

Streamlining Ethical Review

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The review system for human subjects research in the United States has been widely criticized in recent years for requirements that delay research without improving human subject protections. Any major reformulation of regulations may take some time to implement. However, current regulations often allow for streamlined ethics review that does not jeopardize—and may improve—protections for research participants. The authors discuss underutilized options, including research that need not be classified as human subjects research, categories of studies that can be exempt from ethical review, studies that need only undergo expe-

ditied review by 1 institutional review board (IRB) member, and simplifying reviews of multicenter research by using the IRB of 1 institution. The authors speculate on multiple reasons for the underuse of these mechanisms and exhort IRBs and researchers to take advantage of these important opportunities to improve the review process.

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The review system for human subjects research in the United States has been widely criticized in recent years. Many commentators, particularly within the research community, complain of pointless bookkeeping requirements that sap the morale of institutional review board (IRB) members (1) and delay and obstruct lifesaving research (2).

Various diagnoses have been offered and corresponding regulatory changes proposed to deal with what Fost and Levine (3) call the “dysregulation of human subjects research.” However, even if the regulations were to be substantially reformed, such change would take time to implement. In the meantime, ethics review could be streamlined under the current regulations if institutions, IRBs, and researchers adhered strictly to the definition of human subjects research and used the available options for exemptions, expedited review, and centralized review (4)—options that remain underused in biomedical research.

According to Marjorie Speers, President of the Association for the Accreditation of Human Research Protection Programs, many institutions label activities as “human subjects research” that do not fall under the federal definition (5). Although much low-risk human subjects research is exempt from review, some institutions insist on having all their research reviewed by IRBs (6). A 1998 report (7) found that for each category of exempt or expedited research, 25% to 77% of U.S. IRBs “practice some form of review that was more rigorous than specified by the regulations.” There appear to be no data that contradict this picture today.

These options may be underused for several reasons. One key reason is probably lack of awareness, but another is the fear of the consequences if the regulations are deemed to be violated, which can include the complete suspension of an institution’s federally funded research. Our purpose here is to both inform and reassure.

HUMAN SUBJECTS RESEARCH

Institutional board review is legally required for research conducted or funded by certain U.S. federal agencies (8), regulated by the U.S. Food and Drug Administra-

tion, or carried out at institutions that have elected to subject all their research to the Common Rule requirements. The regulations apply only to “human subjects research,” in which investigators obtain data through some “intervention or interaction” with living people or obtain identifiable private information about them (9). Data from people whose identities the investigator cannot “readily ascertain” are not identifiable private information (10). For much medical research, particularly that which uses clinical data, researchers do not need to know the identity of the participants and therefore need not conduct human subjects research. For example, research that uses data from medical records can be conducted in such a way that the researchers cannot identify the person from whom the data comes. Someone not involved in the research could remove the identifiers from the data (such as the 18 specified Health Insurance Portability and Accountability Act identifiers) (11) and agree never to disclose the code that links those data to specific individuals. Researchers could even set up a mechanism for receiving and removing the identifiers from future data without the regulations applying.

EXEMPTIONS AND EXPEDITED REVIEW

Even if a proposed research study is human subjects research, it may fall into 1 of the 6 categories that are exempt from ethical review. Two categories are of particular interest to biomedical researchers. Category 2 exempts research that uses only educational tests, survey procedures, interviews, or observation of public behavior, unless the data recorded are both identifiable and potentially harmful if disclosed. For example, the work of a researcher who interviewed patients with HIV/AIDS about their medications and recorded their names would not be exempt under category 2, because disclosure of the patients’ HIV/AIDS status could harm them. However, if the researcher conducted the interviews anonymously and never recorded the patients’ names or other identifying information, the study would probably be exempt.

Category 4 exempts research “involving the collection or study of existing data, documents, records, pathological

specimens, or diagnostic specimens,” if either the data sources are publicly available or the recorded data do not allow patient identification (9). For example, a retrospective chart review that examined the medications administered to the most recent 50 patients seen at a hospital emergency department for suspected cardiac infarction would be exempt, provided the data were recorded without patient identifiers. Decision charts for these exemptions are available on the Web site of the Office for Human Research Protections (www.hhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm).

If a protocol for conducting human subjects research is not exempt, it may still be possible to expedite its review. Initial and continuing review of certain categories of minimal-risk research, such as that which involves only the collection of blood samples or the noninvasive collection of other biological specimens, can be expedited (12). Expedited review is also permitted for minor changes in already approved research. The same standards are followed as for a full IRB review, but the review is done by just the chairperson or by designated experienced IRB members. Because expedited review can be conducted on an ongoing basis, its use should speed up the review process and reduce the time that the convened IRB spends reviewing minimal-risk research. The sparse data available indicate that for some institutions, expedited reviews save little money (13) and no time (14), which suggests that some IRB procedures also need streamlining.

MULTICENTER RESEARCH

Since the regulations were established, the number of collaborative studies that take place at multiple institutions has greatly increased. Because responsibility for ethical review rests with institutions, multicenter research frequently results in the IRB of each institution reviewing the same protocol (15). This both duplicates work and increases the time and resources spent getting research projects approved, as different IRBs mandate different (often minor) changes to consent documents and researchers go back and forth between them.

Again, regulatory resources for addressing this problem already exist. According to the Common Rule (9), when a research project involves more than 1 institution, “an institution participating in a cooperative project may enter into a joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.” This arrangement is underused mainly because of institutional reluctance to cede control and underlying liability concerns. The Office for Human Research Protections recently published a request for public comments on an amendment to the regulations that would allow it to hold IRBs and the organizations that operate them directly responsible for meeting some regulatory requirements, rather than always enforcing compliance through the institutions engaged in the research (16).

For example, if an independent IRB reviewed a particular study and incorrectly approved it by using expedited review when the study should have undergone review by the convened IRB, any compliance action would fault the IRB—not the institution that hired it to review the study. The amendment’s goal is to encourage more institutions to rely on review by an external IRB by reducing their liability concerns.

One existing “joint review” arrangement is the Central Institutional Review Board (CIRB) Initiative (www.ncicirb.org), sponsored by the National Cancer Institute, which covers certain National Cancer Institute–sponsored multicenter adult and pediatric cancer studies. For studies in the initiative, the CIRB performs a single review of the protocol. Local IRBs may then defer to the CIRB and perform only a “facilitated review” of ethical issues that arise because of the local context. The CIRB generally performs the continuing reviews, amendment reviews, and reviews of serious adverse events for the protocol.

ETHICAL CONCERNS

Medical research pursues the ethically important goal of developing interventions to improve human health. It does so under the constraint of another goal—protecting research participants. Measures that speed up the ethics review process clearly help with the first goal by reducing the time that it takes to develop health care interventions and allowing resources that would otherwise be taken up by ethical review to be directed toward beneficial research. Expending excessive resources on reviewing studies that pose minimal risks or replicating review by other IRBs is ethically troubling.

One concern, however, might be that speeding up ethical review would compromise the welfare of the people it is designed to protect. However, following these measures is unlikely to reduce human subject protections. The categories of research that are exempt or eligible for expedited review are unlikely to include highly unethical studies. For example, studies in these categories almost always pose no more than minimal risk to participants, which should ameliorate concerns about participant harm. Thus, the absolute probability of increased use of these measures leading to more unethical research is low.

In addition, IRBs always have constraints on their time and resources, and any time they spend reviewing one protocol takes away time from reviewing others. Institutional review boards should prioritize their time to focus on protocols that are more likely to generate ethical issues but need a way to determine whether a study will raise ethical issues without actually reviewing the full protocol. The regulatory measures we have detailed identify categories of research that are unlikely to be ethically problematic. Using them therefore frees up resources for reviewing riskier research.

ACTION

This article has 2 main goals: to inform biomedical researchers about the measures through which the ethical review of low-risk and multicenter research could be made more efficient under the existing regulations, and to extol the virtues of these measures to researchers, IRBs, and institutional officials. These measures may not only allow valuable research to be carried out more rapidly but also reduce the cost of protocol review and allow IRBs to focus on research that is more likely to be ethically challenging.

Researchers cannot act alone. Institutional review board offices and the officials who oversee them must be willing to prioritize time and resources by allowing exemptions and developing efficient procedures to expedite reviews. In addition, the institutions that host research must be willing to trust the ethical review systems at other institutions—and that trust must be built. Finally, regulatory bodies need to reassure the research community that their primary concerns lie not with meeting bureaucratic requirements but with genuinely protecting human participants. That message will help encourage institutions to appropriately streamline their policies and procedures by minimizing concerns about being subject to inappropriate regulatory responses.

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