

Keeping Research Subjects Out of Harm's Way

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OBSERVERS OF HUMAN EXPERIMENTATION IN biomedicine and behavior are sounding cautionary notes that demand attention. In scientific research, "continued vigilance [is] critical to protecting human subjects," reports the US General Accounting Office.¹ "The effectiveness of IRBs is in jeopardy," concludes an analysis of institutional review boards (IRBs) by the US Department of Health and Human Services' Office of Inspector General. "With this report, we offer a warning signal," says the inspector general.² In this issue of *THE JOURNAL*, Woodward identifies trends that "erode" human subject protections.³ These are strong words that connote peril. Given that the inspector general also declares, "We do not document, nor do we suggest that widespread harm is being done to human subjects,"² the words are, perhaps, too strong. It is, after all, by any probabilistic measure, relatively safe to be a human research subject. This is precisely the time to take constructive account of the notes of caution being sounded and to reform, correct, revise, and improve the dynamic and evolving system that keeps those who are enrolled in research out of harm's way.

Researchers, research institutions, and research sponsors are together responsible for creating and maintaining an environment that embraces the primacy of the rights and welfare of people who volunteer to be research subjects.⁴ This requires, more than anything else, an enduring program of education. Education is cheap, effective, preventive maintenance for the current system of protecting human subjects. It begins with an understanding that, for activities sponsored by any of 17 federal departments and agencies, the 1991 common Federal Policy for the Protection of Human Sub-

jects⁵ contains regulations that govern human experimentation. "Research" means a systematic investigation designed to develop or contribute to generalizable knowledge, and "human subject" means a living individual about whom an investigator conducting research obtains either data through intervention or interaction with the individual or identifiable private information. Complementary rules of the Food and Drug Administration⁶ define these 2 concepts in ways that differ from the 1991 Federal Policy in specific detail, although not in their basic idea. Because the process of protecting human study subjects essentially begins with a process of prospective self-referral by investigators of themselves and their research to IRBs, it is imperative that all understand precisely when a planned activity will constitute research involving a human subject.

There is no upper limit to the amount of information about the nuances of protecting the rights and welfare of research subjects. There is always more to learn, for example, about communicating risks to prospective subjects in the consent process, about crafting language understandable to the subject, or about protecting the privacy of subjects and confidentiality of personally identifiable data. Consequently, and with cautionary notes now echoing broadly, this is no time to pay mere lip service to the need for education. It is time for action.

Researchers, institutions, and sponsors that do not avail themselves of opportunities for education regarding the ethical aspects of their endeavors are courting trouble, just as they would be if they did not keep up with their science.

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See also p 1947.

Notable among 20 recommendations recently suggested by Moreno et al⁷ to update protections for human subjects involved in research is that research institutions sponsor at least 1 educational session per year for IRB members, local investigators, and other interested persons.

The leaders of research institutions set the tone for the ethical conduct of research under their institutions' auspices. Attentive and creative institutional leadership creates a culture in which both IRBs themselves and the function of protecting human subjects are held in high regard. All personnel need to receive a memorandum in which research involving human subjects is defined. This memorandum should simply parrot the definitions found in federal regulations. There should be wide circulation of the name and telephone number of a specific contact for questions about human experimentation—generally, the IRB office. All personnel need to be periodically reminded of an institution's obligations to safeguard the rights and welfare of human subjects.

IRB records are the best integrated index of how well an institution exhibits compliance with policy on human subjects. One IRB record in particular—the written minutes of IRB meetings—should clarify how the institution is handling protection of human subjects. Physicians know that in the practice of medicine, if it is not documented, it was not done. The maxim is applicable to research as well.

IRB records are required by federal regulation to show attendance, actions taken, votes, the basis for changes or disapprovals, a summary of controverted issues, and any alterations or waivers of informed consent that the IRB approves. The minutes should show certain findings any time research involving children is approved. If inspection of the minutes does not permit determination of precisely how and by whom a research proposal was handled and discussed at an IRB meeting, the IRB actually may not be doing what it is required to do.

Is this an inappropriately bureaucratic emphasis on mountains of paperwork and record keeping? If that were truly the motivation behind the process, it might be inappropriate. For the most part, IRB records are integral to the actual protections conferred on human study subjects. In reviewing proposed research, IRBs require sufficient information to make determinations required for modification, improvement, and approval of research protocols. This includes information regarding (1) procedures that minimize risks to subjects, (2) subject recruitment and enrollment procedures, (3) the equitable selection of subjects, (4) provisions to protect the privacy of subjects and maintain the confidentiality of data, (5) provisions for monitoring data to ensure the safety of subjects, and (6) additional safeguards to protect subjects who are likely to be vulnerable to coercion or undue influence. Absent this information, the IRB cannot perform an informed review and cannot provide direction for revision of research protocols if needed. An IRB review that lacks the required substance is not meaningful.

Institutional review boards review the informed consent process and its signal feature, the informed consent docu-

ment. Federal regulations require that an investigator seeking consent of a prospective subject present multiple elements of information in language understandable to the subject. This means, for example, that prospective subjects who do not speak English should be presented with a consent document written in a language understandable to them. (The fact that this point needs to be mentioned, and that review by the federal Office for Protection from Research Risks of certain IRB files indicates that it does need to be mentioned, is remarkable.) Paperwork? No, this is a matter of serious substance. A telephone call to the local school system can help inform a research institution of the languages spoken in its potential research-subject catchment area. Overall, when properly made, IRB records are a reflection of what is proposed to the IRB, approved by the IRB, and actually taking place in the research reviewed by the IRB.

Protecting research subjects requires resources. Institutional leaders should consider surveying IRB members, administrators, and staff to determine their unmet needs for resources. In the experience of the Office for Protection from Research Risks, inadequate institutional support is the root cause of compliance problems with research subject policy. Protecting human subjects by means of local IRBs began more than 25 years ago as a largely volunteer effort with informal financing. Today, this undertaking is best viewed as a demanding, professional undertaking requiring a formal budget.

In many ways, researchers seeking an individual's consent to experimentation come as strangers at the bedside.⁸ All investigators should recognize the exquisite vulnerability of the prospective research subject that is inherent in his or her situation. Only by prospectively addressing the circumstances surrounding researchers' solicitation of consent to research, and the special relationship that endures throughout the experiment and beyond, can human subjects be fully protected. That is the challenge currently being articulated in strong, cautionary words.

This is not a new challenge. In 1972, Katz et al⁹ asked, "When may a society . . . expose some of its members to harm in order to seek benefits for them, for others, or for society as a whole?" In 1993, Katz added, "Ultimately, it is necessary to conduct human trials in order to acquire the necessary knowledge to alleviate human suffering."¹⁰ Later, Katz warned investigators against "employing the concept of voluntary consent as a deceptive subterfuge to shift moral responsibility for participation in research from themselves to their patient-subjects."¹¹

With great care, this challenge can be met, and the task can be done well. Society has long since agreed that the pursuit of new knowledge in biomedicine and behavior—knowledge that ultimately benefits all—can be performed only in keeping with the highest standards of ethics. Respecting the rights of research subjects and providing for their welfare is to honor a deep obligation to those individuals who make a remarkable contribution to the common good by volunteering to serve as research subjects.

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