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Authorship and Industry Financial Relationships: The Tie That Binds

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Over the past decade, newspaper articles related to the medical profession have turned decidedly negative.¹ Given the questionable behavior of some of our colleagues,²⁻⁷ the mounting opprobrium may be justified. Among the many areas of concern, few topics incite more passionate debate than that of physicians' interactions with the pharmaceutical, biotechnology, and medical device industries and the inevitable potential conflicts of interest (COI) that arise.^{8,9} Financial relationships, including honoraria for speaking or writing about a company's product, payment for participating in clinic-based research, and referrals to medical resources, have the potential to influence a physician's attitudes and practices.¹⁰ Importantly, the potential for COI is present whether or not the individual believes the relationship impacts their scientific judgment.¹¹ Although collaborations between physicians and drug companies clearly benefit society, as evidenced by the remarkable advances we have witnessed in cancer research in just the past few years,¹²⁻¹⁵ the Institute of Medicine (IOM) recently concluded that such conflicts "present the risk of undue influence on professional judgments and thereby may jeopardize the integrity of scientific investigations, the objectivity of medical educa-

tion, the quality of patient care, and the public's trust in medicine."¹⁶ Accordingly, for those of us engaged in clinical research, especially those of us who work closely with the pharmaceutical industry, the prospect of COI (or at least the perception of COI) is omnipresent.

Within this emotionally charged atmosphere, Rose and associates¹⁷ undertook a study examining the relationship between authorship contributions and authors' financial ties to industry in more than 200 cancer clinical trials published in *Journal of Clinical Oncology* (*JCO*) between January 2006 and June 2007. The investigators hypothesized that authors who played "key scientific roles" in oncology trials, defined as involvement in conception and design, analysis and interpretation, or manuscript writing, were more likely to have financial ties to industry than those who played a lesser role. The *JCO* provides an excellent setting in which to carry out this kind of analysis since all authors must now report their contribution to a study's conception and design; financial support; administrative support; provision of study material or patients; collection and assembly of data; data analysis and interpretation; manuscript writing; and final manuscript approval. In addition, information related to financial

relationships is available for each author at the conclusion of each article. What these investigators found is perhaps not at all surprising given that most physicians in the United States have a financial relationship with industry.^{18,19} Authors who performed a key role in the conception and design, analysis and interpretation, or reporting of a trial were nearly four times more likely to have a financial tie to industry than those authors without a key role (odds ratio, 4.3; 99% CI, 3.0 to 6.0). The association was strongest for trials with industry funding but also was observed in studies without industry sponsorship. This relationship persisted even when research funding—the single largest source of industry support—was excluded from the outcome variable. The reason(s) for the difference in financial ties to industry was not possible to discern from the available data. Rose and colleagues speculate that it may be related to interpretation of a *JCO* requirement to disclose “financial and other relationships with entities that have investment, licensing, or other commercial interests in the subject matter under consideration.” They posit that authors of nonindustry-sponsored trials “may appropriately view many of their financial relationships as irrelevant to the subject matter at hand.”

What are we to make of these findings? Using the scientific literature to advance an agenda is always a concern when the author is tied to industry through a financial relationship,^{20,21} and financial ties to industry may bias scientific reporting.^{16,21} In fact, the editors of some of the world’s most prestigious medical journals have expressed concern vis-à-vis the growing influence of industry on the design of clinical trials some of which are undertaken to facilitate regulatory approval or advance the marketing of a specific agent rather than test a specific scientific hypothesis.¹¹ Such relationships can negatively influence physicians’ behavior, establish a sense of entitlement, and undermine the independence and integrity of the profession.²² With all of the concern surrounding physician-industry interactions, are all industry relationships inherently bad? There is a lack of solid empirical data to determine if, on balance, relationships between physicians and industry ultimately harm or benefit society.²³ One might properly ask what the public thinks about disclosure since, after all, the purpose is to “ensure the public trust.” Somewhat surprisingly (at least it is to us), Hampson et al²⁴ found that most patients in cancer-research trials were not worried about financial ties between researchers or medical centers and drug companies and would still have enrolled in the trial if they had known about such financial ties. This may be due to patients’ trust in their physicians, or perhaps a desire to be treated with a new agent to which they may not otherwise have access. Moreover, Blumenthal et al²⁵ found that life-science faculty who received industrial funding were at least as productive academically as those who do not receive such support and are markedly more productive commercially. That study also found that faculty with industry ties were more likely to have a patent licensed, have a product under regulatory review, or have a product on the market. However, they also found that investigators with industry support were at least twice as likely to engage in trade secrecy or to withhold research results from colleagues as are investigators without such support.²⁵ Given the importance of openness to the scientific process, the latter finding is truly disturbing.

Fortunately, there are a number of ways to minimize conflicts of interests including removal, recusal, third-party evaluation, codes of ethics, and disclosure. American Society of Clinical Oncology guidelines, published in 2003, rely heavily on disclosure as the principal method of dealing with perceived COI.²⁶ But is disclosure alone sufficient? Author disclosures are becoming increasingly complex and the

benefits of this increased “transparency” are limited,²⁷ since they are dependent on interpretation of the guidelines as well as the author’s integrity. Moreover, there is not a uniform system for the disclosure of financial information²⁸ that in turn may result in some confusion for authors (as evidenced by several recent high profile cases where the authors failed to properly disclose).^{3,29-32} Even if a uniform system is eventually developed we worry that lengthy disclosures may become the publication industry’s equivalent of the Transportation Security Administration Orange Alert sign now permanently placed at one’s local airport—there, but not really seen. Indeed, it has been suggested that the benefits of disclosure are limited, serving primarily as a prevention against the possibility that a competing interest may eventually come to light and discredit the authors or the journal involved.²⁷

In short, it is simply not possible to read a disclosure statement and fully understand its potential effect on the reporting of a clinical trial. Recently, Psaty²⁷ offered a number of common sense methods for assessing possible biased reporting, which after all is what the reader of any article really wants to know. Psaty argues that an assessment of the trials design, study conduct, and interpretation of the results are the best measures for one to assess the possibility of bias²⁷—and we agree. For example, what are the quality and the scientific merit of the hypothesis addressed by an industry-funded trial? Do the selected hypothesis and its associated outcome address an important public health question? What comparison group was selected for study? If the trial has an active-treatment comparison group, were the control agent and dose appropriate? What is the fit between the results and the discussion points? How do the investigators weigh the balance of risks and benefits? Is the discussion cautious, well-defended, and disinterested? Or are the data used to marshal an argument that has the look and feel of advocacy or promotion? In essence, it is up to the reader to assess and judge the quality of the article...as it should be.

Finally, Rose and colleagues also report that 40% of “authors” failed to meet the International Committee of Medical Journal Editors (ICMJE) authorship criteria.³³ According to the ICMJE guidelines, 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. An “author” should meet conditions 1, 2, and 3. The fact that 40% of the individuals whose names appear on the authorship byline do not meet these criteria is surprising and more than a bit disconcerting. Many claimed authorship by virtue of the “provision of study materials or patients” clause. Is this activity sufficient to claim “authorship?” ICMJE policy suggests that those who have contributed materially to the article but whose contributions do not justify authorship should be listed under headings such as “clinical investigators” or “participating investigators,” and their function or contribution should be described. Rose and her colleagues challenge the editors of *JCO* to clarify the journal’s policy on authorship. We agree.

AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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