EDITORIAL

Institutional Review Boards: A Crisis in Confidence

There is a sense of crisis in the country about the effectiveness of the nationwide system that protects the rights and welfare of human research subjects. Reports of problems appear on television or in newspapers almost weekly and focus attention on the system's centerpiece, the institutional review board (IRB). University hospitals' entire research programs have been suspended on grounds of inadequate IRB performance, and governmental agencies have found that the IRB system is incapable of coping with its workload.

In this issue, Burman and coworkers (1) identify the enormous increase in the number and complexity of multicentered randomized clinical trials (RCTs) as the root cause of the crisis (1). We must be concerned about the capabilities of IRBs to cope with contemporary problems, such as multicentered trials. I disagree, however, that RCTs are the major problem. Institutional review boards have difficulties because low-yield, time-consuming tasks dissipate their energies. This and other factors are eroding the motivation of academics to serve as IRB members.

Many of the aforementioned reports call attention to important problems, but many others stir up needless concerns. About a year ago, several public officials made much of a report stating that no one could estimate the total number of human research subjects in the United States. As one put it, "They can tell us exactly how many animals were used in research! Why do they care more about animals than humans?" Experienced IRB members explained that this was a non sequitur; counting subjects cannot be considered evidence of caring for them. The number of animals is known because they are purchased with grant money and the government requires an annual accounting of how such funds are spent. The IRB members also pointed out that no one had ever before suggested that enumeration of research subjects would help protect their rights or welfare. For a meticulous documentation of the numbers of research subjects, they continued, one should examine the records of the Nazi research physicians. Journalists' accounts of this matter generally repeated the initial non sequitur but omitted the other responses. In a second example of sensational journalism, most press coverage referred to the Office of the Inspector General (OIG)'s Report on IRBs by its original subtitle, "A System in Jeopardy," despite the fact that the OIG had changed the title in response to charges that it seemed hyperbolic. The report had uncovered no instances of exploitation of or injury to research subjects (2).

In examining the recent spate of research program suspensions, Burman and coworkers list the findings of the National Institutes of Health's Office for Protection from Research Risks (OPRR) (which has since been replaced by the Office for Human Research Protections [OHRP] in the U.S. Department of Health and Human Services) and the U.S. Food and Drug Administration. They then select two of these findings for comment. The first is "inadequate continuing review of previously approved protocols," which means a failure to review protocols at convened meetings of the IRB at least once annually (3). Until OPRR decided to make an issue of this, many IRBs used a modified expedited review process to accomplish routine periodic reevaluations—modified in that the reviewer needed to decide only whether review by the convened IRB was warranted.

This modified expedited review is generally adequate for its intended purpose. On the first anniversary of a protocol's approval, the research usually has not yet begun; often, because the funding agency has not yet decided whether to commit funds for the project, there are no data to review. In the absence of data, the major purpose of periodic reevaluation is to determine whether there has been a change in the field of study, such as any reports of research findings that make it necessary to revise or discontinue the protocol. This is decidedly a question for an expert in the field, and most IRB members bring no useful information to this type of discussion. An expert is the one who should be (and once was) called on to conduct the expedited review.

The second problem that Burman and coworkers comment on is "inadequate review of safety reports." Currently, multiple reports of adverse events inundate IRBs, but review yields nearly nothing of value. The Data and Safety Monitoring Board (DSMB) is much better equipped than an IRB to review these reports. An IRB's responsibility to receive and evaluate reports of adverse events should be limited to events that occur in

research subjects enrolled in studies in its own institution. The IRB should also review the results of the DSMB's evaluation.

One of the most vexatious problems for the modern IRB, unrelated to multicenter RCTs, is the "tissue issue" (4). Institutional review boards spend seemingly endless hours trying to determine how to say to a patient, "We want to store a sample of your blood (or other tissue removed at clinically indicated surgery) with the hope that we might be able to do genetic studies on it sometime in the future. We don't know exactly what genetic studies we might want to do, but in case it turns out to be something about which the IRB feels you should be consulted, we will ask for additional informed consent." This is difficult enough when the tissue is sampled in the course of a formal research protocol, but what about the more common cases, in which the tissue is removed by a surgeon or other physician who lacks sufficient sophistication in genetics to respond adequately to the patient's questions?

Another problem not related to RCTs was presented by OPRR's recent ruling involving "secondary research subjects." If in the course of conducting survey or interview research an investigator asks a research subject sensitive questions about other persons, the other persons are considered secondary research subjects and must therefore provide informed consent (5). When asked to explain this new policy, OPRR responded that it was not new and that the regulations had for many years defined *subject* as "an individual about whom an investigator . . . obtains . . . identifiable private information." Although this is technically correct, OPRR's interpretation was indeed new. In my view, the appropriate action would have been to revise the faulty definition rather than enforce a novel reading of it.

The most important problem for the human subjects protection system is that the workers—the IRB members—are frustrated and disillusioned. These people, most of whom agreed to become IRB members because they felt a responsibility to uphold the values of their institutions, have received no reward apart from the satisfaction of doing something important (6). Now, they are weary of reading repeatedly that public opinion, as expressed by politicians and journalists and in governmental reports, sees them as largely incompetent. Worse yet, the criticism increasingly comes from within. As OPRR closed down one university research program after another, faculty colleagues began to hold the IRB and its members accountable for their troubles. While it seems fair to close down seriously unethical research, OPRR's suspension of an institution's entitlement to conduct all research necessarily disrupts many projects that are being conducted satisfactorily. In addition, much important data generated at considerable expense to the public are lost. Other "innocent victims" include postdoctoral fellows who moved to the institution to learn how to do research, only to find that that research can no longer be carried out

Outsiders say that we could manipulate the reward system to make serving as an IRB member more attractive. We could pay members more or give them "release time" from other academic responsibilities. Such proposals simply fail to recognize the nature of teaching in an academic medical center and do not consider the fact that money is not the most important coin of the academic realm.

I have long argued that the development of a successful IRB depends most heavily on nurturing the attitude that the IRB consists primarily of researchers' colleagues and that its mission is to provide guidance on how an institution's values are to be honored and upheld while research is conducted (6). This attitude cannot be sustained if IRB members feel that they are simply agents of the government compelled to enforce compliance with sometimes faulty interpretations of regulations. It further saps the energy and self-respect of IRB members if they are required to spend increasingly large portions of their limited time doing relatively unimportant things, such as dealing with periodic reevaluations and reports of adverse events as prescribed by current policy interpretations.

My response to the IRB crisis would be to reevaluate and restate the charges to the IRBs. These charges should be reasonable and should be designed to focus the IRBs' attention on important matters that match their capabilities (6). I would add a high-quality system of education for IRB staff and members and eventually, after we have learned how to do these things well, I would add an accreditation system for IRBs and a certification system for IRB staff. The burden on local IRBs could be alleviated by delegating some of their responsibilities, particularly those pertaining to multicentered

RCTs, to what Burman and coworkers call central IRBs (7). Finally, I would attempt to tone down the rhetoric of the criticism of IRBs or, if this cannot be done, attempt to balance this rhetoric by including the other side of the story. Critics who seem to insist on perfection as the standard for IRB performance must be reminded that perfection is generally the worst enemy of "good enough."

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