

## Sponsorship, authorship and accountability

Frank Davidoff, Catherine D. DeAngelis, Jeffrey M. Drazen, M. Gary Nicholls, John Hoey, Liselotte Højgaard, Richard Horton, Sheldon Kotzin, Magne Nylenna, A. John P.M. Overbeke, Harold C. Sox, Martin B. Van Der Weyden, Michael S. Wilkes

As editors of general medical journals, we recognize that the publication of clinical-research findings in respected peer-reviewed journals is the ultimate basis for most treatment decisions. Public discourse about this published evidence of efficacy and safety rests on the assumption that clinical-trials data have been gathered and are presented in an objective and dispassionate manner. This discourse is vital to the scientific practice of medicine because it shapes treatment decisions made by physicians, and drives public and private health care policy. We are concerned that the current intellectual environment in which some clinical research is conceived, study subjects are recruited, and data are analyzed and reported (or not reported) may threaten this precious objectivity.

Clinical trials are powerful tools; like all powerful tools, they must be used with care. They allow investigators to test biologic hypotheses in living patients, and they have the potential to change the standards of care. The secondary economic impact of such changes can be substantial. Well-done trials, published in high-profile journals, may be used to market drugs and medical devices, potentially resulting in substantial financial gain for the sponsor. But powerful tools must be used carefully. Patients participate in clinical trials largely for altruistic reasons—that is, to advance the standard of care. In the light of that truth, the use of clinical trials primarily for marketing, in our view, makes a mockery of clinical investigation and is a misuse of a powerful tool.

Until recently, academic, independent clinical investigators were key players in design, patient recruitment and data interpretation in clinical trials. The intellectual and working home of these investigators, the academic medical centre, has been at the hub of this enterprise, and many institutions have developed complex infrastructures devoted to the design and conduct of clinical trials.<sup>1,2</sup> The academic enterprise has been a critical part of the process that led to the introduction of many new treatments into medical practice and contributed to the quality, intellectual rigor and impact of such clinical trials. But, as economic pressures mount, this may be a thing of the past.

Many clinical trials are performed to facilitate regulatory approval of a device or drug rather than to test a specific novel scientific hypothesis. As trials have become more sophisticated and the margin of untreated disease harder to reach, there has been a great increase in the size of the trials and consequently in the costs of developing new drugs.

It is estimated that the average cost of bringing a new drug to market in the United States is about \$500 million.<sup>3</sup> The pharmaceutical industry has recognized the need to control costs and has discovered that private, nonacademic research groups (i.e., contract research organizations [CROs]) can do the job for less money and with fewer hassles than academic investigators. Over the past few years CROs have received the lion's share of clinical-trial revenues. For example, in 2000 in the United States, CROs received 60% of the research grants from pharmaceutical companies, as compared with only 40% for academic trialists.<sup>1</sup>

As CROs and academic medical centres compete head to head for the opportunity to enroll patients in clinical trials, corporate sponsors have been able to dictate the terms of participation in the trial, terms that are not always in the best interests of academic investigators, the study participants or the advancement of science generally.<sup>4</sup> Investigators may have little or no input into trial design, no access to the raw data, and limited participation in data interpretation. These terms are draconian for self-respecting scientists, but many have accepted them because they know that if they do not, the sponsor will find someone else who will. And, unfortunately, even when an investigator has had substantial input into trial design and data interpretation, the results of the finished trial may be buried rather than published if they are unfavourable to the sponsor's product. Such issues are not theoretical. There have been a number of recent public examples of such problems, and we suspect that many more go unreported.<sup>5,6</sup>

As editors, we strongly oppose contractual agreements that deny investigators the right to examine the data independently or to submit a manuscript for publication without first obtaining the consent of the sponsor. Such arrangements not only erode the fabric of intellectual inquiry that has fostered so much high-quality clinical research, but also make medical journals party to potential misrepresentation, since the published manuscript may not reveal the extent to which the authors were powerless to control the conduct of a study that bears their names. Because of our concern, we have recently revised and strengthened the section on publication ethics in the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication," a document developed by the International Committee of Medical Journal Editors (ICMJE) and widely used by individual journals as the basis for editorial

policy. The revised section follows this commentary. (The entire "Uniform Requirements" document is currently undergoing revision; the revised version should be available at the beginning of 2002.) As part of the reporting requirements, we will routinely require authors to disclose details of their own and the sponsor's role in the study. Many of us will ask the responsible author to sign a statement indicating that he or she accepts full responsibility for the conduct of the trial, had access to the data and controlled the decision to publish.

We believe that a sponsor should have the right to review a manuscript for a defined period (e.g., 30 to 60 days) before publication to allow for the filing of additional patent protection, if required. When the sponsor employs some of the authors, these authors' contributions and perspective should be reflected in the final paper as are those of the other authors, but the sponsor must impose no impediment, direct or indirect, on the publication of the study's full results, including data perceived to be detrimental to the product. Although we most commonly associate this behaviour with pharmaceutical sponsors, research sponsored by governmental or other agencies may also fall victim to this form of censorship, especially if the results of such studies appear to contradict current policy.

Authorship means both accountability and independence. A submitted manuscript is the intellectual property of its authors, not the study sponsor. We will not review or publish articles based on studies that are conducted under conditions that allow the sponsor to have sole control of the data or to withhold publication. We encourage investigators to use the revised ICMJE requirements on publication ethics to guide the negotiation of research contracts. Those contracts should give the researchers a substantial say in trial design, access to the raw data, responsibility for data analysis and interpretation, and the right to publish — the hallmarks of scholarly independence and, ultimately, academic freedom. By enforcing adherence to these revised requirements, we can as editors assure our readers that the authors of an article have had a meaningful and truly independent role in the study that bears their names. The authors can then stand behind the published results, and so can we.

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The authors are members of the International Committee of Medical Journal Editors. Dr. Davidoff is Editor Emeritus, *Annals of Internal Medicine*; Dr. DeAngelis is Editor, *Journal of the American Medical Association*; Dr. Drazen is Editor-in-Chief, *New England Journal of Medicine*; Dr. Nicholls is Editor, *New Zealand Medical Journal*; Dr. Hoey is Editor, *Canadian Medical Association Journal*; Dr. Højgaard is Editor-in-Chief, *Ugeskrift for Læger* (Journal of the Danish Medical Association); Dr. Horton is Editor, *The Lancet*; Dr. Kotzin is Executive Editor, MEDLINE/Index Medicus; Dr. Nylenna is Editor-in-Chief, *Tidsskrift for Den norske lægeforening* (Journal of the Norwegian Medical Association); Dr. Overbeke is Executive Editor, *Nederlands Tijdschrift voor Geneeskunde* (Dutch Journal of Medicine); Dr. Sox is Editor, *Annals of Internal Medicine*; Dr. Van Der Weyden is Editor, *Medical Journal of Australia*; and Dr. Wilkes is Editor, *wjm western journal of medicine*.

**Competing interests:** None declared for Drs. Davidoff, DeAngelis, Nicholls, Hoey, Højgaard, Horton, Kotzin, Nylenna, Overbeke, Sox, Van Der Weyden or Wilkes. Before July 2000, Dr. Drazen received speaker fees from Merck Frosst and consultancy fees from Merck Frosst, Immunex and Roche Bioscience, and was a member of the scientific advisory boards of Aerocrine, Aradigm, Entelos, Inspire Pharma-

ceuticals and Lifemasters; he currently has no arrangements with any commercial entity in the health care sector other than his current employer, the Massachusetts Medical Society.

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**Correspondence to:** Dr. John Hoey, CMAJ, 1867 Alta Vista Dr., Ottawa ON K1G 3Y6; fax 613 565-5471; john.hoey@cma.ca

*The section on publication ethics from the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication" was adopted as policy on May 11, 2001, and follows below. The full revised "Uniform Requirements" will be published later.*

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