Central IRBs: Why Are Some Institutions Reluctant To Sign On?

There are several good reasons why hospitals and cancer centers would want to use central institutional review boards (IRBs) to supplement their often overburdened local boards that are charged with overseeing research involving human subjects. What’s more, several national agencies support central IRBs: The U.S. Food and Drug Administration issued a draft guidance in March to help increase awareness of central IRBs, the Office for Human Research Protections (OHRP) looks favorably on them, and the American Society of Clinical Oncology officially endorses their use. So does the National Cancer Institute, which has established two central IRBs for institutions participating in its phase III cooperative group trials.

Centralized review, according to representatives from all of these organizations, can be more efficient and more effective in protecting clinical trial participants because it reduces the burdens on local IRBs, eliminates duplication of effort, and can bring to bear expertise that may not be available at the local level.

Nevertheless, “lots of institutions are not buying into it,” said Ernest Prentice, M.D., associate vice chancellor for academic affairs at the University of Nebraska Medical Center and chairman of the Health and Human Services Secretary’s Advisory Committee on Human Research Protections (SACHRP). Worries about liability, confusion over how local and central IRBs should work together, and concerns about administrative hassles account for some of their reluctance, according to Prentice and others who have been involved in IRBs.

In addition, local IRBs have traditional ties to and a sense of responsibility for their own communities. Decades ago when institutional review of clinical trials became mandatory, most trials took place at a single academic institution and the IRB regulations were “founded on the premise of local autonomy,” said Prentice. “The idea was that IRBs would know their own culture and participants best.”

Increase in Trials

But in the 1990s, clinical trials proliferated and IRB workloads increased dramatically. Multicenter trials became more common, and IRBs at dozens of institutions were reviewing the same protocols. Staffing did not keep pace, and the review process slowed down, Prentice said.

In the meantime, trials sponsored by pharmaceutical companies were increasing in number and moving away from academic centers and into the private sector. That created a need for IRBs that private-practice physicians could use. One result was the growth of independent or “commercial” IRBs that provide reviews for a fee.

At first there was a tendency to suspect independent IRBs of bias in favor of industry sponsors, Prentice said. “But there is no longer that prejudice,” he said. “It is clear that many independent IRBs are better than academic IRBs.” In fact, some now argue that local IRBs are the ones that may be biased. The Consortium to Examine Clinical Research Ethics, a group established in 2002 under the auspices of Duke University Medical Center, points out that local IRBs can have an inherent conflict of interest because the IRBs are funded by the same institution that conducts and oversees the research under review. In an editorial that appeared in the *Annals of Internal Medicine* a year ago, Ezekiel Emanuel, M.D., chief of clinical bioethics at the National Institutes of Health, and other members of the consortium recommended that central IRB review be required for multisite trials.

The SACHRP took up the central versus local IRB issue at its meeting last October, and the panel agreed to hold a national workshop—which is now scheduled for this fall and will be sponsored by OHRP, ASCO, and the Association of American Medical Colleges—to clarify the value of centralized review and understand barriers to its use. Encouraging centralized review also appears to be one goal of the FDA’s draft guidance.

“What we are trying to do is get people to think about this possibility,” said Bonnie Lee, associate director for human subjects protection policy at the
FDA. “This might be a way to increase both efficiency and effectiveness of human research protections.”

**Barriers to Use**

Although these nudges from national organizations could help, getting institutions to make greater use of central IRBs may take a while. A recent AAMC survey of U.S. medical schools found little enthusiasm for the idea. Survey authors Evangeline D. Loh, Ph.D., and Roger E. Meyer, M.D., both of AAMC, concluded that “in spite of much discussion about the advantages of central IRBs … the majority of medical schools surveyed had never used a central IRB and expressed no interest in doing so.”

The NCI’s central IRB for cooperative group phase III trials also seemed to receive a lukewarm response when it first convened in 2001. The number of participating institutions has risen sharply in the past year—in May 2005, there were 535 participating sites compared to 254 reported in April 2004—but so far just 139 have accepted a review from the central body. NCI recently instituted another central IRB for pediatric trials that now has 92 participants, 19 of which have accepted a centralized review.

Experts cite several reasons for institutional reluctance to use any central IRB. One, the fear of liability, stems from an increasing number of lawsuits brought by clinical trial participants against institutions. Also, the shutdown of trials at places like Johns Hopkins and Duke by the OHRP “put the fear of God into lots of institutions,” said Prentice. “The feeling was that if we’re going to be liable, we should do it ourselves.”

Many institutions may be confused relate to each other. “There’s an erroneous impression that when you accept a central IRB review, you give up everything,” Prentice said, “and that’s not true.” This confusion over the roles of central and local IRBs is addressed in the FDA draft guidance, which gives examples of several models showing how the relationship can work.
that encourages ethical conduct. Robert Levine, M.D., co-chair of the Yale University Interdisciplinary Project in Bioethics and longtime IRB participant, sees the advantages of local control. “You are getting the word out that these are our values, that we are not merely a deputy sheriff to FDA,” he said in an interview. With central review, “you lose a sense of a community of compliance, the ability to influence people within the institution,” he said.

Nevertheless, central review can be practical, Levine acknowledged, especially for the multisite trials common in cancer research. “The oncologists have a point,” he said.

—Caroline McNeil