Ethical Standards for Healthcare Journal Editors: A Case Report and Recommendations

Donald W. Light, PhD and Rebecca N. Warburton, PhD

Unfair and biased editing is not new. Over many decades, authors have occasionally suffered from prejudice, favoritism, negligence, deception, and other editorial offenses. We know that most editors do outstanding work under difficult, conflict-ridden conditions inherent in their role. We, like all researchers, have been the beneficiaries of excellent, helpful, honest, and fair editing and review many times. Counterexamples rarely come to light for three reasons. First, few authors dare speak out against editors; editors can use their position and status to influence future efforts to publish. Second, the alleged offenses are usually poorly documented, because so much editing occurs behind the scenes. This is why a recent article about editorial bias called for publishing earlier versions of articles in manuscript, together with reviewers' and editors' comments.[1] Finally, editors have near absolute power and can do what they like, in part because most journal boards do not provide oversight or an appeal process.

Ethical Standards for Editing

While authors have occasionally suffered at the hands of editors, editors have themselves suffered increasingly at the hands of hired ghost-writers, fronted by academic "authors" paid for their cooperation, notably by the pharmaceutical industry.[2] The development of good editorial standards has been driven by revelations of pharmaceutical industry influence, including suppression of negative findings, falsification of data, and control of analysis and conclusions. Commercial influence has become so pervasive that Richard Horton, editor of the Lancet (and a leader in setting standards to defend the integrity of science and its journals), bemoaned, "Journals have devolved into information laundering operations for the pharmaceutical industry."[3] Marcia Angell, past editor of the New England Journal of Medicine, decries the evolution of the pharmaceutical companies from science-based innovators to primarily marketing machines that co-opt any institution that might stand in their way.[4]

Dr. Donald W. Light is a Fellow at the Center for Bioethics at the University of Pennsylvania and Professor of Comparative Health Systems and Policy in the Division of Social & Behavioral Medicine at the University of Medicine & Dentistry of New Jersey. Dr. Rebecca N. Warburton is an Associate Professor and Health Economist as well as a Michael Smith Foundation for Health Research Scholar, School of Public Administration.

In response, the editors of leading journals have formed international bodies to set standards for editorial conduct. With each revision, these standards have been broadened and strengthened, and now include guidelines for editors that go well beyond the handling of authors and reviewers.

The International Committee of Medical Journal Editors (ICMJE) is a small working group of general medical journal editors who have met regularly since 1978 to develop widely used guidelines for researchers and editors.[5] From time to time ICMJE members have written influential joint editorials on threats to the integrity of research and journals.[6] According to the ICMJE:

> Public trust in the peer review process and the credibility of published articles depend in part on how well conflict of interest is handled during writing, peer review, and editorial decision making… Conflicts exist when an author (or an author's institution), reviewer, or editor has financial or personal relationships with other persons or organizations that inappropriately influence (bias) his or her actions… The potential for conflict of interest can exist whether or not an individual believes that the relationship affects her or her scientific judgment…[7]

The Council of Science Editors (CSE) states that editors "are responsible for ensuring that the content of their publications is of high quality: accurate, valid, reliable, credible, authoritative…", and "[e]ditors must treat all submitted material fairly, consistently, and in a timely manner, avoiding bias, conflict of interest, and external pressure in making editorial decisions."[8] In addition, editors should:

- Treat authors with fairness, courtesy, objectivity, and honesty.
- Render timely decisions and responses.
- Protect the privileged nature of every author's work, keeping it confidential while under review.
- Require authors, editors, and reviewers to provide full disclosure of all potential financial and nonfinancial conflicts of interest and causes of bias.

The World Association of Medical Editors (WAME) has a mission to help train editors in developing countries and at small journals, and more than 1400 editors representing 890 journals from ninety countries are members. A major theme is transparency, of the editorial process as well as of the research and authorial process. WAME emphasizes "publishing corrections, retractions, and critiques of published articles," and calls for authors to disclose sources of financial support including any financial relationship or affiliation with organizations that might have a vested interest in the conduct or results of the research."[9]

Finally, the Committee on Publication Ethics (COPE) "supports and encourages editors to report, catalogue and instigate investigations into ethical problems in the publication process."[10] COPE provides a unique resource for member journals, an independent, nonbinding review in case of disputes. COPE urges journals to publish a de-

scription of their review and appeal processes, and to publish corrections, retractions, apologies, and critical responses to published material. A recent review called for all journals to join COPE to level the playing field for authors.[11]

This body of work has clarified the nature of good conduct, and ended any justification for contrary behavior by journal editors. "I was that wicked editor," admitted Richard Smith, one of the editors who played a central role in establishing ethical standards for editing and helped to form COPE. An author had filed a complaint against him for going back on a promise to publish a paper. Smith had his reasons, but agreed to live by the criteria he had helped create, and published the paper. This may be the first example of self-regulation by a journal editor.[12]

In recent years, more and more journals are refusing to consider papers based on data to which journals and reviewers do not have access, as a fundamental check on quality and bias. This requirement is not yet included in the above standards.

An Exceptional Case?

The Journal of Health Economics (JHE) is read worldwide and has high citation impact factors in both Economics and Health Policy and Services.[13] The journal publishes on a wide range of topics, including pharmaceuticals, and some papers have been influential, especially a 1991 article that set a new high for the estimated cost of research and development (R&D) for new drugs.[14] The JHE editors likely knew that this would be a much-cited paper, and placed it as the lead article. The many citations of the 1991 JHE paper in turn contributed to the journal's citation impact rating.

The authors of the 1991 paper used confidential cost data submitted to the industry supported Tufts Center for the Study of Drug Development (CSDD) to estimate the expected average R&D costs for new drugs. The authors included costs, in 1987 dollars, for investments in drugs that fail as well as those that succeed, and then added the cost of capital at 9% annually (because R&D precedes sales). These adjustments increased the average $11 million cost per drug to an average capitalized cost of $231 million for each newly-approved drug–more than four times the highest previous estimate.[15] This JHE article was quickly publicized worldwide by the industry's trade association, and used to support claims that high drug prices and long patent protection are necessary to pay for the R&D that creates new drugs.

Our analysis of this article led us to question its validity for a number of reasons. As a health economist and an economic sociologist concerned about the role of high prices in limiting access to medicines and making them unaffordable to millions worldwide, we began in 2002 to prepare a critique of the paper. Then, in 2003, an update was published in the JHE, raising the estimated cost of a new drug from $231 million to $802 million, in 2000 dollars.[16] The press release issued by the Center reported that it "stunned many experts on the industry."[17,18]

We amended our work to address this new paper, and submitted it to JHE. The Journal has five editors, three of whom are at Harvard University and work closely as a team on American

submissions: Dr. Joseph Newhouse, the John D. McArthur Professor of Health Policy and Management, Dr. Thomas McGuire, professor of Health Economics, and Dr. Richard Frank, the Margaret T. Morris Professor of Health Economics. McGuire, the editor who had handled the review, acceptance, and editing of the 2003 DiMasi et al. paper, was assigned to our critique–contradicting the spirit of guidelines on editorial impartiality laid down by all four international organizations concerned about the ethics of editing.

In our critique (as submitted to JHE on February 10, 2004), we made five points about the data and methods of the DiMasi et al. paper, and then discussed issues of potential conflict of interest due to industry funding. The content of this first draft is summarized below to allow readers to make sense of subsequent events.

First, we stated that the comparability and reliability of the cost data had to be questioned because cost allocation methods vary over time and across companies, and because the use of confidential data allowed no independent verification. In addition, there was wide variation between the costs for the different unnamed drugs, rendering a point estimate (the $802 million) uninformative.

Second, we noted that the study was based on data from a small, nonrandom sample of only ten pharmaceutical companies; it was not clear which firms had been invited to participate or why half of those invited had declined. The authors' claim that they had used a "random sample" of new chemical entities (NCEs) was misleading, because the companies providing the data were self-selected.

Third, we highlighted the fact that the authors' study used only NCEs discovered and developed entirely in-house. These drugs are a small subset (8-13% [19, 20]) of all newly approved drug products, many of which are either developed elsewhere and licensed-in, or simply reformulate existing compounds, change dosages, or add timed release. The authors had explained earlier that R&D costs of in-house NCEs are much higher than for other drug products, hence the 1991 and 2003 published cost estimates were higher than the average for all newly approved drug products.[21]

Fourth, we pointed out that the $802 million estimate did not take into account government subsidies or support for industry research from the National Institutes of Health.

Finally, we noted that the estimate was not adjusted for tax deductions and credits, estimated by the U.S. Office of Technology Assessment to offset nearly 50% of R&D spending.[22]

Our short critique closed with a discussion of competing interests. Journals owe their readers full disclosure of financial interests.[23] The authors had stated that they "…did not receive any external funding to conduct this study," yet the web site of the Tufts CSDD explains clearly that pharmaceutical and biopharmaceutical companies are major funders of the organization.[24] While most are "unrestricted grants", the only way to get more is to please those who pay. We also cited published evidence that funding affects research results. [25, 26]

Act One: Commercial Influence Deleted

On March 2, 2004 we received a letter from McGuire, stating that "Your commentary makes some good points and deserves to be published. It is thoughtful, concise and well-written. Thank you for preparing it and sending it to JHE." He then asked, however, for "major modifications" to the passages quoted above concerning the funding of the Tufts Center; guidelines that called for funding to be disclosed to readers; the fact that this funding had not been disclosed when the DiMasi et al. paper was published in JHE; and the research evidence that funding biases results. We protested that the question of commercial influence was central to both the unverified industry data and the methods. We provided evidence that the paper's authors had helped found the Center with pharmaceutical company support, and that three of them had been doing research widely cited to support industry interests since the mid-1970s.[27-32] McGuire replied in a second letter on Harvard Medical School stationary that "I will not accept a paper that includes what I regard as unfair claims about the motives of the DHG authors. Joe Newhouse, Richard Frank and I are of one mind about this." We replied that we had made no claims about the authors' motives, but had cited research substantiating the influence of funding on results.[33, 34] The editors would not budge or explain.

Next, McGuire wrote and asked us to "correct" passages which DiMasi considered erroneous, revealing that, without telling us ahead of time, he had sent our draft critique to DiMasi. The editor was relying on the original author as his expert adviser, yet some of the "errors" had been fully documented and in fact appeared at the Tufts Center web site. We wrote back to re-assert that these were not errors, but were told we had to "correct" them anyway if our submission was to proceed.

Act Two: Protecting the Authors

By the end of April 2004, our critique was accepted by JHE editors, and went to the authors for their reply. Five months later, on September 29, 2004, McGuire sent us the authors' reply. It was nearly double the length of our commentary and went well beyond it, introducing new material on new topics, new unpublished sources allegedly supporting the authors' original data and conclusions, rhetorical repetitions, several statements we believed were misrepresentations or errors concerning our critique, as well as personal attacks on our professionalism and competence. The editors accepted this "reply," and McGuire wrote that no further response from us "would be necessary or desirable." If we felt it was, he stated that "the bar is being set very high" for any rejoinder, and he gave us two weeks to do it.

The bias in favor of the authors was striking, no tight focus on the issues for them versus addressing only "errors" for us; little editing of their rhetoric, redundancy, new materials, or ad hominem remarks, versus major cuts and a high bar for us; prohibiting us to even comment on their new material aside from errors; and twenty weeks of leisurely time for them versus two weeks for us at one of the busiest times of the academic year.

We worked overtime to send back a brief rejoinder that challenged only the

errors and misleading statements we had found in the authors' reply, chiefly concerning data validity, the potential for financial support to influence research results, the nonrandom nature of the drugs sampled (because companies were self-selected), the proper handling of R&D related tax savings and government funding of research, and our competence in understanding the original paper.

The editors prohibited us from addressing problems with the extensive new points and materials that the authors had been allowed to include in their expansive reply. Moreover, McGuire sent back our short rejoinder, having deleted the following:

1) our asking who funded the big landmark study we were critiquing,
2) our statement that DiMasi was Director of Economic Analysis at the Center (his exact title on its website),
3) our explanation of why R&D tax savings were real, not illusory (as the authors claimed),
4) our documentation of industry influence on the OTA's review of the authors' research, which they cited repeatedly as independent validation of their work.[35]

We protested against these extensive deletions, but McGuire replied in an email on November 10th that we could choose "to basically accept my chops on your rejoinder and get it published soon in the jhe" or take our critique elsewhere. We sent a detailed email of protest and spent the day agonizing over yet another example of ultimatum editing. McGuire replied, in part, that "…it is time to end the back and forth between you two and me (even if productive) so as not to delay publication…" We thus decided to accept (under protest) these deletions so that what remained of the critique could be published.

Then, a reversal occurred. The editors sent the three-part set off to Elsevier in Ireland for copy editing for the next issue. After that, page proofs were sent, (December 2004) but we were not shown the authors' reply, leaving us concerned that the editors might have allowed them to make revisions. Then suddenly on January 6, 2005, McGuire wrote that the editors were pulling the entire set out of production, giving no reason.

Act Three: Eviscerating the Rejoinder

After more than two months of silence, McGuire (in March 3, 2005) wrote a letter on Harvard stationary on behalf of himself, Newhouse and Frank, demanding massive cuts marked by large Xs that crossed out 100 of 132 lines in our rejoinder, in order "to have the package make sense for the reader and be fair to both sets of authors." We protested but once again the editors did not budge. Under threat of losing a year of work with the editors (and over a year preparing the initial comment), we reluctantly accepted.

Act Four: A Strike for Academic Freedom?

While deciding what to do, we had searched frantically for some avenue of recourse or appeal. We called the American Association of University Professors (AAUP) and the Canadian Association

of University Teachers (CAUT), and learned that neither could offer practical support; academic freedom is essentially a noble idea with little or no legal standing. We called eminent editors who reaffirmed that we were powerless. When it comes to free speech, editors apparently have total and unaccountable power to deny it. We also consulted colleagues at the Center for Bioethics at the University of Pennsylvania, and called a few lawyers recommended to us. Nice conversations but no progress, until we called Alan Milstein.[36]

A litigator nationally known for his creative and aggressive style, Milstein thought that academic freedom was critical to higher education and a free society. He found in the emails between us and McGuire the terms of a contract – "accept my chops…and get it published in the jhe." JHE's subsequent withholding of publication and deletions of the finalized text violated that contract. This, Milstein concluded, provided a rare chance to litigate on behalf of academic freedom and challenge academic censorship. He thought the case was clear and winnable, but how to pay for it? There were no substantial financial damages which might pay for trying the case, and we could not bear the costs of litigation. Milstein then made an extraordinary offer: "This is an important case. I'll pay for it myself."

Heartened, we wrote the three editors at Harvard on Thursday, March 17th that we were rescinding our consent, stating that their cuts were "unacceptable violations of our academic freedom…" McGuire replied, "This is a poor decision on your part."

Milstein acted with remarkable speed, drafting a full legal complaint by the next day. We sent back clarifications on Friday, he worked all weekend, and by Monday he had a finished complaint alleging multiple breaches of contract and violations of academic freedom by the editors personally, the Journal, its Editorial Board, and Elsevier. He did not expect much in monetary damages, but expected to win before a jury, revealing to the world how leading economists handled an independent critique of a key article concerning the high costs of drug development from an industry sponsored research center.

While we thought a landmark federal case for academic freedom would be invaluable, we also worried (and friends warned) that it would consume at least two years of our lives and should be avoided if possible. We identified members of JHE's Editorial Board who we respected, and sought their advice. We then approached Tony Culyer, one of the five senior editors of JHE and a prominent non-American economist, requesting that he take on an ombudsman-like role, and he agreed. He saw merit in our rejoinder, but thought it could be more succinct. In regard to the original article having been published despite being based on proprietary data, he emailed on March 24th "that JHE is at fault (I am a party to this) in not barring material that is not independently verifiable…"

We called McGuire and let him know that a prominent trial lawyer was ready to litigate in federal court. He seemed stunned, said he was sure something could be worked out, and would talk it over with Newhouse and Frank. The next week McGuire sent a letter on Harvard stationary to make "an attempt to get the publication of your comment and rejoinder back on track." The editors asked for changes to our com-

mentary (saying we were accusing the authors of bias) and proposed sending it back to the authors to "go through a similar process with them." This amounted to starting the commentary-reply-rejoinder process all over again! We decided that if we accepted this proposition, it would effectively replace the earlier "contract" and could well destroy the legal basis for the lawsuit. We therefore refused but kept working with Culyer on the rejoinder.

In early April, we sent Culyer a revision that he thought was "much better." We then sent our comment and revised rejoinder to JHE editors, with the offer either to publish this new set, or the original three-part set from December; otherwise we would go to court. McGuire's reply on behalf of the editors indicated that, unbeknownst to us, the editors had asked the authors of the original paper whether they would like to make any changes in their original reply. After asking repeatedly to see the revised reply, we were finally sent it, and we saw that the changes were minor and did not require changes to our rejoinder. The set was, we thought, complete.

Act Five: Covert Action

The three-part set went forward in the usual way, copy editing then page proofs, though again we were only sent our pieces, not the authors' reply, until we asked for it. We turned to other work until the issue appeared on the web (July 2005) in advance of the print edition being available. There we discovered that the set now included a fourth piece, an answer to our rejoinders before, the editors had allowed the other authors greater length and latitude for their wide-ranging, sharply-worded, and, in our view, misleading "last word" response.[37-40] The editors had not notified us in any way and have never provided any explanation.

Recommendations

The editors of JHE violated, in our opinion, almost every ethical standard established for editors. Yet they remain accountable to no one. Richard Smith,[38] in his insightful book on the ethics of medical journals, writes that "Some say that editors are as unaccountable as kings," but he thinks they are more so. How exceptional is this case, or the various parts of it, such as heavy editing or deletions with little or no explanation? How many other authors have suffered from similar editorial practices? How often are editorial boards or publishers informed or involved? Smith, in his chapter on editorial misconduct, provides examples that are worse than our case.

Our recommendations:

- ICMJE, CSE, COPE, and WAME should require authors to make their data available to reviewers and readers, as a check on data quality and validity.
- Journal publishers and owners should protect the integrity of their journals by requiring all of them to join COPE. The traditional hands off stance of publishers and academic societies towards the editors of journals they own is absolutely right, except when it comes to the ethics of editorial conduct. To date, Blackwell's and BMJ Publications have signed up their journals. Why not Elsevier (JHE's publisher), Kluwer, Wiley or Springer-Verlag?
- Academic researchers should urge

their professional associations (AAUP, CAUT, etc.) to formally request publishers of journals to join COPE and adopt the COPE and WAME standards.

- Finally, journal publishers and owners (particularly academic research associations that publish journals) should create an ombudsman function, as The Lancet has. An ombudsman could make many contributions to the journal, the editors, and to the field. 

References

1. Lexchin J, Light DW. Commercial influence and the content of medical journals. BMJ. 2006;332:1444-1447.
2. Smith R. The Trouble with Medical Journals. London: Royal Society of Medicine Press; 2006.
3. Horton R. The dawn of McScience. New York Review of Books. 2004;51(4):7-9.
4. Angell M. The Truth About the Drug Companies: how they deceive us and what to do about it. New York: Random House; 2004.
5. International Committee of Medical Journal Editors. Uniform Requirements for manuscripts Submitted to Biomedical Journals. www.icme.org Accessed 15 Sept, 2006.
6. DeAngelis CD, Drazen JM, Frizelle FA, Haug C, al. e. Clinical trial registration: a statement from the International Committee of Medical Journal Editors. Canadian Medical Association Journal. 2004;171(6):606-607.
7. Davidoff F, DeAngelis CD, Drazen JM, Hoey J, al. e. Sponsorship, authorship and accountability. Journal of American Medical Association. 2001;286:1232-1234.
8. Council of Science Editors. Editorial Policy Statements Approved by the CSE Board of Directors. www.councilscienceeditors.org Accessed 15 Sept., 2006.
9. World Association of Medical Editors. WAME Policy Statements www.wame.org Accessed 15 Sept, 2006.
10. Committee on Publication Ethics. A code of conduct for editors of biomedical journals www.publicationethics.org.uk/guidelines Accessed 15 Sept, 2006.
11. Lexchin J, Light DW. Commercial influence and the content of medical journals. BMJ. 2006;332:1444-1447.
12. Godlee F. Dealing with editorial misconduct. BMJ. 2004;329:1301-1302.
13. Thomson Scientific. Journal Citation Reports: Social Science Edition for 2004 and 2005: Thomson Scientific; 2006.
14. DiMasi JA, Hansen RW, Grabowski HG, Lasagna L. Cost of innovation in the pharmaceutical industry. Journal Of Health Economics. 1991;10:107-142.
15. Hansen RW. The pharmaceutical development process: estimates of current development costs and times and the effects of regulatory changes. In: Chien RI, ed. Issues in Pharmaceutical Economics. Lexington, MA: Lexington Books; 1980:151-187.
16. DiMasi JA, Hansen RW, Grabowski H. The price of innovation: new estimates of drug development costs. Journal Of Health Economics. 2003;16:151-185.
17. The ballooning price tag. Tufts e-news; 2001:1-2.
18. Love J. IRS Data Shows Drug Industry Cost Estimates Exaggerated. IP-health [http://lists.essential.org/pipermail/ip-health/2001-November/00248
19. Hunt MI. Prescription Drug Costs: Federal Regulation of the Industry. Washington, DC: The Blue Cross Blue Shield Association; Sept 2000 2000.
20. Prescrire International. A review of new drugs and indications in 2002: Financial speculation or better patient care? Prescrire International. 2003;12(64):74-77.
21. Thomson Scientific. Journal Citation Reports: Social Science Edition for 2004 and 2005: Thomson Scientific; 2006.
22. U.S. Office of Technology Assessment. Pharmaceutical R&D: Costs, Risks and Rewards. Washington DC: OTA; 1993.

NTIS #PB93-163376.
23. International Committee of Medical Journal Editors. Uniform Requirements for manuscripts Submitted to Biomedical Journals. www.icme.org Accessed 15 Sept, 2006.
24. Tufts Center for the Study of Drug Development. About Tufts CSDD Financial Disclosure. http://csdd.tufts.edu/About/FinancialDisclosure.asp. Accessed 14 October, 2007.
25. Bekelman JE, Li Y, Gross CP. Scope and impact of financial conflicts of interest in biomedical research: a systematic review. Journal of the American Medical Association. 2003;289:454-465.
26. Lexchin J, Bero LA, Djulbegovic B, Clark O. Pharmaceutical industry sponsorship and research outcome and quality: systematic review. BMJ. 2003;326:1167-1170.
27. Hansen RW. The pharmaceutical development process: estimates of current development costs and times and the effects of regulatory changes. In: Chien RI, ed. Issues in Pharmaceutical Economics. Lexington, MA: Lexington Books; 1980:151-187.
28. Wardell WM, ed. Controlling the Use of Therapeutic Drugs: An International Comparison. Washington DC: American Enterprise Institute 1978.
29. Wardell WM, Lasagna L, eds. Regulation and Drug Development Washington DC: American Enterprise Institute; 1975.
30. Helms RB, ed. Drug Development and Marketing. Washington D.C.: American Enterprise Institute; 1975.
31. Grabowski H, ed. Drug Regulation and Innovation: Empirical Evidence and Policy Options. Washington DC: American Enterprise Institute; 1976.
32. Grabowski H, ed. Drug Regulation and Innovation: Empirical Evidence and Policy Options. Washington DC: American Enterprise Institute; 1976.
33. Bekelman JE, Li Y, Gross CP. Scope and impact of financial conflicts of interest in biomedical research: a systematic review. Journal of the American Medical Association. 2003;289:454-465.
34. Lexchin J, Bero LA, Djulbegovic B, Clark O. Pharmaceutical industry sponsorship and research outcome and quality: systematic review. BMJ. 2003;326:1167-1170.
35. U.S. Office of Technology Assessment. Pharmaceutical R&D: Costs, Risks and Rewards. Washington DC: OTA; 1993. NTIS #PB93-163376.
36. Sherman, Silverstein, Kohl, Rose & Podolsky, corporate web site, http://www.sskrplaw.com/attorneys/milstein/, accessed 10 May 2008.
37. Light DW, Warburton RN. Extraordinary claims require extraordinary evidence. Journal of Health Economics. 2005;24:1030-1033.
38. DiMasi JA, Hansen RW, Grabowski HG. Reply: extraordinary claims require extraordinary evidence. Journal of Health Economics. 2005;24:1034-1044.
39. Light DW, Warburton RN. Setting the record straight in the reply by DiMasi, Hansen and Grabowski. Journal Of Health Economics. 2005;24:1045-1048.
40. DiMasi JA, Hansen RW, Grabowski H. Setting the record straight to setting the record straight: response to the Light and Warburton rejoinder. Journal Of Health Economics. 2005;24:1040-1053.
41. Smith R. The Trouble with Medical Journals. London: Royal Society of Medicine Press; 2006.