

**Uniform Requirements
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About the ICMJE**URM Journals List****Sponsorship, Authorship, and
Accountability**

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 participants are recruited, and the data 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 center, has been at the hub of this enterprise, and many institutions have developed complex infrastructures devoted to the design and conduct of clinical trials (1, 2). 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 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 (3). The pharmaceutical industry has recognized the need to control costs and has discovered that private nonacademic research groups--that is, 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 (1).

As CROs and academic medical centers 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 (4). 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 unfavorable 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 (5, 6).

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 editorial. (The entire "Uniform Requirements" document is 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 (for example, 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 behavior with pharmaceutical sponsors, research sponsored by government 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 section on publication ethics from the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication" follows below. The full revised "Uniform Requirements" will be published later.

Conflict of Interest

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. Conflict of interest exists when an author (or the 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 of such relationships to create bias varies from negligible to extremely great; the existence of such relationships does not necessarily represent true conflict of interest, therefore. (Relationships that do not bias judgment are sometimes known as dual commitments, competing interests, or competing loyalties.) The potential for conflict of interest can exist whether or not an individual believes that the relationship affects his or her scientific judgment. Financial relationships (such as employment, consultancies, stock ownership, honoraria, paid expert testimony) are the most easily identifiable conflicts of interest and the most likely to undermine the credibility of the journal, the authors, and science itself. Conflicts can occur for other reasons, however, such as personal and family relationships, academic competition, and intellectual passion

All participants in the peer review and publication process must disclose all relationships that could be viewed as presenting a potential conflict of interest. Disclosure of these relationships is particularly important in connection

with editorials and review articles, because bias can be more difficult to detect in those publications than in reports of original research. Editors may use information disclosed in conflict of interest and financial interest statements as a basis for editorial decisions. Editors should publish this information if they believe it will be important to readers in judging the manuscript.

Potential Conflicts of Interest Related to Individual Authors' Commitments

When authors submit a manuscript, whether an article or a letter, they are responsible for disclosing all financial and personal relationships between themselves and others that might bias their work. To prevent ambiguity, authors must state explicitly whether potential conflicts do or do not exist. Authors should do so in the manuscript on a conflict of interest notification page that follows the title page, providing additional detail, if necessary, in the accompanying cover letter. Investigators should disclose potential conflicts to study participants, and should state in the manuscript whether they have done so.

Editors also need to decide when to publish information disclosed by authors about potential conflicts. If doubt exists, it is best to err on the side of publication.

Potential Conflicts of Interest Related to Project Support

Increasingly, biomedical studies receive funding from commercial firms, private foundations, and government. The conditions of this funding have the potential to bias and otherwise discredit the research.

Scientists have an ethical obligation to submit credible research results for publication. As the persons directly responsible for their work, researchers therefore should not enter into agreements that interfere with their access to the data or their ability to analyze the data independently, to prepare manuscripts, and to publish them. Authors should describe the role of the study sponsor(s), if any, in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the report for publication. If the supporting source had no such involvement, the authors should so state. Biases potentially introduced when sponsors are directly involved in research are analogous to methodological biases of other sorts; some journals therefore choose to include information about the sponsor's involvement in the methods section of the published paper.

If a study is funded by an agency with a proprietary or financial interest in the outcome, editors may ask authors

to sign a statement such as, "I had full access to all of the data in this study and I take complete responsibility for the integrity of the data and the accuracy of the data analysis." Editors should be encouraged to review copies of the protocol and/or contracts associated with project-specific studies before accepting such studies for publication. Editors may choose not to consider an article if a sponsor has asserted control over the authors' right to publish.

Conflicts of Interest Related to Commitments of Editors, Journal Staff, or Reviewers

Editors should avoid selecting external peer reviewers with obvious potential conflicts of interest, for example, those who work in the same department or institution as any of the authors. Authors often provide editors with the names of persons they feel should not be asked to review a manuscript because of potential conflicts of interest, usually professional. When possible, authors should be asked to explain or justify their concerns; that information is important to editors in deciding whether to honor such requests.

Reviewers must disclose to editors any conflicts of interest that could bias their opinions of the manuscript, and they should disqualify themselves from reviewing specific manuscripts if they believe such disqualification would be appropriate. As in the case of authors, silence on the part of reviewers concerning potential conflicts may mean either that such conflicts exist that they have failed to disclose, or that conflicts do not exist. Reviewers must therefore also be asked to state explicitly whether conflicts do or do not exist. Reviewers must not use knowledge of the work, before its publication, to further their own interests.

Editors who make final decisions about manuscripts must have no personal, professional, or financial involvement in any of the issues they might judge. Other members of the editorial staff, if they participate in editorial decisions, must provide editors with a current description of their financial interests (as they might relate to editorial judgments) and disqualify themselves from any decisions where they have a conflict of interest. Editorial staff must not use the information gained through working with manuscripts for private gain.

Editors should avoid submitting to their own journal reports of original research to which they have contributed as authors. If they do so, they should recuse themselves from the editorial process, and delegate editorial decisions on those manuscripts to other members of the editorial staff. Editors should publish regular disclosure statements about potential conflicts of interests related to the commitments of journal staff.

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