

Commentaire

Continuing review of research approved by Canadian research ethics boards

Charles Weijer

‡ See related article page 1321

The research ethics board is a social oversight mechanism to ensure that all human research subjects are protected. To achieve this end, research ethics boards must go beyond merely reviewing the paper protocols submitted by investigators. Continuing review of approved research is essential to ensure that research is conducted as planned, that research subjects comprehend the information presented to them in the consent process, and that the potential benefits and risks of study participation remain acceptable.¹

The imperative to conduct continuing review of research was first recognized almost 25 years ago by the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, which existed from 1974 to 1978, in its report on institutional review boards.² Building on the work of the National Commission, the Medical Research Council of Canada (MRC), in its publication *Guidelines on Research Involving Human Subjects 1987*,³ set out for Canadian research ethics boards detailed requirements for continuing review. Recognizing that trust is an important component of the relationship between the board and the investigator, the MRC guidelines implied that such trust is verifiable. They stated: "It is expected ... that the institution's monitoring will be more active than simply seeking investigator's assurances."³ Article 1.13 of Canada's current research ethics guidelines, the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*,⁴ specifies that research be subject to review on a continuing basis, that researchers propose to the research ethics board the type of review required and that this not be less than an annual written report. When research poses more than minimal risk, the research ethics board has a variety of review mechanisms open to it, including review of the consent process, creation of a safety monitoring committee, periodic review of study documents, review of adverse event reports, chart review and random audit of the consent process.

Despite the importance of continuing review, it seems that few research ethics boards fulfill this responsibility. In 1995 the National Council on Ethics in Human Research published a 4-year review of Canadian research ethics boards.⁵ Of the 68 boards included in the study, 53% (24/45) reported that they required an annual report from investigators — the bare minimum for continuing review.

Only 18% (8/44) stated that they performed "ongoing review or audit" of research, and 7% (2/29) reported periodic review of patient charts. These results are consistent with findings from Australia and Scotland.^{6,7} A 1998 review of US research ethics boards found that "[I]n the current system, [research ethics boards] have no way of knowing whether those participating in research truly understand that they are research subjects, and that there may be risks associated with their participation."⁸

In an attempt to meet this challenge, a number of research ethics boards have reported successful strategies for continuing review. A Scottish report detailed a program in which the research ethics board sent a questionnaire to 311 project investigators.⁹ A stratified sample of 10% of the projects were followed up by 2 members of the board, who reviewed questionnaire responses with the investigator, completed a more detailed questionnaire and inspected consent forms and case records. The authors estimated that each detailed review required on average of 6 person-hours, at a cost of £120 (Can\$260). A New Zealand publication reported on qualitative interviews with investigators for 16 research projects approved by a research ethics board.¹⁰ The authors concluded that an active monitoring program can detect deviations from the approved protocol not disclosed in the annual report and can fulfill educational objectives.

The report by Jane McCusker and colleagues in this issue of *CMAJ* (page 1321) is the first detailed report from a Canadian research ethics board of a continuing review program.¹¹ The Research Ethics Committee at St. Mary's Hospital Centre in Montreal asks investigators to submit a list of all patients enrolled in studies, and these lists are cross-checked to determine if any subjects are enrolled in more than one study. Patient charts are audited to check whether a signed consent form and cover sheet are included. If study participation poses more than minimal risk, subjects may be interviewed to assess their understanding of the research project. The results reported, including a variety of problems with consent and other procedures, are consistent with those of similar studies in the literature.^{9,10} Importantly, most of the investigators at St. Mary's (67%) believed that the monitoring activities were important, although few (19%) thought that research grants should cover the associated costs.

Without question, the main impediment to wide-scale implementation of continuing review is the increasing workload of research ethics boards and the cost of such programs. Yet it seems from the results reported by McCusker and colleagues that a research ethics board need make only a modest investment of resources to achieve suitable continuing review of approved studies. More detailed information on the cost of continuing review and the scripts used for subject interviews ought to be provided. There is an urgent need, therefore, for other research ethics boards to publish their experiences with continuing review.

Two mechanisms in particular might be considered for covering the costs of continuing review. First, the Canadian Institutes of Health Research (CIHR) should set up a committee to address the need for continuing review of health research and its financial implications. The committee should provide CIHR Governing Council with advice on setting guidelines for the choice of research to be continually reviewed and setting guidelines for appropriate costs to be covered by CIHR in its operating grants to health researchers. In addition, research ethics boards may choose to pay for continuing review by charging for such activities. For example, some Canadian boards now charge pharmaceutical companies \$1000 or more to review a protocol. In addition to paying the direct costs of continuing review, such revenue would allow the boards to increase administrative staff and to computerize the tracking of protocols, thereby increasing the efficiency of review.

Other obstacles require further study and clarification. For example, what should be the board's role in reviewing reports of adverse drug reactions? What continuing review should be conducted for a multi-institutional protocol? What is the relation between a data and safety monitoring board and the research ethics board?

To ensure adequate protection of Canadians serving as research subjects, we must seek answers to these questions in

a timely fashion. We must also develop guidelines for determining the extent of continuing review and acceptable costs.

Dr. Weijer is Assistant Professor of Medicine, Department of Bioethics, Dalhousie University, Halifax, NS.

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Correspondence to: Dr. Charles E. Weijer, Department of Bioethics, Dalhousie University, 5849 University Ave., Halifax NS B3H 4H7; fax 902 494-3865; charles.weijer@dal.ca