In spring 2012 the Standing Senate Committee on Social Affairs, Science and Technology started holding hearings on a wide range of issues dealing with pharmaceutical policy. November saw the release of the first in a series of reports (PDF 1.44MB) from these hearings on clinical trials in Canada. (Full disclosure: I appeared before the Committee and am briefly cited in the report.) The report raises a number of issues and makes some useful recommendations. It calls for trial registration for all trials being conducted in Canada, something that Health Canada has been studying since June 2005 without, however, coming to any conclusions.

Currently there is very little in the way of national standards for Research Ethics Boards (REBs), the bodies that are supposed to ensure that trials are conducted in accordance with ethical standards. Here the Senate Committee correctly recommends that the Minister of Health call on Health Canada to “immediately undertake to develop an accreditation program for” REBs. Following in a long line of recommendations from Health Canada’s now defunct Science Advisory Committee and the House of Commons Standing Committee on Health, the report calls for more transparency in the entire clinical trial process including public access to data from clinical trials. Finally, the Senate wants better monitoring and
follow-up of adverse reactions that occur during clinical trials, a deficiency that the November 2011 Report of the Auditor General identified.

All of this is to say that the Senate Committee Report makes some very important recommendations so it would be a mistake to dismiss it out of hand. At the same time, there are some serious gaps in the report that need to be addressed. One of the over-riding concerns in the report seems to be that Canada is losing out on clinical trials as they increasingly move to developing countries, especially India and China. In order to redress this development the report calls for the establishment of a “National Framework for Coordinating Clinical Trials to establish Canada as a preferred site for clinical trials, and provide a point of contact between industry and networks” among academic institutions, research networks and patient groups.

In their presentations to the Senate, the Best Medicines Coalition and the Canadian Organization for Rare Disorders called for the government to promote increased clinical trial activity. In response, the Senate report suggests one benefit of such promotion would be that health care professionals might become more familiar with the product and presumably better able to prescribe it once approved. However, this rationale makes two assumptions — first that the drug will in fact be approved and second that the drug will offer a significant advantage over existing products. According to industry sources about 4 out of 5 drugs that enter the clinical trial process fail to get approved and about 85%–90% of new drugs offer little to no therapeutic advantage over existing products.

Clinical trials are very important: that’s how the data is generated to show the safety and efficacy of products that are in the development stage. But at the same time, it is well-known that not all products are created equal. As noted above, somewhere between 85%–90% of all the new drugs approved in any given year are largely unnecessary. The successful completion of clinical trials on these products only benefits the pocket books of the drug companies, not patients. Clinical trials of therapeutically important new drugs should be encouraged but the distinction between the two types of drugs is nowhere to be found in the Senate Report. Readers would be left with the conclusion that all trials are of equal value.

Moreover, the report does not comment on the multiple studies that have found that clinical trials paid for by the pharmaceutical industry (at present about 80% of all trials are funded by industry) are much more likely to produce positive results (the drug is safe and efficacious) than are trials with any other source of funding. (A Cochrane report due to appear in mid December will reinforce this point. Another disclosure: I’m one of the authors of the report.) Finally, groups in Europe are uncovering the uncomfortable truth that the European Medicines Agency is overlooking questionable ethical practices used in trials done in
developing countries and approving products based on these trials. Is the same thing happening with Health Canada? The Committee Report is silent on this issue.

Although the report does address some of the issues around REBs there are other questions about these boards that it failed to look at. The 70% of all clinical trials that are done in a community setting do not go through an institutional (hospital, medical school, etc.) REB for the simple reason that they are not conducted in an institution. Instead they go to a commercial for-profit REB. Concerns have been raised that these commercial REBs may be reluctant to be too critical of ethical deficiencies for fear of losing future contracts. One proposal to remedy this situation would be the creation of a province-wide public REB run by an independent organization that would oversee ethical approval for all community-based trials.

Finally, the report does not talk about clinical trials that are terminated early. Commercially funded trials are sometimes stopped early allegedly because the benefits from the new product should be available sooner to the public. An analysis of cancer trials that were stopped before their anticipated endpoint suggests that there might be a commercial component behind their premature termination; shorter trials lead to lower costs and also allow for earlier registration and an earlier start to revenue from the product. What's the case for RCTs in cancer is happening with RCTs more generally. A systematic review of RCTs stopped for benefit found that they were typically industry-funded and failed to give a full account of the decision to terminate the trial early and often showed “implausibly large treatment effects”. In the 1980s the most common reason for terminating trials in the late stages of research was not efficacy or safety but economics — including a limited commercial market, insufficient anticipated return on investment and a change in research priorities following drug company mergers. Termination solely on economic grounds can be viewed as a violation of the Declaration of Helsinki, the ethical "bible" for clinical trials.

The Senate Committee has just finished hearings on the post-approval monitoring of prescription pharmaceuticals and will later focus its attention on the off-label use of prescription pharmaceuticals and the nature of unintended consequences in the use of prescription pharmaceuticals. Let’s applaud what the Committee has done but also hope that it does better in the future.

About the Contributor

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