Debate Over Institutional Review Boards Continues as Alternative Options Emerge

By Caroline McNeil

On Jan. 1, the University of Minnesota launched a major overhaul of its institutional review boards (IRBs) with the goal of increasing efficiency, quality, and—most importantly—for many IRB critics—the speed with which it reviews new clinical trial protocols.

The reforms represent one approach to fixing the problems that have been plaguing IRBs everywhere for more than a decade. Charged with protecting human research subjects, IRBs have been facing increasing workloads, difficulty attracting qualified members, and lack of expertise in specific areas of medicine.

The University of Minnesota’s local reforms buck the growing trend toward use of external or “central” IRBs to solve these problems. Outsourcing review to central IRBs, including the independent, for-profit boards that charge a fee, is increasingly common and has the explicit support of federal agencies including the Office for Human Research Protections (OHRP), the U.S. Food and Drug Administration, and the National Cancer Institute.

Nevertheless, the debate over local versus central review continues, as does the search for alternative models that might include the advantages of both. What happens in Minnesota in the next few years, as well as with the growing number of alternatives, will be closely watched by the entire clinical trial community.

At the University of Minnesota, the new IRB has started meeting once a week rather than once a month. Several boards have been consolidated into one, with its members rotating according to the expertise needed. Its members, all senior investigators, will be paid. These reforms and others—the use of electronic forms and assistance with applications, for example—should speed up the clinical research process, improve the expertise of the review, and lessen pressure to use central IRBs, said Richard Bianco, associate vice president for research.

Over the next few years, he will be collecting data to help gauge the success of this approach, including the time it takes for each stage of the process; for example, how long it takes the IRB staff to present the application to the board members, the time it takes the IRB to approve the trial with stipulations, and the total time to final approval.

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Champions of central IRBs cite a range of advantages. In addition to eliminating duplicate reviews for multisite trials, they can more easily include members with a broad range of expertise, said Lowell Schnipper, M.D., of Harvard Medical School. They also ensure consistency across sites and free up more time for local IRBs to focus on local trials.

Schnipper, speaking at the OHRP conference, also pointed to a new factor in the debate—the growing number of targeted drugs. The need to test these agents on patients whose tumors have those molecular targets means recruiting participants from a wide geographic area. “We can’t waste time, money, and effort testing drugs on patients without the target,” he said. And with so many emerging targets and candidate drugs, “speed and high-quality data become the essence of doing research.”

Range of Advantages

On the other side of the debate, advocates argue that central IRBs make more sense for today’s clinical trials. When an IRB review of trials became mandatory in the 1970s, there were fewer trials and most took place at one institution. But in the 1990s, multicenter trials became more common. IRBs’ workloads shot up, and the review process slowed down. For multicenter trials, local IRBs were duplicating each other’s work, sometimes producing conflicting modifications that needed to be resolved. Trials were often delayed by months.

In an effort to tackle these issues, many institutions looked beyond their own walls. More began outsourcing reviews to independent or “commercial” IRBs, such as the Western IRB, in Olympia, Wash., the largest and oldest of the independent IRBs. In oncology, another approach was the creation of central IRBs at the National Cancer Institute, one for adult and one for pediatric trials. These central IRBs provide an initial review of phase III cooperative group trials that local boards can either adopt or modify.

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Under all the models, local boards continue to monitor adverse events and address local issues, but by using central IRBs they avoid the long initial review process.

Issue of Responsibility

On the other side of the debate are those who worry about issues of liability—fear of lawsuits makes some institutions reluctant to relinquish control over any aspect of...
their trials. Another barrier to the use of central IRBs is confusion over how local and nonlocal boards can work together.

But the single biggest barrier appears to be concern over the loss of a close connection between local investigators and the principles and processes of human subject protection.

“It is an issue of responsibility,” Bianco said. “These are our patients. The local IRB knows the principal investigators and the patients—you can’t get that in a commercial IRB.”

Robert Levine, M.D., codirector of Yale University’s Interdisciplinary Bioethics Center, puts it in terms of institutional culture. The local IRB serves as an “institutional presence” to remind people of and serve as a resource on ethics, he said. “My greatest fear is that the IRB will come to be seen like the Internal Revenue Service—a distant bureaucracy that you’ve got to reckon with even though its objectives may be at odds with your own. Many otherwise honest people think it’s okay to withhold information from such an agency.”

Advocates of external IRBs maintain that a culture of responsibility for human subject protection stems less from the influence of a local IRB and more from well-trained investigators. “We outsource [IRB review] but concentrate resources on where the rubber meets the road—the training and support of investigators,” said Stuart Horowitz, Ph.D., who was chief of the Miami Children’s Hospital Research Institute, speaking at the OHRP meeting.

Horowitz, now with Huron Consulting Group in Chicago, and others pointed out that local IRBs may be more prone to bias than external boards. Local academic politics, for instance, could influence their approval or disapproval of a trial. Moreover, the dollars that a particular trial sponsor is bringing to the institution could introduce a bias in a local board.

**Spirited Experimentation**

While the debate continues, the acceptance of external review boards in some form is growing. NCI’s two central IRBs now have 295 institutions enrolled, up from 261 a year ago, said Jacquelyn Goldberg, J.D., administrator of the central IRBs. Almost 60% of the Children’s Oncology Group institutions have joined the pediatric group, she said.

Likewise, the Western IRB now supports 31 academic medical institutions compared with just one in 1996, said its president, Angela Bowen, M.D. Another 150 nonacademic medical centers have joined WIRB in the same period. The WIRB also provides regulatory support staff for the NCI’s two central IRBs.

At the same time, new models of review are emerging, including regional consortia and reciprocal arrangements. “We’re now in a period of spirited experimentation,” Levine said. “People are trying all sorts of permutations.”

In fact, one purpose of the national conference was to raise awareness of the range of alternatives. “It was our intent to have people realize that there are many models, a growing number of models,” said OHRP director Bernard Schwetz, D.V.M., Ph.D.

One of these models is the Multicenter Academic Conical Research Organization, or MACRO, a group of four institutions—Vanderbilt University in Nashville; the University of Alabama at Birmingham; Washington University in St. Louis; and the University of Pennsylvania Medical School in Philadelphia—that have a “limited reciprocity” agreement. If a protocol is approved at one of the four, it is considered approved at the others, according to the MACRO website.

Another alternative model, Michigan State University’s Community Research Institutional Review Board, comprises representatives from member organizations from throughout the state. Other members and expertise are added as needed, and online postings of protocols and other materials help maintain collaboration between the members, said Peter Vasilenko, Ph.D., Michigan State’s director of its human research protection program. New York also has a statewide consortium, the Biomedical Research Alliance of New York.

Even institutions that still rely primarily on their local IRB may be increasingly open to accepting some aspects of central review. At the University of Minnesota, for instance, Bianco said that he did not expect long reviews or changes to multisite protocols that had been approved by central boards.

**Local Context**

In fact, with the growth of central IRBs, the focus of the discussion may be shifting from whether to use them to how best to work with them. At the OHRP conference, several panels emphasized the need for detailed agreements or contracts since local institutions retain some responsibilities under any system.

One of the hot issues in IRB collaboration is how external reviewers can gain knowledge of local conditions—i.e., how the central IRB assesses the “local context” of the proposed research. Local context, which review boards must take into account, can include cultural norms, community sensitivities, the adequacy of facilities and resources, and competence and qualifications of investigators.

Local context can be difficult to convey. For instance, “the reputation of investigators is elusive and hard to assess,” said Joan Rachlin, J.D., the executive director of Public Responsibility in Medicine and Research, a professional association for human subject protection. “That is difficult to do remotely … the local IRB has to play some part.”

“It’s a challenge,” Bowen agreed, and one that independent IRBs have grappled with for some time. The WIRB uses regular site visits, both by regional representatives and by its own staff over the course of a study, to stay on top of local context issues. A database with information on investigators and research facilities, as well as records gathered in the initial application, also help with local context. And good communication with local sources is vital, Bowen said.

Other participants at the OHRP meeting also stressed the need for good communication between local IRBs and whatever sort of central IRB they may turn to for help. Horowitz, for instance, a champion of central review boards, urged local IRBs to be in frequent contact with any outside IRB that they used. “My advice on that front is to treat an outsourced IRB no differently than you would an in-house IRB. Consider them as ‘your IRB,’ not as a separate entity,” he said.

Bianco agreed that no matter what form you decide upon, “it’s not us versus them; it’s how can we best protect human subjects together.”

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