Scientific harassment by pharmaceutical companies: time to stop

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The timely and accurate synthesis of clinical trial results and of other information on new drugs and new devices is essential to informed decision-making on the appropriate use of these products. However, 2 alarming trends are already impeding such assessments. First, the results of applied medical research — which, increasingly, is being funded by the private sector — are being released only selectively to the public. Findings that support manufacturers' claims are widely disseminated, while others may be withheld. Second, some companies appear to be ready to stifle scientific discussion by turning to the courts, seeking injunctions to prevent the release of reports or threatening researchers with legal action.

More and more, the development of drugs and medical devices is being carried out by private industry. In Canada, pharmaceutical firms spent almost $1 billion on research and development in 1999,[1] dwarfing the $19 million set aside by the publicly funded Medical Research Council (shortly to be transformed into the Canadian Institutes of Health Research).[2,3] Most clinical trials undertaken to establish the safety and efficacy of these products are funded by industry. What happens to the results of such research? In an editorial in the *Journal of the American Medical Association*, Drummond Rennie draws attention to the publication bias generated by the multiple publication of some studies, selective publication of only some of the results, the tendency for studies that obtain favourable results to be reported more frequently and more quickly than studies with negative results, and failure to cooperate with other researchers seeking to clarify issues of study design.[4] In an editorial in this issue of *CMAJ* (see page 209) Allan Sniderman recounts his similarly unsuccessful attempts to obtain information from authors and pharmaceutical firms.[5] These trends can inappropriately skew the balance of opinion in favour of new drugs. Rennie suggests that this practice, which serves commercial interests so well, is deliberate and must stop. One way to do this is to register trials before they are carried out and to publish the results of all of them.[6] I endorse this proposal. We cannot properly assess the benefits and risks of new technologies without having all of the evidence.

The second problem, that of blocking the release of information and opinion, is even more worrisome. In a recent article[7] my colleagues and I drew attention to the fact that industry is using litigious means to dispute research findings and block the dissemination of results. One case was the now well-known situation in which Bristol-Myers-Squibb Canada, Inc., tried to prevent the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) from releasing a summary report on statins. This report was prepared after CCOHTA had made a full assessment available to industry for review and comment. The court refused to grant an injunction against the release of the summary document, and an appeal of this decision was denied. However, publication of the summary report was delayed for almost a year, and CCOHTA was faced with legal costs equivalent to a substantial proportion of its budget. In addition, other assessment work at CCOHTA was delayed as a result of the demands on staff made by the court case.

A more recent case centered on the proton pump inhibitor omeprazole, a highly successful drug marketed in Canada by AstraZeneca under the name Losec; Canadian sales totalled $280 million in 1997.[8] The Ontario Ministry of Health struck an independent panel of specialists familiar with relevant evidence, family physicians, pharmacists and consumers to formulate guidelines for Ontario for the treatment of heartburn, ulcers and related conditions. The panel was chaired by Anne Holbrook, a physician–scientist at McMaster University in Hamilton, Ont. In a preliminary report circulated widely for comment to government and industry, the panel concluded that there were no important differences in the clinical effectiveness of omeprazole and 2 other drugs in its class. This finding would mean that physicians might choose to prescribe the cheaper proton pump inhibitors. Each of these stakeholder groups were asked to provide comment with supporting evidence. AstraZeneca did, but they also hired a Toronto law firm to write a letter to Holbrook asking her to "refrain from finalizing and distributing the guidelines." If she persisted, the letter continued, they would instigate "appropriate legal proceedings."

In a letter to the *British Medical Journal*,[9] the company said that it "has never prevented nor had the intention of preventing, any doctor or researcher from publishing or communicating the results of their studies." They should have told their lawyers about this policy. Although the company says that it apologized to Holbrook for sending the letter directly to her rather than to the ministry, the letter was certainly intimidating and has not been formally withdrawn.

It costs pharmaceutical companies a lot of money to develop new drugs. AstraZeneca, a major international pharmaceutical firm, reports worldwide spending of more than US$2 billion a year on research and development.[10] This investment, a business expense, represents a substantial contribution to research by the companies and their shareholders. Likewise, insofar as it allows manufacturers to reduce their taxes, it represents a major contribution to research by taxpayers. It is important that new drugs and technologies yield both health care benefits (the return for public investment in research) and financial returns for those who invest money in industry.

In the short term, manufacturers can gain an advantage over their competitors by virtue of publication biases and the selective or delayed dissemination of trial results. In the long term, however, the truth about a health technology will emerge, and clinical practice and financial support for a product will be adjusted accordingly. However, the long term may be a matter of many years, during which time patients may be exposed to inappropriate interventions and the health care system burdened with needless expenditures.

What can be done about this unsatisfactory state of affairs? Legal challenges should be a last resort, and industry should be encouraged to use scientific channels to challenge results it deems unsound or opinions it considers unfair. Industry has a wealth of research expertise, and detailed scientific responses from the private sector substantially contribute to the quality of the debate on the efficacy and efficiency of new technologies. Two pharmaceutical companies — Schering Health Care and Glaxo Wellcome — have taken important steps in making information available about ongoing trials in which they are involved. It is to be hoped that other companies that provide support for clinical trials will follow this lead.

Cooperative efforts between government, industry and academic researchers (such as the not-for-profit Institute of Health Economics in Edmonton) might provide a more constructive environment in which to assess new technologies and provide advice to patients and health care decision-makers. Cooperation of this sort may provide a better opportunity to build bridges and avoid the harm caused by the use of legal threats to stifle scientific discussion.

Lastly, researchers who head scientific government panels dealing with drugs and devices should be encouraged to submit their reports to peer review, as was done in the Holbrook case, including, where possible, medical journals. This avoids any perception on the part of industry, even if misguided, that recourse to the courts may appear to be the only option.

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