. 2007;82(12):1460-1462.
- Waisel D. Physician participation in capital punishment. *Mayo Clin Proc*. 2007;82(9):1073-1082.
- Caplan AL. Should physicians participate in capital punishment? [published correction appears in *Mayo Clin Proc*. 2007;82(10):1291] [editorial]. *Mayo Clin Proc*. 2007;82(9):1047-1048.
- Lanier WL, Berge KH. Physician involvement in capital punishment: simplifying a complex calculus [published correction appears in *Mayo Clin Proc*. 2007;82(11):1434] [editorial]. *Mayo Clin Proc*. 2007;82(9):1043-1046.
- Camilleri M, Cortese DA. Managing conflict of interest in clinical practice. *Mayo Clin Proc*. 2007;82(5):607-614.
- Stossel TP. Divergent views on managing clinical conflicts of interest [letter]. *Mayo Clin Proc*. 2007;82(8):1013-1014.
- Romano TJ. Divergent views on managing clinical conflicts of interest [letter]. *Mayo Clin Proc*. 2007;82(8):1013-1014.
- Camilleri M, Cortese DA. Divergent views on managing clinical conflicts of interest [letter reply]. *Mayo Clin Proc*. 2007;82(8):1014-1015.
- Holtby S, Wakewich P. Publication of market-driven research in medical journals [letter]. *Mayo Clin Proc*. 2006;81(6):850.
- Yawn BP. Publication of market-driven research in medical journals [letter reply]. *Mayo Clin Proc*. 2006;81(6):850-851.
- Lanier WL. Editor’s note: industry support of articles published in *Mayo Clinic Proceedings*. *Mayo Clin Proc*. 2006;81(6):851-852.
- Ross JS, Hill KP, Egilman DS, Krumholz HM. Guest authorship and ghostwriting in publications related to rofecoxib: a case study of industry documents from rofecoxib litigation. *JAMA*. 2008;299(15):1800-1812.
- DeAngelis CD, Fontanarosa PB. Impugning the integrity of medical science: the adverse effects of industry influence [editorial]. *JAMA*. 2008;299(15):1833-1835.
- Nature Publishing Group. Nothing to see here: based on one company’s past poor publishing practices, a top-tier medical journal misguidedly stigmatizes any paper from industry [editorial]. *Nat Biotechnol*. 2008;26(5):476.
- Fitzgerald GA. Guest authorship, mortality reporting, and integrity in rofecoxib studies [letter]. *JAMA*. 2008;300(8):900-901.
- Patrono C. Guest authorship, mortality reporting, and integrity in rofecoxib studies [letter]. *JAMA*. 2008;300(8):901.
- Hawkey CJ. Guest authorship, mortality reporting, and integrity in rofecoxib studies [letter]. *JAMA*. 2008;300(8):901.
- Ferris S, Galasko D, Kirby L. Guest authorship, mortality reporting, and integrity in rofecoxib studies [letter]. *JAMA*. 2008;300(8):901-902.
- Ong HT, Cheah JS. Guest authorship, mortality reporting, and integrity in rofecoxib studies [letter]. *JAMA*. 2008;300(8):903-904.
- Ross JS, Egilman DS, Harlan M, Krumholz HM. Guest authorship, mortality reporting, and integrity in rofecoxib studies [letter reply]. *JAMA*. 2008;300(8):904-905.
- DeAngelis CD, Fontanarosa PB. Guest authorship, mortality reporting, and integrity in rofecoxib studies [letter reply]. *JAMA*. 2008;300(8):905-906.
- International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals: writing and editing for biomedical publication: updated October 2008. ICMJE Web site. www.icmje.org. Accessed July 8, 2009.
- Berenson A. Trial lawyers are now focusing on lawsuits against drug makers. *New York Times*. May 18, 2003. <http://www.nytimes.com/2003/05/18/us/trial-lawyers-are-now-focusing-on-lawsuits-against-drug-makers.html>. Accessed July 8, 2009.
- Thompson DF. Understanding financial conflicts of interest. *N Engl J Med*. 1993;329(8):573-576.
- Cohen JJ. Trust us to make a difference: ensuring public confidence in the integrity of clinical research. *Acad Med*. 2001;76(2):209-214.
- DeAngelis CD, Fontanarosa PB, Flanagan A. Reporting financial conflicts of interest and relationships between investigators and research sponsors [editorial]. *JAMA*. 2001;286(1):89-91.
- Conflict of interest in medical research, education, and practice. Institute of Medicine of the National Academies Web site. Washington, DC: National Academies Press, 2009. <http://www.iom.edu/CMS/3740/47464/65721.aspx>. Accessed July 8, 2009.
- Horton R. Conflicts of interest in clinical research: opprobrium or obsession? *Lancet*. 1997;349(9059):1112-1113.
- Smith R. Conflict of interest and the *BMJ*: time to take it seriously [editorial]. *BMJ*. 1994;308(6920):4-5.
- Harris Interactive. The 9th annual RQ: reputations of the 60 most visible companies: a survey of the US general public. HarrisInteractive Web site. www.harrisinteractive.com/news/mediaaccess/2008/HI_BSC_REPORT_AnnualRQ_USASummary07-08.pdf. Accessed July 8, 2009.
- Dong BJ, Hauck WW, Gambertoglio JG, et al. Bioequivalence of generic and brand-name levothyroxine products in treatment of hypothyroidism. *JAMA*. 1997;277(15):1205-1213.
- Rennie D. Thyroid storm [editorial]. *JAMA*. 1997;277(15):1238-1243.

37. Kahn JO, Cherng DW, Mayer K, Murray H, Lagakos S. Evaluation of HIV-1 immunogen, an immunologic modifier, administered to patients infected with HIV having 300 to 549 x 10⁶/L CD4 cell counts: a randomized controlled trial [published correction appears in *JAMA*. 2001;285(17):2197]. *JAMA*. 2000;284(17):2193-2202.
38. Silverstein FE, Faich G, Goldstein JL, et al. Gastrointestinal toxicity with celecoxib vs nonsteroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis: the CLASS study: a randomized controlled trial. *JAMA*. 2000;284(10):1247-1255.
39. Hrachovec JB, Mora M. Reporting of 6-month vs 12-month data in a clinical trial of celecoxib [letter]. *JAMA*. 2001;286(19):2398.
40. Davidoff F, DeAngelis CD, Drazen JM, et al. Sponsorship, authorship, and accountability [editorial]. *Ann Intern Med*. 2001;135(6):463-466.
41. The Lancet. Depressing research [editorial]. *Lancet*. 2004;363(9418):1335.
42. Martinez B. Spitzer charges Glaxo concealed Paxil data. *The Wall Street Journal*. June 3, 2004:B1. <http://www.moralgroup.com/NewsItems/Drugs/p3.htm>. Accessed July 8, 2009.
43. DeAngelis C, Drazen JM, Frizelle FA, et al. Clinical trial registration: a statement from the International Committee of Medical Journal Editors [editorial]. *Lancet*. 2004;364(9438):911-912. http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=PubMed&list_uids=15364170&dopt=Abstract.
44. Curfman GD, Morrissey S, Drazen JM. Expression of concern: Bombardier et al. "Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis." *N Engl J Med*. 2000;343:1520-8 [editorial]. *N Engl J Med*. 2005;353(26):2813-2814. Epub 2005 Dec 8.
45. Bombardier C, Laine L, Burgos-Vargas R, et al. Response to expression of concern regarding VIGOR study [letter]. *N Engl J Med*. 2006;354(11):1196-1199. Epub 2006 Feb 22.
46. Reicin A, Shapiro D. Response to expression of concern regarding VIGOR study [letter]. *N Engl J Med*. 2006;354:1198-1199. Epub 2006 Feb 22.
47. Armstrong D. How the New England Journal missed warning signs on Vioxx: medical weekly waited years to report flaws in article that praised pain drug: Merck seen as "punching bag." *The Wall Street Journal (East Ed)*. 2006;A1:A10.
48. US Department of Health and Human Services. Food and Drug Administration. Food and Drug Administration Amendments Act of 2007, P.L. 110-85. http://fwrwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid=f:publ085.110. Accessed July 8, 2009.
49. Hirsch L. Trial registration and results disclosure: impact of US legislation on sponsors, investigators, and medical journal editors. *Curr Med Res Opin*. 2008;24(6):1683-1689. Epub 2008 May 6.
50. Bekelman JE, Li Y, Gross CP. Scope and impact of financial conflicts of interest in biomedical research: a systematic review. *JAMA*. 2003;289(4):454-465.
51. Lexchin J, Bero LA, Djulbegovic B, Clark O. Pharmaceutical industry sponsorship and research outcome and quality: systematic review. *BMJ*. 2003;326(7400):1167-1170.
52. Kjaergard LL, Als-Nielsen B. Association between competing interests and authors' conclusions: epidemiological study of randomised clinical trials published in the *BMJ*. *BMJ*. 2002;325(7358):249.
53. Montori VM, Smieja M, Guyatt GH. Publication bias: a brief review for clinicians. *Mayo Clin Proc*. 2000;75(12):1284-1288.
54. Krzyzanowska MK, Pintilie M, Tannock IF. Factors associated with failure to publish large randomized trials presented at an oncology meeting. *JAMA*. 2003;290(4):495-501.
55. Chan AW, Krleža-Jerić K, Schmid I, Altman DC. Outcome reporting bias in randomized trials funded by the Canadian Institutes of Health Research. *CMAJ*. 2004;171(7):735-740.
56. Hirsch L. Randomized clinical trials: what gets published, and when? *CMAJ*. 2004;170(4):481-483.
57. Chan AW, Hróbjartsson A, Haahr MT, Gøtzsche PC, Altman DC. Empirical evidence for selective reporting of outcomes in randomized trials: comparison of protocols to published articles. *JAMA*. 2004;291(20):2457-2465.
58. Fontanarosa PB, Flanagan A, DeAngelis CD. Reporting conflicts of interest, financial aspects of research, and role of sponsors in funded studies [editorial]. *JAMA*. 2005;294(1):110-111.
59. Loew CJ. Conflicts of interest and independent data analysis in industry-funded studies [letter]. *JAMA*. 2005;294(20):2575.
60. Molenberghs G, Imrey P, Drake C. Conflicts of interest and independent data analysis in industry-funded studies [letter]. *JAMA*. 2005;294(20):2575-2576.
61. Fontanarosa PB, DeAngelis CD. Conflicts of interest and independent data analysis in industry-funded studies [letter reply]. *JAMA*. 2005;294(20):2576-2577.
62. Rothman KJ, Evans S. Extra scrutiny for industry funded trials: JAMA's demand for an additional hurdle is unfair—and absurd [published correction appears in *BMJ*. 2006;332(7534):151] [editorial]. *BMJ*. 2005;331(7529):1350-1351.
63. DeAngelis CD. The influence of money on medical science [editorial]. *JAMA*. 2006;296(8):996-998. Epub 2006 Aug 7.
64. Goozner M, Caplan A, Moreno J, Kramer BS, Babor TF, Cowles Science W. A common standard for conflict of interest disclosure. Center for Science in the Public Interest Web site. http://www.cspinet.org/new/pdf/20080711_a_common_standard_for_conflict_of_interest_disclosure_final_for_conference.pdf. Accessed July 8, 2009.
65. Califf R. The changing academic landscape. Presented at: 4th Annual Meeting of the International Society for Medical Publication Professionals; Philadelphia, PA; April 28-30, 2008. <http://www.ismpp.org/pdf/4th%20Annual%20Meeting%20Highlights%20Newsletter%20FINAL.PDF>. Accessed July 8, 2009.
66. Cohen LS, Altschuler LL, Harlow BL, et al. Relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment [published correction appears in *JAMA*. 2006;296(2):170]. *JAMA*. 2006;295(5):499-507.
67. Cohen LS, Nonacs R, Viguera AC, et al. Antidepressant treatment and relapse of depression during pregnancy [letter reply]. *JAMA*. 2006;296(2):166-167.
68. Armstrong D. Financial ties to industry cloud major depression study: at issue: whether it's safe for pregnant women to stay on medication: *JAMA* asks authors to explain. *The Wall Street Journal (East Ed)*. July 11, 2006:A1, A9. <http://research.unm.edu/coi/private/Articles/WSJ%202006.07.11%20Fin%20Ties%20Industry.pdf>. Accessed July 8, 2009.
69. Armstrong D. *JAMA* to tighten rules on author disclosure. *The Wall Street Journal*. July 12, 2006. <http://online.wsj.com/article/SB115266504840504116-search.html?KEYWORDS=david+armstrong&COLLECTION=wsjie/6month>. Accessed April 18, 2009.
70. Leo J, Lacasse J. Clinical trials of therapy versus medication: even in a tie, medication wins [letter]. http://www.bmj.com/cgi/eletters/338/feb05_1/b463#208503. *BMJ*. Mar 5 2009. Accessed July 8, 2009.
71. Armstrong D. *The Wall Street Journal* Health Blog. *JAMA* editor calls critic a "nobody and a nothing." March 13, 2009. <http://blogs.wsj.com/health/2009/03/13/jama-editor-calls-critic-a-nobody-and-a-nothing/>. Accessed July 8, 2009.
72. Armstrong D. Medical journal decries public airing of conflicts. *The Wall Street Journal*. March 22, 2009. <http://online.wsj.com/article/SB123776823117709555.html#articleTabs%3Darticle>. Accessed July 8, 2009.
73. Armstrong D. Nonprofit hits *JAMA* editors, urges inquiry. *The Wall Street Journal*. March 27, 2009. <http://online.wsj.com/article/SB123810131860651487.html>. Accessed July 8, 2009.
74. Armstrong D. Medical group seeks probe of its journal. *The Wall Street Journal*. March 28, 2009. <http://online.wsj.com/article/SB123819137827260883.html>. Accessed July 8, 2009.
75. Robinson RG. Re: Clinical trials of therapy versus medication: even in a tie, medication wins [letter reply]. http://www.bmj.com/cgi/eletters/338/feb05_1/b463#208503. *BMJ*. April 15, 2009. Accessed July 8, 2009.
76. DeAngelis CD, Fontanarosa PB. Conflicts over conflicts of interest [published online ahead of print March 20, 2009] [editorial]. *JAMA*. doi:10.1001/jama.2009.480.
77. DeAngelis CD, Fontanarosa PB. Resolving unreported conflicts of interest [editorial]. *JAMA*. 2009;302(2):198-199.
78. Armstrong D. Medical journal eschews rule silencing filers of complaints. July 7, 2009. *The Wall Street Journal.com* <http://online.wsj.com/article/SB124700923018308521.html>. Accessed July 13, 2009.
79. Psaty BM, Kronmal RA. Reporting mortality findings in trials of rofecoxib for Alzheimer disease or cognitive impairment: a case study based on documents from rofecoxib litigation. *JAMA*. 2008;299(15):1813-1817.
80. Instructions for Authors. *JAMA* Web site. <http://jama.ama-assn.org/misc/fora.dtl#AuthorshipCriteriaandContributionsandAuthorshipForm>. Accessed July 8, 2009.
81. Krumholz HM, Ross JS, Presler AH, Egilman DS. What have we learnt from Vioxx? *BMJ*. 2007;334(7585):120-123.
82. Mayer TVH. On selective learning [letter]. *BMJ*. 2007;(February):24. <http://www.bmj.com/cgi/eletters/334/7585/120#160396> [published online ahead of print]. Accessed April 18, 2009.
83. US Department of Health and Human Services, Food and Drug Administration. Guidance for the public, FDA Advisory Committee members, and FDA staff on procedures for determining conflict of interest and eligibility for participation in FDA Advisory Committees. August 2008. <http://www.fda.gov/oc/advisory/guidancepolicyregs/acwaivercriteriafinalguidance080408.pdf>. Accessed July 8, 2009.
84. Wright M. Controversy surrounds witness in Vioxx trial. The Facts.com Web site. July 31, 2005. <http://thefacts.com/story.lasso?ewcd=c2feba40a6deb92e>. Accessed July 8, 2009.
85. Declaration of David Egilman. MD, MPH. Case 1:07-cv-00504-JBW-RLM Document 79-2 Filed 09/07/2007. <http://lawprofessors.typepad.com/tortspof/files/EgilmanAffidavit.pdf>. Accessed July 8, 2009.

86. Thomas L Jr. Judge rules drug documents must be returned to Eli Lilly. *The New York Times*. February 14, 2007. http://www.nytimes.com/2007/02/14/business/14lilly.html?_r=1. Accessed July 8, 2009.
87. Doctor who leaked documents will pay \$100,000 to Lilly. *The New York Times*. September 8, 2007. <http://www.nytimes.com/2007/09/08/business/08lilly.html>? Accessed July 8, 2009.
88. Henderson D. He's taking on Vioxx maker on its home turf: lawyer's winning Texas style to be tested in New Jersey. *The Boston Globe*. February 26, 2006. http://www.boston.com/news/nation/articles/2006/02/26/hes_taking_on_vioxx_maker_on_its_home_turf/. Accessed July 8, 2009.
89. Smith R. Medical journals are an extension of the marketing arm of pharmaceutical companies. *PLoS Med*. 2005;2(5):e138. Epub 2005 May 17.
90. Hill KP, Ross JS, Egilman DS, Krumholz HM. The ADVANTAGE seeding trial: a review of internal documents. *Ann Intern Med*. 2008;149(4):251-258.
91. Angell M. Shattuck lecture: evaluating the health risks of breast implants: the inter-play of medical science, the law, and public opinion. *N Engl J Med*. 1996;334(23):1513-1518.
92. Kastelein JJ, Akdim F, Stroes ES, et al; ENHANCE Investigators. Simvastatin with or without ezetimibe in familial hypercholesterolemia [published correction appears in *N Engl J Med*. 2008;358(18):1977]. *N Engl J Med*. 2008;358(14):1431-1443. Epub 2008 Mar 30.
93. O'Keefe JH, Bybee KA, Lavie CJ. Intensive lipid intervention in the post-ENHANCE era [editorial]. *Mayo Clin Proc*. 2008;83(8):867-869.
94. Stein EA. Low-density lipoprotein cholesterol reduction and prevention of cardiovascular disease [editorial]. *Mayo Clin Proc*. 2009;84(4):307-309.
95. The speech that maimed Schering and Merck. *Forbes.com* Web site, April 3, 2008. http://www.forbes.com/2008/04/03/vytorin-merck-schering-biz-healthcare-cx_mh_0402schering.html. Accessed July 8, 2009.
96. Dentzer S. Communicating medical news—pitfalls of health care journalism. *N Engl J Med*. 2009;360(1):1-3.
97. Saul S. Merck wrote drug studies for doctors. *The New York Times*. April 16, 2008. <http://www.nytimes.com/2008/04/16/business/16vioxx.html>? Accessed July 8, 2009.
98. Merck guidelines for publication of clinical trials and related works. http://www.merck.com/mlr/swf/clinical_trial_publication_guidelines.swf. Accessed July 8, 2009.
99. The “file drawer” phenomenon: suppressing clinical evidence [editorial]. *CMAJ*. 2004;170(4):437, 439.
100. Principles on conduct of clinical trials and communication of clinical trial results. PhRMA Web site. http://www.phrma.org/files/042009_Clinical%20Trial%20Principles_FINAL.pdf. Accessed July 8, 2009.
101. Van Loon T, Maisonneuve H. An authors' and editors' problem: authorship [editorial]. *Europ Sci Editing*. 2003;29(1):4. http://www.ease.org.uk/pdfese/ESE29_1p1-32.pdf. Accessed July 8, 2009.
102. Strange K. Authorship: why not just toss a coin? *Am J Physiol Cell Physiol*. 2008;295(3):C567-C575.
103. Levisky ME, Rosin A, Coon TP, Enslow WL, Miller MA. A descriptive analysis of authorship within medical journals, 1995-2005. *South Med J*. 2007;100(4):371-375.
104. Yank V, Rennie D. Disclosure of researcher contributions: a study of original research articles in *The Lancet*. *Ann Intern Med*. 1999;130(8):661-670.
105. Bhopal R, Rankin J, McColl E, et al. The vexed question of authorship: views of researchers in a British medical facility. *BMJ*. 1997;314(7086):1009-1012.
106. Bates T, Anić A, Marusić M, Marusić A. Authorship criteria and disclosure of contributions: comparison of 3 general medical journals with different author contribution forms. *JAMA*. 2004;292(1):86-88.
107. Mowatt G, Shirran L, Grimshaw JM, et al. Prevalence of honorary and ghost authorship in Cochrane reviews. *JAMA*. 2002;287(21):2769-2771.
108. Sismondo S. Ghost management: how much of the medical literature is shaped behind the scenes by the pharmaceutical industry? *PLoS Med*. 2007;4(9):e286.
109. Information for Authors. *Neurology* Web site. <http://www.neurology.org/misc/auth2.html>. Accessed July 13, 2009.
110. Wager E. Medical writers and peer-reviewed journals: understanding the rules and responsibilities. Keyword Pharma Web site. June 2007;3-13. http://www.keywordpharma.com/qrg/wager_sample.pdf. Accessed July 13, 2009.
111. AAMC Task Force. Industry funding of medical education: report of an AAMC Task force, Page 22. Published June 2008. https://services.aamc.org/publications/index.cfm?fuseaction=Product.displayForm&prd_id=232&cfid=1&cfoken=B97CA0DA-CCD3-0978-F90E246611633B1D. Accessed July 13, 2009.
112. Chaudhry S, Schroter S, Smith R, Morris J. Does declaration of competing interests affect readers' perceptions? A randomised trial. *BMJ*. 2002;325(7377):1391-1392.
113. Meilof JF, Hylkema MN. The Lancet and advertorials [published correction appears in *Lancet*. 2009;373(9678):1848] [letter]. *Lancet*. 2009;373(9668):1004.
114. Ferrari MD, Dodick DW, Winner P, Koppen H. Response from academic authors [letter reply]. *Lancet*. 2009;373(9668):1004-1005.
115. Writing for the Lancet. *Lancet* web site. <http://www.thelancet.com/writing-for-the-lancet>. Accessed July 13, 2009.
116. Drazen JM, Curfman GD. Financial associations of authors [editorial]. *N Engl J Med*. 2002;346(24):1901-1902.
117. The editors. Publishing commentary by authors with potential conflicts of interest: when, why and how [editorial]. *Ann Intern Med*. 2004;141(1):73-74.
118. Rothman KJ. Conflict of interest: the new McCarthyism in science. *JAMA*. 1993;269(21):2782-2784.
119. Angell M. The pharmaceutical industry: to whom is it accountable? [editorial]. *N Engl J Med*. 2000;342(25):1902-1904.
120. Kolata G. Citing ethics, some researchers are rejecting industry pay. *The New York Times* April 15, 2008. http://www.nytimes.com/2008/04/15/health/15conf.htm?_r=1&scp=26&sq=April%2015,%202008&st=cse. Accessed July 13, 2009.
121. Berenson A. Courts reject two major Vioxx verdicts. *The New York Times*. May 30, 2008. <http://www.nytimes.com/2008/05/30/business/30drug.html>? Accessed July 13, 2009.
122. PhRMA clinical study results database proposal. Pharmaceutical Research and Manufacturers of America Web site, 2004. http://www.clinicalstudyresults.org/primers/Clinical_Study_Results_Database.pdf. Accessed July 13, 2009.
123. European Federation of Pharmaceutical Industries and Associations (EFPIA) International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) Japanese Pharmaceutical Manufacturers Association (JPMA) Pharmaceutical Research and Manufacturers of America (PhRMA). Joint position on the disclosure of clinical trial information via clinical trial registries and databases. January 2005. http://www.ifpma.org/Documents/NR2205/joint%20position_clinical%20trials.pdf. Accessed July 13, 2009.
124. PhRMA. Revised clinical trial principles reinforce PhRMA's commitment to transparency and strengthen authorship standards [press release]. Washington, DC: April 20, 2009. http://www.phrma.org/news_room/press_releases/revised_clinical_trial_principles_reinforce_phrma%92s_commitment_to_transparency/. Accessed July 13, 2009.
125. Nissen SE, Wolski K. Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes [published correction appears in *N Engl J Med*. 2007;357(1):100]. *N Engl J Med*. 2007;356(24):2457-2471. Epub 2007 May 21.
126. Diamond GA, Bax L, Kaul S. Uncertain effects of rosiglitazone on the risk for myocardial infarction and cardiovascular death. *Ann Intern Med*. 2007;147(8):578-581. Epub 2007 Aug 6.
127. Mulrow CD, Cornell JE, Localio AR. Rosiglitazone: a thunderstorm from scarce and fragile data [editorial]. *Ann Intern Med*. 2007;147(8):585-587.
128. Hennekens CH, DeMets DL, Bairey Merz CN, Borzak SL, Borer JS. Doing more good than harm: need for a cease fire. *Am J Med*. 2009;122(4):315-316.
129. Werner M, Stern A. Is sunlight always the best disinfectant? Are financial conflicts of interest in research inherently unhealthy? *Science Progress*. Published February 18, 2009. http://www.scienceprogress.org/2009/02/is-sunlight-always-the-best-disinfectant/#_edn10. Accessed July 13, 2009.
130. Stossel TP. Regulating academic-industrial research relationships—solving problems or stifling progress? *N Engl J Med*. 2005;353(10):1060-1065.
131. Goozner M. Submitted statement of the Center for Science in the Public Interest. Institute of Medicine Board on Health Science Policy - Committee on Conflicts of Interest in Medical Research, Education and Practice. March 13, 2008. <http://www.iom.edu/CMS/3740/47464/49428/52483.aspx>. Accessed July 13, 2009.
132. Lock S. Research misconduct 1974-1990: an imperfect history. In: Lock S, Wells F, Farthing M, eds. *Fraud and Misconduct in Biomedical Research*. 3rd ed. London, England: BMJ Books; 2001:51-63.
133. Sox HC, Rennie D. Research misconduct, retraction, and cleansing the medical literature: lessons from the Poehelman case. *Ann Intern Med*. 2006;144(8):609-613. Epub 2006 Mar 6.
134. Lurie P, Almeida CM, Stine N, Stine AR, Wolfe SM. Financial conflict of interest disclosure and voting patterns at Food and Drug Administration drug advisory committee meetings. *JAMA*. 2006;295(16):1921-1928.