Carolyn Gretton

Watching the PROTECTORS

Increased regulation and decentralized data-collection processes are just some of the challenges faced by institutional review boards (IRBs) in safeguarding the rights and welfare of clinical trial participants.

Ever-changing clinical-trial regulations and continued growth in multicenter and international studies have resulted in an exponential increase in the volume of data generated for IRB review, including large numbers of individual adverse event (AE) reports, which often lack the context and detail needed for full analysis and thus limit the IRB's ability to ensure patient protection.

In January 2009, the FDA issued recommendations for sponsors and investigators conducting clinical research on how to identify which AEs represent "unanticipated problems" and must be reported to the IRB, as well as how best to convey the information. According to the FDA's guidelines, sites should report an AE to the IRB if it is unexpected, serious, and has a major impact on the conduct of the study, like a significant – usually safety-related – change in trial protocol.

However, the guidelines also acknowledge the difficulty in interpreting which AEs are isolated occurrences and which indicate more widespread risk. The FDA guidelines note that AEs "generally require an evaluation of their relevance and significance to the study, including an aggregate analysis of other occurrences of the same (or similar) event, before they can be determined to be an unanticipated problem involving risk to human subjects."

While these guidelines have helped clarify the AE reporting process for clinical sites and IRBs, they have done little to address the challenge of multisite trial overview. Under the current framework, there is often little or no central supervision or coordination of the individual IRBs involved in monitoring each center participating in a multicenter trial, resulting in wasteful redundancies and increasing the potential for miscommunication or misuse of data.

The Department of Health and Human Services recently warned that the need for separate IRB reviews at each clinical site involved in multicenter trials may compromise patient safety instead of offering additional protection. In a Perspective article published in the Oct. 13, 2010, issue of the New England

AAHRPP's Principles for Accreditation of Human Research Protection Programs

What AAHRPP expects from organizations

- Protecting the rights and welfare of research participants must be an organization's first priority. An organization should promote a research environment where ethical, productive investigation is valued.
- Protecting research participants is the responsibility of everyone within an organization and is not limited to the IRB. Accreditation examines whether the policies and procedures of the organization as a whole result in a coherent, effective system to protect research participants, and that all individuals know their roles and responsibilities.
- Striving to exceed the federal requirements and continually seeking new safeguards for protecting research participants while advancing scientific progress must be integrated into an organization's mission.

What organizations can expect from AAHRPP

- The standards for protecting participants in human research will be clear, specific, and applicable to research across the full range of settings. Standards will address any special concerns (e.g., the use of vulnerable populations or heightened risk to privacy and confidentiality) that may arise in each setting.
- The standards will identify outcome measures that organizations can use to assess and demonstrate quality improvement over time.
- The standards will be performance-based using objective criteria and measurable outcomes to evaluate whether a human research protection program effectively implements the standards. The evaluation will result in a grade of pass or fail for each standard and, where appropriate, will also include commendations or recommendations for meeting the standards.
- The accreditation process will provide a clear, understandable pathway to accreditation, along with equally clear pathways for appeal and the remediation of identified shortcomings.
- The accreditation process will be educational involving collegial discussion and constructive feedback. The accreditation process will identify areas in which the human research protection program does not yet meet the standards and give organizations the opportunity to discuss potential program improvements.
- The accreditation process will be responsive to changes in federal regulations and to standards that will evolve based on what AAHRPP learns from accrediting organizations from research settings.

Source: Association for the Accreditation of Human Research Protection Programs. For more information, visit aahrpp.org.

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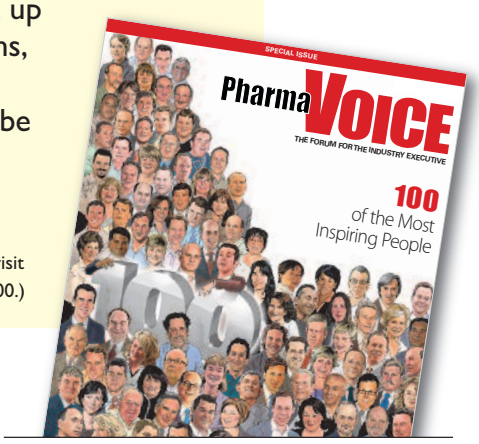

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Read. Think. Participate.

Journal of Medicine, Jerry Menikoff, M.D., J.D., director of the Office for Human Research Protections in HHS, offered two potential solutions to the problem: establishing a central IRB for multisite studies or allowing the HHS to take action against IRBs that per-

VIEWPOINTS

Technology to Improve Patient Safety

I believe the more an IRB can use technology to reduce repetitive tasks in the IRB process the more time the IRB will have to focus on subject safety. If an IRB can find ways to reduce time staff are spending on administrative work, more time will be available for reading the details and looking for trends. Using technology allows for human eyes to spend more time looking at what is going on with actual subjects, as opposed to spending time generating documents.

MATT BAKER
President and CEO
CompassIRB

Adhering to the Highest Standards

Ensuring patient safety involves a complex matrix of best practices. IRBs must continually and consistently evaluate research to ensure all criteria for approval are met, including making sure that risks to subjects are minimized. IRBs must have systematic processes to ensure that investigators are qualified to conduct research in accordance with applicable regulations and IRB requirements. Accreditation provides an evaluation process that IRBs use to ensure the highest standards of subject protection.

ERIN BROWER, M.S., CIP
Director of Operations
New England IRB

Defining SOPs

IRBs should have clearly defined SOPs and procedures which require principal investigators and/or sponsors to properly report data to it that may affect subject safety. Proper reporting should be limited to data that genuinely affect subject safety, such as unanticipated problems involving risks to subjects and others, significant protocol deviations, and investigator noncompliance. Once safety data are received, IRBs should have procedures and training to thoughtfully and promptly review it and respond appropriately.

JOHN ISIDOR
Senior Director and Founder
Schulman Associates IRB

What is an "Accredited" IRB?

The accreditation of IRBs began several years ago. One of the goals of accreditation is the improvement and continuing education of the organizations that seek it. Accreditation is usually voluntary and is granted for a specific period of time, generally three or more years, following which the organization must repeat the process. Accreditation is a long-term, continuous activity, both for the accrediting body and for organizations under review. Protecting the public is the goal of accrediting organizations.

Source: Association for the Accreditation of Human Research Protection Programs (AAHRPP). For more information, visit aahrpp.org.

mit violations of ethical standards. HHS is considering the second option, though no formal action has been taken on the proposal.

Seal of Approval

Academic medical centers and hospitals have traditionally maintained internal IRBs to review the research of investigators affiliated with their institutions. More recently, as research has moved into community-based clinics, independent IRBs have been established to provide review services to investigators not affiliated with an academic institution or research organization. These independent IRBs are subject to the same federal and state regulatory requirements applicable to all IRBs.

One way in which both independent and internal IRBs strive to indicate their commitment to patient safety is by voluntarily seeking accreditation from organizations such as the Association for the Accreditation of Human Research Protection Programs (AAHRPP) and the Consortium of Independent Review Boards (CIRB). These agencies conduct periodic reviews of member IRBs to determine whether they are committed to improving the systems that protect the rights and welfare of clinical study participants.

It should be noted, however, according to Marjorie Speers, Ph.D., president and CEO, of the AAHRPP, applying for accreditation is not indicative of an organization's ability to earn accreditation. Organizations must meet a total of 98 standards and elements. These standards and elements meet or exceed the U.S. federal requirements and are consistent with ICH-GCP guidelines for protecting human research subjects. PV

EXPERTS

JERRY MENIKOFF, M.D., J.D. Director of the Office for Human Research Protections, The Department of Health and Human Services (HHS), the United States government's principal agency for protecting the health of all Americans and providing essential human services, especially for those who are least able to help themselves. For more information, visit hhs.gov.

MARJORIE A. SPEERS, PH.D. President and CEO, the Association for the Accreditation of Human Research Protection Programs Inc. (AAHRPP), which promotes high-quality research through an accreditation process that helps organizations worldwide strengthen their human research protection programs (HRPPs). For more information, visit aahrpp.org.