

Profits, Pressure, and Perception: Expensive Research Collides with Medicine



In this issue of *The Journal*, Duncan Gordon provides a comprehensive, instructive, and engaging review of the many aspects of research misconduct and publication ethics¹. One doesn't have to be an editor long to encounter improprieties ranging from data fabrication and falsification to plagiarism, ghost and gift authorship, duplicate publication or "salami science" (the multiple publication of identical or very similar data). Some transgressions arise, at least in part, from author ignorance². Other misconduct, such as failure to disclose financial conflicts of interest, arise from a persistent belief on the part of some authors and educators that their professional activities are impervious to the influence of money: the direct compensation, research funding, and other benefits they receive from pharmaceutical companies³. However, there is accumulating evidence that the influence of financial conflicts of interest in research and education is subtle, often unrecognized or disguised, and increasingly pervasive.

WHY THE INTEREST IN FINANCIAL CONFLICTS OF INTEREST?

Getting a new drug to market has become very expensive. Estimates vary but are likely in the range of about Cdn \$1 billion⁴. When a new product is finally approved for clinical use, the pressure on marketing departments to convince doctors to become loyal prescribers before the patent period expires must be enormous. Off-label drug trials, pharmaceutical detailing, journal advertising, and, increasingly, pharmaceutical company sponsorship of continuing medical education (CME) for physicians (read prescribers) are used to increase sales.

INFLUENCE ON RESEARCH

When the International Committee of Medical Journal Editors (ICMJE, also known as the Vancouver Group) met in 2001, we discussed the increasing influence of companies, foundations, and government departments on research that was being submitted for publication in our journals. There were many examples of research contracts that limited the researchers' freedom to publish or denied researchers access to all study data. In an attempt to counteract this trend, the ICMJE established new guidelines for the publication of sponsored research⁵. These guidelines require editors to

verify (if necessary, by inspecting research contracts and study protocols)⁶ that researchers had full access to all study data and that there were no restrictions on publication.

PUBLIC PERCEPTION OF CONFLICT OF INTEREST: THE JESSE GELSINGER CASE

Although the new ICMJE guidelines are important, they address only the most egregious forms of sponsor influence on research and publication. Changes in the relationships between universities and health sciences centers on the one hand and pharmaceutical companies on the other are occurring on a broader front, as increasing amounts of money from commercial sponsors flow to universities and health sciences centers and, more recently, directly to community-based practitioners⁷.

After the death of Jesse Gelsinger, an 18-year-old child with ornithine transcarbamylase deficiency, 48 hours after he received via his portal vein a virus carrying a replacement gene⁸, universities have begun to reexamine their policies governing sponsored clinical research.

In the Gelsinger case, the problem was not one of uninformed consent, misleading protocols, publication gag clauses, or the like. The study had been duly approved by the university. Arthur Caplan, an internationally recognized expert on the ethics of research on children, had supported the research. Jesse was not the first patient to enter the trial, and the protocol had passed the required scrutiny for human gene research of the US National Institutes of Health. The science and the process met acceptable standards.

The problem was one of perception. Several months after Jesse's death, the family filed a lawsuit against the university. On legal discovery, it became clear that James Wilson, the lead investigator and an internationally recognized expert in this field, was also the president and major shareholder of a private company (Genova, Inc.) that held patents for the procedure and supplied the funding for the research. It also emerged that the university and some members of its board of governors owned stock in Genova, and that Genova had granted research funds to Caplan.

Although there was no evidence that the complex financial relationships between the university and its commercial sponsor were a factor in Gelsinger's death, the university quickly settled the lawsuit and Wilson resigned his post at

the university. But the university went further, instituting strict guidelines for clinical research⁹ that explicitly prohibit faculty from participating in clinical research if they (or members of their family) have any material financial interest in a private company whose product they are evaluating. Harvard has recently followed suit. The University of Toronto, following the fiasco¹⁰ involving contracts between researchers Nancy Olivieri and Gideon Koren and Apotex, a pharmaceutical firm, are revising their policies^{11,12}. Other Canadian universities will undoubtedly follow. There are calls for even stricter reforms and for regulation of clinical research funding¹³.

CONTINUING PROFESSIONAL DEVELOPMENT

Probably most readers of this journal have been involved in CME, whether as pharmaceutical company consultants, course leaders, speakers, or participants. CME is necessary and expensive, so it is understandable that physicians look for financial support for tuition, travel, and accommodation. And it is equally understandable that pharmaceutical firms, eager to convince physicians of the benefits of their products, like to “help out” by paying these costs. Recently, the Canadian “Rx&D” pharmaceutical firms have succeeded in persuading the Royal Colleges and the Canadian Medical Association to weaken their stance on CME funding by pharmaceutical companies¹⁴⁻¹⁶. However, both the literature on the influence of money on professional behavior in medicine and the public perception of gifts and incentives are decidedly negative. In my view, this recent ethical wobble by the physician associations is damaging to the profession.

I would venture to say that medical journal editors have been slow to tackle ethical issues in research, publication, and continuing professional development. A search of the almost 11,000 *Journal of Rheumatology* articles listed in PubMed since 1971 revealed only 6 coded under the MeSH Major Topic heading of “ethics”¹⁷⁻²². Granted, this was a crude search that may have missed some. But I suspect that, had I done this search for most specialty medical journals, the results would have been equally sparse.

By writing more about ethical issues in research and publication, by reporting on some of the most egregious misconduct, and by encouraging debate in their pages about the role of pharmaceutical companies and other sponsors in the professional lives of physicians and their patients, medical journals can promote more responsible behavior and acquire a cleaner public image. Journals that neglect this self-critique and study may risk a more painful examination by others.

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