Symposium: Bioethics in Scientific Research: Conflicts between Subject’s Equitable Access to Participate in Research and Current Regulations

Looking into the Institutional Review Board: Observations from Both Sides of the Table

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ABSTRACT

Institutional review board (IRB) reviews offer the benefit of perspective afforded by the board’s distance from the research and the research subjects. At the same time, distance from research subjects that is geographic, socioeconomic, cognitive, linguistic, and cultural can undermine the positive role of perspective. In addition, distance between IRB and investigators, largely a result of attitudes and communication, can prolong the review process and can obscure its message. The tension that often characterizes IRB–investigator relationships is due, in part, to variability in the application of federal regulations by IRBs across institutions and, on the part of investigators, inexperience, communication problems, and difficulties in anticipating the needs of their subjects. Contributing to the variability are the demographics and the culture of the IRB, attitudes that influence IRB–investigator relationships, and the adequacy of support from the institution. The effects of these factors on review decisions and on the performance of the human subjects protection system are largely unstudied. The movement for IRB accreditation is causing institutions to examine their overall research protection system and promises a more collaborative approach, where IRB and investigators accept their common charge to meet the needs of subjects and to improve the quality of research. J. Nutr. 135: 921–924, 2005.

KEY WORDS: • IRB • human subjects • research protection

This symposium focuses on the current state of the research human subjects protection system and its effect on subject access to the presumed benefits of research. My article explores 2 major themes of relevance to this topic: characteristics that influence the process and outcome of institutional review board (IRB) review and interactions between investigators and review boards. I propose that much of the tension that often characterizes IRB–investigator relationships is due to variability in the application of federal regulations by IRBs across institutions and, on the part of investigators, inexperience, communication problems, and difficulties in anticipating the needs of their subjects. Contributing to the variability are the demographics and the culture of the IRB, attitudes that influence IRB–investigator relationships, and the adequacy of support from the institution. The effects of these factors on review decisions and on the performance of the human subjects protection system are largely unstudied. The movement for IRB accreditation is causing institutions to examine their overall research protection system and promises a more collaborative approach, where IRB and investigators accept their common charge to meet the needs of subjects and to improve the quality of research. J. Nutr. 135: 921–924, 2005.

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The basis for these observations and advice is 13 y as a participant observer, including serving as a reviewer for 3 IRBs and developing an IRB for a new institution. A review of the literature describing the results of research on the IRB demonstrates that the great majority of research on human subject protection examines the consent process: subject comprehension and cognitive capacity, language level of consent forms, communication, and enrollment bias (1–11).

Unfortunately, systematic research with the IRB as the subject is sparse, despite, as Oakes (12) points out in his thoughtful guide for social scientists approaching a world of biomedical review procedures, the many interesting questions...
raised by applying social science methods to study the operations of IRBs.

Variability in the review outcomes

Both IRBs and investigators are operating under a set of rules: the rules of scientific investigation and the scientific method govern protocol design. Regulations, spelled out in Title 45 of the Code of Federal Regulations Part 46, dictate the responsibilities, operations, and composition of IRB in the United States. Within that regulatory framework, IRBs are given wide procedural and decisional latitude. Some resulting inconsistencies in approval decisions, documentation provided to investigators, and applications of standards have been documented in a few studies (13–16). Investigators whose research involves multiple institutions and those who have served as IRB members in multiple settings may have experienced these inconsistencies firsthand. Some variability is intended and desirable, allowing flexibility and responsiveness to local circumstances. However, even as we know very little about the range and the characteristics of this variation, we know even less about its effect on either the scientific enterprise or on the experience of human subjects. Several factors contribute to variability, including the demographics and the culture of the IRB, the attitudes that influence IRB–investigator relationships and the adequacy of support from the institution.

Attitudes, beliefs, and the problems of perspective

Although an investigator disturbed by the process at his institution may feel differently, IRBs do not exist to frustrate investigators, to fund bureaucrats, or to add paperwork burden. The human subject protection movement that IRBs endeavor to address did not evolve alongside advances in scientific inquiry but developed within the last 30 y in response to documented abuses and ethical violations (17). The regulatory environment that exists today is a direct result of horrific ethical violations, hubris on the part of investigators, and lack of attention to detail. This sorry history of exploitation and corrective responses by individuals and government is well described and forms the basis for all educational programs in research ethics in the United States (18).

Whereas no scientist is likely today to deny the need for human subject protection, investigators often fail to appreciate the relevance and the importance IRB review and the consent process bring to their own research. The result is a cognitive dissonance in investigators characterized by the attitude that, “Yes, this is important in the grand scheme but is not a priority for me because: (a) my work does not really involve humans, just their blood or tissue samples; (b) I know my patients/subjects well, and they trust that I would not do anything to harm them; or, perhaps, (c) my research assistant takes care of this type of thing.”

In my experience, investigators, and, in particular, new investigators, approach the IRB with attitudes ranging from annoyance and impatience (“they want me to jump through hoops”) to fear (most common with residents and graduate students, who have been filled with tales about the horrors of IRB review). In most circumstances, looming deadlines add an overlay of haste and anxiety to the interaction.

In light of the sometimes contentious rhetoric that characterizes investigator frustration with IRBs, it is worth noting that IRBs are as much a part of the scientific review process as is a sponsor review committee. As Oakes (12) notes, “IRBs are peer/community review mechanisms analogous to journal editors who require changes to an article or NIH/National Science Foundation scientific review groups who determine the fate of grant applications. . . . That scientists are constantly required by others to make (occasionally silly) changes to their work but squawk and flap loudly when IRBs require the same is astonishing.”

At the same time, attitudes among individual reviewers can reinforce investigator misgivings. The reviewer approaches a protocol with an eye critical not only to the science but also in judgment of the investigators’ motivations, perhaps holding a preconceived skepticism (if not downright suspicion) about the investigators’ concern for subjects. These attitudes may be more or less ameliorated, depending on the reviewer’s own experience with research, but they can be reinforced by group dynamics.

The IRB as a social entity takes on a distinct culture that is influenced by the culture of the institution it serves. The likelihood that this is true becomes apparent when we consider the variety of institutions that are represented by IRBs, including universities, hospitals, research institutes, and government agencies, not to mention the independent, for-profit IRBs. Although IRBs are charged with representing the interests of research subjects, they operate on behalf of these institutions. For example, in hospitals where physicians tend to hold more decision-making power, the IRBs may have a different orientation than those whose culture is more explicitly nursing oriented. The IRB chair may represent powerful interests in the scientific hierarchy of the institution or may tend to favor basic over applied or clinical science in academic settings. IRB leadership often overlaps with institutional research leadership, positions that are responsible for research advocacy and that are likely to be supported with research revenues. IRB reviewers are generally scientific peers who serve as volunteers, a situation that tends to favor persons who are older and more advanced in their careers. Lay or nonscientific members of the IRB present a unique set of issues. They must be of an educational level sufficient to understand complex protocols, be assertive in the face of fellow members who may tower above them in income and prestige, and, at the same time, provide the important perspective of those who have nothing to gain from protocol approval.

Perspective from many sources and relevant points of view is a primary function of the IRB. The value of perspective is apparent in all areas of review. IRBs are mandated to consider a broad definition of risk that goes beyond physical risk or potential loss of confidentiality. Some IRBs will take the position that research participants should not be subject to scientific methods that will likely produce useless results and may reject or suggest revisions to improve scientific quality, validity, and value. In addition to concerns about methodology, IRBs are also concerned that statistical power and sample size calculations justify proposed enrollments, especially in protocols they define as posing more than minimal risk.

IRB review is intended to identify the implications of the research, as well as risks and benefits, for both individuals and communities, and to ensure that they are clearly spelled out in the consent process. Ethical implications invariably involve operational issues. Will there be nonreimbursed costs to the subject? Is the time commitment accurately spelled out, and is any compensation commensurate with time spent? Are there discomforts associated with participation that the investigators

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3 Some of this variability is reflected in nomenclature. I will refer to committees charged for the protection of human subjects in research as IRB, however they are often entitled Human Investigation Committee, Medical Ethics Board or similar.
have not considered? Will participation raise expectations among the subjects and the community that cannot be met by the research project, the investigators, or the institutions involved? What will happen to subjects when the study is completed? Finally, does the consent form contain the answers to these questions? There is growing interest in incorporating procedures to evaluate subject cognitive capacity, literacy and the degree of agreement between the research protocol and a subject’s understanding of the personal implications of participation (7,11,19). In many cases, investigators will have considered these aspects before review, but the additional perspective provided by a multidisciplinary group of experienced reviewers invariably expands and improves upon the consent process.

In addition, the IRB grapples with conflict of interest issues, such as the amount of financial or professional gain to the investigators and when this should be disclosed to subjects. Based on the questions that appear on IRB listservs, there is little consensus on how much subjects should be told about budgetary issues.

Perspective vs. distance

The IRB offers perspective on the research due to its relative distance from the research and the research subjects. At the same time, distance may have a negative influence that can overwhelm the positive role of perspective. Such distance may be geographic, socioeconomic, cognitive, linguistic, and cultural. In general, IRBs reflect the makeup of the institution rather than the subjects of research. Demographically, IRBs tend to be white, male, and from the upper strata of education and income (20,21). Citations for lack of diversity among IRB rosters are common sources of the federal Office of Human Research Protections findings of noncompliance. Members of minority groups selected to serve on IRBs are likely to be from higher socioeconomic levels, compared with community norms. There may be only one person of a specific ethnicity on an IRB, yet that one person is expected to represent the voice of “the community.” Nor is this strictly a problem of ethnic minorities. Within my own institution, an academic children’s hospital, many studies involve adolescents and young adults. Our patients are drawn from inner city, largely Latino, neighborhoods surrounding the hospital. In this situation, which is by no means unique, the IRB reviewers need to act as anthropologists seeking to understand the worldviews of diverse research subjects. Few biomedical scientists assume this role easily. Investigators often face similar challenges, but the distance between them and their subjects may be decreased by frequent interaction, common ethnicity, or insights from their research. We have only anecdotes to evaluate the extent to which these factors influence the review process.

IRB oversight and concern increase in proportion to their perception of subject vulnerability. Children, the incarcerated, and persons unable to speak for themselves are accorded special regulatory protection, a position that is relatively uncontroversial when vulnerability is clear-cut, but one that is often complicated to apply (22,23). Studies involving adolescents are more complex, involving issues of privacy, disclosure, and legal status to consent (24,25). In general, as distance of any type increases, both the IRB and the investigators are more likely to err in their assessment of subject needs, expectations, comprehension, and attitudes toward research. An IRB may overestimate vulnerability in cross-cultural situations, because they lack knowledge of the culture or the situation in the field. Although IRBs are charged with possessing “sufficient knowledge of the local research context” to meet the requirements of their federally approved assurance, scientists whose research involves subjects in disadvantaged communities of the developing world may confront an IRB whose concern for protection results in unrealistic strictures placed on the consent process or on the protocol itself (26). Confronted with this situation, the responsibility lies with the investigators to educate the IRB about their research communities, in addition to presenting specific research protocols.

Culture and beliefs can pose barriers that increase distance between the IRB and the research participants. The IRB model, developed in the United States and other Western nations, is based on values of individuality (autonomy) and is centered on the concept of individual informed consent. The IRB model can be at odds with cultural values that emphasize importance of family, clan, or community over those of individuals (27). An individual consent approach can result in decreased enrollment and can, in the worst case, put subjects at risk. Similarly, cultural and linguistic barriers contribute to low participation rates in clinical research among minority groups in Western countries (28). These issues are increasingly important as the research community and the pharmaceutical industry struggle to adapt the Western biomedical ethics model in clinical trials throughout the world.

Communication between IRBs and investigators can pose another type of distance problem. IRB review should improve research quality, but a positive result is largely determined by quality of communication between the IRB and the investigators. The first IRB challenge is to arrive at an understanding, if not consensus, about what changes they will require. Secondly, they must clearly convey this understanding. Their work is not helped by protocols and consents that do not meet even minimum standards. Too often a common theme in meeting is, “What is this investigator trying to do,” only to be followed by its corollary from the investigator, “What does the IRB want from me?” Communication barriers can be clerical or operational, and tend to increase with IRB workload. Recent studies have confirmed the growing workloads that IRB staff and reviewers are forced to manage. In my experience, institutions must be convinced to support the IRB with sufficient resources to meet their responsibilities.

What are IRBs doing to decrease distance?

Coalitions led by health care, private, and governmental organizations are taking responsibility to improve the review process. The movement toward quality improvement has resulted in new standards and accreditation for IRBs (29). Though still voluntary, accreditation is likely to become an institutional standard demanded by research sponsors. In preparing for accreditation, institutions are forced to look at their overall research protection system, including safety and compliance, and to address any gaps.

Beyond system issues, IRBs need to do more to let investigators know how they operate and to make the review process clear for applicants. Review outcome, approval contingencies, and expectations should clearly communicate what is needed for approval. Examples of model consent forms, suggestions for appropriate language level, and educational approaches that respect the time demands on investigators are a few ways to improve the overall quality of applications and to reduce frustrations on both sides. Both IRB and investigators need to view the process as collaborative, where both parties are working together to meet the needs of subjects and to improve the quality of research.
What can investigators do?

The first step toward a more collaborative approach is for investigators to approach the IRB with the expectation that they will learn something from the review and that their research will benefit. Investigators who make an effort to become familiar with relevant ethical issues discussed in the literature will have an advantage negotiating the review process. Applications should go beyond describing the study; investigators should be prepared to document special considerations or information that will assist the reviewers and should not assume that these factors will be self-evident. An IRB will be forced to assume the worst case in the absence of good data on risk (12). The rationale behind the proposed consent process ought to be explained clearly. Consent forms should be written for subjects, not for scientific peers on the IRB, and should be pretested with a nonscientist. If investigators can make the time, it is recommended that they serve on IRBs. This service will clarify all those issues about IRB review that seem so opaque, and the insights brought to the process by investigators may make a difference.

If we are to continue to refine human subject protection and to improve the quality of our research, IRBs and investigators need to look for ways to build trust. IRBs trust that investigators will follow the human subjects aspects of their protocol as stated. Investigators need evidence to trust that IRBs are interested in advancing research (30). Investigators can reasonably demand more information from IRBs about their operations, procedures, and culture. In turn, IRBs can demand that investigators become educated about human subject protection and do a better job anticipating and meeting the needs of research subjects.

LITERATURE CITED