

Conflict of Interest and Scientific Publication: A Synopsis of the CSE Retreat

A retreat by the Council of Science Editors with funding from the Greenwall Foundation, the American Heart Association, and the American Society of Clinical Oncology

29-31 October 2004

Hyatt Lodge at the McDonald's Campus, Oak Brook, Illinois

Retreat cochairs: Jessica Ancker and Annette Flanagin

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In science, *conflict of interest* (COI) refers to “situations in which financial or other personal considerations may compromise, or have the appearance of compromising, an investigator’s professional judgment in conducting or reporting research”,¹ according to guidelines of the Association of American Medical Colleges. The Council of Science Editors,² the World Association of Medical Editors,³ and others also have defined and delineated COI. Researchers, reviewers, editors, journals, institutions, and funders all can have COI.

To address COI in scientific publication, the Council of Science Editors held a retreat on 29-31 October 2004. The Greenwall Foundation, the American Heart Association (AHA), and the American Society of Clinical Oncology supported the retreat with \$20,000 in grants. The grants made the attendance of four international editors possible and helped to fund the speakers.

The goal, as stated in the program, was for participants to discuss “the effects of

financial conflicts on scientific research and editorial and publication decisions, and to review and debate current strategies for managing conflicts of interest in scientific publication”. The 78 attendees—including editors, researchers, representatives of private and government funding agencies, representatives of pharmaceutical companies, legal experts, and journalists—discussed and debated such questions as the following: What constitutes a COI for an author, reviewer, editor, or institution? What are the effects of COI on scientific research and publication? What policies and procedures are in place for managing COI? Are they sufficient? Can we draw any conclusions from current practices and come up with better strategies?

After the keynote address on Friday evening, other presentations started the following morning and continued until about noon on Sunday. (The retreat program can be viewed at www.CouncilScienceEditors.org.) Presentations ran consecutively and lasted 10 to 25 minutes. A 10-minute question-and-answer session followed each presentation or group of presentations. To promote open discussion of the issues, all participants were guaranteed that what they said would not be quoted or paraphrased without their permission. That made for thought-provoking presentations and lively discussions. Speakers and other participants discussed study results, recounted anecdotes, and expressed a variety of opinions.

FRIDAY, 29 OCTOBER

Evening Session: Keynote Address: Conflict of Interest Policies in Science and Medical Journals Presented by Sheldon Krimsky, Professor of Urban and Environmental Policy and Planning, Tufts University

Sheldon Krimsky provided an overview of the topic of COI in science and medical

journals. Krimsky has been studying the interface between science and technology, ethics, and public policy for more than 30 years. He is the author of more than 140 reviews and essays and seven books on the subject. His most recent book, *Science in the Private Interest: Has the Lure of Profits Corrupted Biomedical Research?* published in 2003, focuses on COIs in biomedical research.

Through examples and published studies, including some of his own, Krimsky posed a series of questions, such as the following, and offered some partial answers:

- How have journals responded to COIs? One of Krimsky’s studies showed that 16% of the 1396 high-impact journals that he and his coauthor selected had COI policies in 1997.
- What types of COI policies do journals have? Journals’ COI statements to authors vary widely. They include one-sentence requests for information (for example, “The journal requests information about the authors’ professional and financial affiliations that may be perceived to have biased the presentation.”), lists of COIs that the authors must check off, and more complex statements with multiple questions.
- How well do authors comply with COI policies? In a study of 181 peer-reviewed journals with COI policies, authors of 0.5% of the articles had something to disclose. In a study of 192 writers of a total of 44 clinical guidelines, 90 of the 100 writers who responded “had financial ties to companies whose drugs were either considered or recommended in the guidelines they wrote”. However, a COI was reported in only one of the 44 guidelines written.
- Why is disclosure of COIs important? It is especially important because of the increasing financial links between for-profit corporations and the research

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community and because journals are the “gatekeepers of certified knowledge”.

Krimsky concluded his remarks by drawing an analogy between COIs in scientific publishing and the Enron affair, in which the energy giant Enron Corporation, in collusion with its accounting firm, Arthur Andersen, released false financial reports that hid serious problems. He noted that “we no longer tolerate disclosures of auditing companies that audit financial houses [but] have other financial relationships with those houses. . . . So we have to decide in the publishing arena when disclosure is enough and when prohibition is appropriate.”

SATURDAY, 30 OCTOBER

Morning Session: Evidence and Experiences of Researchers and Institutions
Moderated by Faith McLellan, North American Senior Editor, *The Lancet*, and President, Council of Science Editors

The morning began with a presentation by Cary P Gross, associate professor of internal medicine at the Yale University School of Medicine, who discussed the prevalence and seriousness of financial COIs. He said that the existence of a COI doesn't necessarily lead to bias. He did, however, describe how COI can lead to bias at each step in the bench-to-bedside process of clinical research: during study design, participant recruitment, study conduct, data analysis and interpretation, publication and dissemination, and interpretation and synthesis of evidence. He illustrated with such examples as the Celecoxib (Celebrex) Long-term Arthritis Safety Study of 2000. A paper on the study, submitted to *JAMA* with 6 months of data, indicated a lower incidence of “ulcer complications” among Celebrex users than among users of other nonsteroidal anti-inflammatory drugs. In fact, 12-month data showing a less favorable result were not made available to *JAMA* by the paper's authors, all of whom were either employees of the drug's manufacturer or paid consultants.

Lisa Bero, professor of clinical phar-



Retreat cochair Jessica Ancker and participant Anju Sharma

macy and health policy at the University of California, San Francisco, gave the next presentation, which focused on how academic institutions manage their faculties' financial disclosures. She noted that disclosure (as opposed to restrictions or bans) is the most commonly used means of dealing with COI in universities; this is not surprising, she said, given the culture of academic institutions, where “bias is considered to be conscious” and therefore manageable. Bero discussed work in which she found that studies funded by private sponsors were about five times as likely to have favorable results as studies funded by nonprivate sponsors. And these, she noted, were the results of studies in which there was disclosure! She also discussed a 1981 study that demonstrated an association between second-hand smoke and lung cancer and the tobacco-industry-funded study created to refute it. To hide the connection to the tobacco industry in the second study, not all authors were disclosed, and the disclosures that were published were misleading. Bero concluded that disclosure does not prevent bias.

Drummond Rennie, deputy editor of *JAMA* and a professor in the Department of Medicine in the Institute for Health Policy Studies, University of California, San Francisco, gave a thoughtful presenta-

tion titled “Why What We Think Works Doesn't”. He said that we need money to flow to inventors and developers of new drugs. The problem comes when that money flows from the manufacturers of the new drugs to those who *test* them by conducting trials in humans. The public must be able to trust those who test drugs to conduct the most appropriate tests and to report their results faithfully. But in this new world, because of the direct influence of money, the trust between the public, scientific journals, and clinical researchers has been repeatedly broken by monetary interests competing for the loyalty and attention of the researchers. A basic problem was exemplified by what happened when *JAMA* published, in 1990, an editorial calling some postvaccination neurologic problems “a myth”. First, a newspaper pointed out that the researcher had worked for a vaccine manufacturer, but there was no disclosure of that. The researcher then admitted that he was wrong to sign the *JAMA* forms stating that he had no such conflicts. And finally, none of those who wrote to protest his failure to disclose his financial conflicts declared any financial conflicts themselves, although almost all, when pressed, admitted to having testified on this very issue for money on numerous occasions. That episode and others show

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that we are simply unable to see our own conflicts, although we are quick to see them in others: “You have a conflict, but I don’t. I’m pure, but you’re not.” Rennie discussed a problem with disclosure: the burying of the receipt of one huge sum of money from one sponsor among pages listing relatively trivial connections. To reestablish trust, Rennie said, he has long supported the creation of an independent agency to do drug testing and supports a publicly accessible registry of all clinical trials initiated.

The final speaker of the session was C K (Tina) Gunsalus, adjunct professor and special counsel at the University of Illinois. Gunsalus presented examples of COI problems that cropped up repeatedly in university settings over a 20-year period and concluded that universities have not been and are not likely to be able to solve the problems as they present themselves in our current funding and policy environment. Unless journals take a stand, she concluded, we will not see much substantial change; the actors with the ability and the will to make changes are journal editors, ideally acting collectively.

Midmorning Session: The Experiences, Concerns, and Policies of Funders
Moderated by Catherine D DeAngelis, Editor-in-Chief, *JAMA*

After a short break, the discussion moved on to funders’ experiences, policies, and concerns. The first speaker was Rita Redberg, professor of medicine and director of Women’s Cardiovascular Services at the University of California, San Francisco, School of Medicine. As a member of the AHA Scientific Publishing Committee and chair of the AHA COI working group, Redberg discussed the AHA COI standards for research funding, scientific publishing, scientific statements, and professional education. She noted that over the last few years, the COI working group has been “working on tightening COI standards”; for example, it has “better defined what is conflict, in terms of levels of money”, and verified that COI disclosures are



Retreat cochairs Annette Flanagin and Jessica Ancker, participant Anju Sharma, and CSE president Faith McLellan

being gathered. She recalled the summer 2004 publication of the updated National Cholesterol Education Program (NCEP) guidelines—endorsed by AHA—which was followed by mass-media criticism of the NCEP’s failure to reveal the financial ties of guideline-committee members. Upon becoming aware of the situation, the AHA focused on ensuring that its COI standards—which include publishing disclosures with guidelines—were being applied and increased the amount of formal discussion about COIs.

Paul T Antony, chief medical officer of Pharmaceutical Research and Manufacturers of America (PhRMA), presented a pharmaceutical-industry perspective. He noted that pharmaceutical companies recoup research and development costs on only three of 10 medicines. He also expressed industry concerns about clinical-trial registration proposals that weakened intellectual-property protection. Antony talked about the “implied contract” between the individual and the pharmaceutical industry: In exchange for industry’s accepting regulation and sharing innovation to the extent that it is financially feasible, the pharmaceutical industry has a right to treat some infor-

mation as proprietary and to achieve a “reasonable” profit. In response to a question about bringing the PhRMA Principles on Conduct of Clinical Trials up to date, Antony said that PhRMA had revised the document in June 2004 and that future revisions could be expected.

The final speaker of the session was Joan P Schwartz, assistant director of the Office of Intramural Research at the National Institutes of Health (NIH). She indicated how COI is addressed in the NIH intramural-research program. She also presented a draft of new guidelines for preventing financial COI in human-subjects research at NIH. The draft outlined prohibited activities of scientific staff and their immediate families, such as receiving honoraria from commercial sponsors of their research, and listed guidelines for handling NIH intellectual property and royalties. She finished by outlining the NIH rules established to safeguard the objectivity of NIH-funded research.

Afternoon Session: Regulatory and Legal Concerns

Moderated by C K (Tina) Gunsalus, Adjunct Professor and Special Counsel, University of Illinois

The afternoon sessions began with three speakers discussing regulatory and legal issues. Steven Nissen, of the Section of Clinical Cardiology at the Cleveland Clinic, spoke about the Food and Drug Administration (FDA) regulation process. As a member of the FDA Cardiovascular and Renal Drug Advisory Committee, Nissen has had opportunities to compare actual trial data submitted to FDA with data reported in scientific journals. He listed some ways in which researchers have manipulated their results to report more favorable results to journals: serious adverse effects are incompletely reported, inappropriate emphasis is placed on nonprespecified subgroups, and unfavorable results are not reported. Nissen made a number of suggestions: Researchers should give editors and reviewers the study protocol and statistical analysis plan; in industry-sponsored studies, editors should demand an independent data analysis (by an academic coordinating center, for example); and editors should require commercial sponsors to place data into the public domain in 5 years. Also, Nissen said, editors should be aware that some of researchers' "real conflicts" are not financial; for example, the researcher's ego might be involved, the funder of the study may be a potential employer, or the researcher may want to please the sponsor.

James R Ferguson, partner in the law firm Mayer, Brown, Rowe & Maw, spoke about the growing use of patents in biomedical research, in particular DNA patents held by universities. Although patents can serve as an incentive for research, he recognized some people's concern that patents can impede rather than promote biomedical research by preventing use of the results of the research; several observers have noted that as universities have become more aggressive in enforcing their patents, they have also become more vulnerable to patent-infringement claims.⁴ Still, Ferguson said, "we shouldn't be quick to eliminate the patent system" without replacing it with a better one. He noted that the Federal Trade Commission and other government agencies have proposed

changes to improve the system, such as having the Patent and Trademark Office apply a higher burden of proof for granting patents or providing alternatives to litigation to those who would challenge the validity of patents.

Richard Painter, professor at the University of Illinois College of Law, began by addressing an issue raised earlier in the day: whether and, if so, under what conditions a journal has the right to sanction an author who has violated its COI policy. He noted that one approach to misconduct is to refuse to publish work by an author for some period, after which the journal editor might exercise higher scrutiny when reviewing the author's work. Painter stressed that he would not publish a notice of such action and that the less said to other people, the better, from the standpoint of reducing liability exposure in a possible action for libel or restraint of trade. The editor, however, could respond to another journal's inquiry about the author with such a comment as "we don't feel comfortable publishing that author's work". Furthermore, because truth of the matter asserted is a defense against an action for libel, Painter said that a journal should keep documentation of the author's violation and be able to prove it.

Painter then turned to the issue of insider trading. This, he said, is a potential problem for journals that either have embargo policies for journalists or send out prepublication information to a select group of subscribers. In either case, if the material is used for financial gain, the journal is exposed to charges of facilitating insider trading; therefore, Painter does not favor embargo policies. With respect to prepublication materials sent out to some subscribers, his solution, which drew an appreciative chuckle from the audience, would be to send out any of this material to the largest base possible, essentially getting the information into the public domain.

Midafternoon Session: Journal Policies and Experiences
Moderated by Annette Flanagin, Managing Senior Editor, JAMA

A session on journal policies and experiences followed. The retreat cochairs, Annette Flanagin, managing senior editor at JAMA, and Jessica Ancker, of the Mailman School of Public Health, Columbia University, began the session by presenting some data on current journal COI policies. Of 84 high-impact-factor journals they reviewed, only 28 (33%) publish COI policies in or with the instructions for authors.

After Flanagin and Ancker's presentation, editors of six scientific journals spoke about the COI policies of their journals. The speakers were Faith McLellan, senior editor of *The Lancet*; Catherine D DeAngelis, editor-in-chief of JAMA; Juan Carlos Lopez, editor of *Nature Medicine*; Katrina Kelner, deputy editor, life sciences, of *Science*; Rita Hanson, managing editor of *Environmental Health Perspectives*; and Martin Blume, editor-in-chief at the American Physical Society (APS). Most gave examples of COIs at their journals. Although a few editors, particularly Blume, noted nonfinancial COIs, the discussion centered on financial issues. Highlights of the discussion included the following:

- Most editors noted that their journals had either created or updated their COI policies in recent years. But differences in addressing COIs were notable, in part because different journals face different issues. Blume noted that APS has both the means and the time that medical journals do not have to replicate questionable results and publish corrections: "No lives are at stake."
- Journals owners differ in their attitudes toward accepting funding. For example, Lopez noted that, to fund special supplements for which no money is appropriated in the annual budget, *Nature* approaches commercial and noncommercial funders. JAMA does not.
- Another issue was access to original data. JAMA requires that at least one author without any commercial funding have full access to the data.
- Differences existed with respect to disclosure, the focus of much of the discussion. All six editors agreed that some type of disclosure was necessary,

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perhaps to inform readers and let them decide for themselves, as Lopez noted, or to act as a deterrent. Disclosure may also help to establish trustworthiness, which DeAngelis said is critical: “The heart of research lies in altruism and trust. Without that we’re doomed.” But there the policies parted ways. What was to be disclosed varied. Most of the six editors agreed that employment by a funder or stock held in a funder’s company was a COI that a researcher should disclose. But, McLellan asked, is it a COI for a researcher to own, or apply for, a patent for a product related to his or her research if the researcher’s institution requires this (as an increasing number do)? Who was to disclose COIs also varied: *The Lancet*, among others, requires reviewers, as well as authors, to disclose COIs. In addition, it was noted that editors are expected to disclose conflicts of interest or recuse themselves.

- Where should the line be drawn? Again, it depends on whom you ask. For example, during his keynote address, Krinsky had noted that in 2002, the *New England Journal of Medicine*, after 10 years of not accepting review articles and editorials from authors with financial ties to industry, began doing so from authors who earn up to \$10,000 annually in speaking and consulting fees from a company that manufactures a product written about in the article. (Editors of the journal found that it had become difficult to find experts who had no financial ties.⁵)
- Methods differed for encouraging compliance: When submitting papers to *Science*, authors must complete an online form that requires them to answer questions about COI; some other journals still require submission of a paper form with a signature. Deterrents to nondisclosure also varied: Some journals publish a retraction and an online notice if prepublication disclosure of a COI would have resulted in the article’s being rejected. Of the journals represented at the session, only *Environmental Health Perspectives* prohibits researchers guilty of willful failure to disclose COIs from publishing in its

pages; the prohibition lasts for 3 years.

- Is disclosure sufficient? Most of the editors agreed with earlier presenters in saying that, although necessary, it is not sufficient. Many examples attest to that, as the speakers demonstrated. At the very least, they said, systematic research should be performed on the effectiveness of disclosure and other methods in discouraging noncompliance; the methods could include prohibiting the publication of papers for which COIs exist. Kelner stated that the peer-review process and the replication of data might be more powerful than disclosure in validating data. And, as Rennie noted, “naming and shaming” researchers who fail to disclose can be more effective than more severe measures, which may not be warranted. Not all researchers, it was noted, fail to disclose out of bad intent; they may do so out of ignorance. (For example, guidelines may be too vague or too narrow or may lack examples; it is not always obvious what a “relevant” conflict is.) It was observed that editors have some responsibility for educating authors about COI.

SUNDAY, 31 OCTOBER

Morning Session: Policies, Experiences, and Interests of the News Media

Moderated by Annette Flanagan, Managing Senior Editor, JAMA

Sunday began with presentations by two journalists on COI issues and the media. Lindsey Tanner, a medical writer with the Associated Press who covers about a dozen journals in the Chicago area, began by speaking about the standards of integrity in the news media. Although editors want every financial tie reported, she said, not all such ties are equal—for example, earning a small one-time fee from a company differs from owning stock in a company—and the reader may find long disclosures boring. She feels that a consensus among science journal editors as to what constitutes a COI would be helpful, along with full disclosure of COIs. That information would help newspapers to decide what to publish.

Noting that “the appearance of conflict is as big as the actual thing”, Snigdha Prakash, a reporter with National Public Radio, spoke about how journalists approach and manage COIs. She noted that some COIs are obvious and others are not. In any case, “not only must [journalists] be fair and balanced; the public must believe they are.” Why does COI in scientific publication interest her? As a journalist, she said, she has the job of understanding the issues and asking tough questions. “We know that money talks”, she said. “But what is it saying? . . . If [scientific-journal editors] don’t know or try to know, how can I?”

Midmorning Session: Wrapup Session
Moderated by Drummond Rennie, Annette Flanagan, and Jennifer Ancker

The final session was devoted to refining a list of questions, generated by Flanagan and Ancker, that science editors could ask themselves when updating or creating COI policies for their journals. The resulting “consensus document” is ultimately to serve as a framework, not a prescription. It will appear in a forthcoming issue of *Science Editor* and on the CSE Web site. 

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References

1. Guidelines for dealing with faculty conflicts of commitment and conflicts of interest in research. Adopted by the Executive Council of the Association of American Medical Colleges February 22, 1990. www.aamc.org/research/dbt/coi.htm. Accessed 22 November 2004.
2. Editorial policy statements approved by the Council of Science Editors board of directors. www.councilofscienceeditors.org. Accessed 23 November 2004.
3. World Association of Medical Editors recommendations on publication ethics policies for medical journals. www.wame.org/pubethicrecom.htm#conflicts. Accessed 22 November 2004.
4. Eisenberg RS. Patent swords and shields. *Science* 2003;299:1018-9.
5. Drazen JM, Curfman GD. Financial associations of authors. *N Engl J Med* 2002;346:1901-2.