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Protecting subjects without hampering research progress: Guidance from the Office for Human Research Protections

ABSTRACT

The Office for Human Research Protections (OHRP) within the US Department of Health and Human Services aims to protect human research subjects without hampering scientific progress. Institutions can foster safe and efficient research by guarding against conflicts of interest, making research subject safety a priority, having a well-staffed institutional review board, and continually training new investigators. The OHRP provides education on its Web site (www.hhs.gov/ohrp/) and is available to make site visits to offer guidance on federal regulations.

Scientific and technological advances have created new challenges in the area of human subject protection. Protecting subjects who participate in the testing of new medical products is essential for maintaining public trust and is regulated by both the US Food and Drug Administration (FDA) and the US Department of Health and Human Services (DHHS). These two government entities have similar, but not identical, regulations governing human subject protection.

The Office for Human Research Protections (OHRP) within the DHHS is obliged to protect subjects and ensure that they understand their rights as research participants. Because medical innovation is also an important goal, the challenge for the federal government is to balance protecting research subjects with facilitating medical product development.

This article discusses issues that often impede medical products from moving smoothly through the development, testing, review, and approval processes, including conflicts of interest and delays involving either research institutions or the investigators themselves. Suggestions for enhancing efficiency while remaining compliant with human subject protections are covered, as are ways in which institutions can work with the OHRP to meet their goals.

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CONFLICTS OF INTEREST IN HUMAN RESEARCH

The OHRP continually tries to identify and minimize issues that undermine the public trust. A known or potential conflict of interest on the part of investigators is often an important concern. Although financial conflicts are the first to come to mind, other conflicting interests can arise in research, including institutional, professional, and administrative types.

For example, an institutional review board (IRB) itself may be put in a conflict-of-interest situation: a member of the IRB may be urged to approve a research protocol by administrators or colleagues because a specific investigator who is needed by the institution may go elsewhere if approval is not granted. Both the FDA and the DHHS regulate conflicts of interest that arise from being a member of an IRB.

How OHRP handles complaints

When the OHRP receives a complaint about a potential conflict of interest in a research project, an initial investigation is performed to determine if enough evidence exists to pursue the matter. As for any complaint, we try to gather as much specific information as possible, preferably in writing, about the people and institutions involved and the exact nature of the problem.

The next step is to inform the research institution that a complaint has been made about a conflict of interest, and to ask if it is aware of the problem. If the institution is aware, we ask what actions have already been taken to resolve the problem. If it is not aware, we request that it investigate the matter and get back to the OHRP within a specific time period to discuss how it intends to handle the matter.

OHRP's purview

The OHRP has jurisdiction over studies that are conducted or supported by DHHS funds unless an institution has agreed, through the Federalwide Assurance agreement, to comply with the DHHS regulations for all research involving human subjects, regardless of the source of funding. If the OHRP does not have jurisdiction over a study in which a complaint arises, we can only inform the institution that a problem has arisen. If we have jurisdiction, we gather more information to determine whether we should pursue the matter further.

We also contact the FDA to determine if it has jurisdiction over the matter. We may transfer the case to the FDA, or, in some cases, both the FDA and the DHHS handle it, such as if the study is funded by the National Institutes of Health and involves a product controlled by the FDA.

IRBs CAN HINDER PROGRESS

The IRB sometimes hinders institutional research. A fine line exists between appropriate research oversight and actions that end up impeding research progress. Certain problems tend to arise that reduce efficiency:

Overinterpretation of regulations by institutions is a common problem. For example, some kinds of research are exempt from IRB oversight, but an institution may insist that it become involved regardless. This rightly upsets investigators and unnecessarily consumes the time and energy of the IRB. Often, extraneous burdens are added to avoid liability.

Treating guidance as regulation. Often the FDA or the OHRP issues a guidance that the IRB interprets as a regulation, resulting in the choice of a course that the investigator would not normally take. The purpose of guidance is to allow for flexibility in appropriate circumstances.

If an IRB spends too much of its time on tasks that are not mandated, it may not devote enough attention to its real work, which not only might contribute to research delays but may jeopardize the safety of research subjects.

INSTITUTIONS CAN FOSTER PROGRESS

Institutions can take a number of steps to promote good research practices and thereby create an environment that is conducive to safe and efficient product development:

Establish an institutional culture of concern for subject safety. Sometimes the OHRP team—after meeting with an institution's administrators, IRB members, and investigators—senses a culture of indifference to protecting research subjects. Institutions of this type tend to get into trouble later with conflicts of interest and noncompliance with regulations.

Ensure a supply of well-trained investigators. Continuous training and mentoring of young investigators ensures that a continued pool of educated scientists is available, which is critical for good institutional research.

Achieve accreditation from the Association for the Accreditation of Human Research Protection Programs (AAHRPP). Voluntary participation in the accreditation program run by the nonprofit AAHRPP (www.aahrpp.org) helps ensure that procedures are in place to identify conflicts of interest before problems arise. An increasing number of institutions are becoming accredited, raising standards nationwide.

Very few institutions have been shut down due to noncompliance with OHRP regulations; our goal is to prevent problems.

WHAT DELAYS RESEARCH PROJECTS?

IRB obstacles

The slow timing of IRB review is a major complaint on the part of investigators, delaying product development.

Lack of expertise among IRB members is often the primary problem. A common mistake committed by inexperienced IRB members is to send protocols back to investigators for revision without providing specific directions to resolve the issues.

IRB overwork is another common problem. Understaffing the IRB leads to delays.

Antagonism may arise between the investigators and the IRB members, often because investigators believe that their protocols are returned for revision for trivial reasons. The antagonism may become an obstacle in itself, getting in the way of solving the problems and moving the protocol through.

Investigator obstacles

Investigators themselves often contribute to delays in the approval process.

Lack of knowledge on the part of investigators of federal regulations and guidelines, state and local laws, and institutional standard operating procedures often hinders protocol approval. Investigators may believe that they personally do not need expertise in regulatory matters so long as someone on their research team does. However, understanding how to minimize subject risk is critical for designing and writing an acceptable protocol. Most researchers have minimal training

in medical ethics, which often leads to trouble when coupled with a lack of knowledge of regulations.

Lack of experience. Mentoring of young investigators by experienced investigators is critical. Inexperienced investigators not only need information, they need training to think through problems for themselves.

Rogue investigators. Occasionally an investigator unpredictably makes a poor decision, putting subjects—and the research sponsor—at risk.

OHRP FACILITATES RESEARCH

The OHRP continuously seeks input from the research community to learn about ways to improve the oversight process. Very few institutions have been shut down because of noncompliance with our regulations in the past several years; our goal is to prevent problems.

Site visits possible

We offer educational materials on our Web site (www.hhs.gov/ohrp/) and hold educational conferences and workshops. We also have a quality improvement program: an institution can invite us to spend a day and a half at their site so that we can examine standard operating procedures and IRB meeting minutes and discuss questions from investigators.

We are happy to discuss issues with IRB members and investigators as well as with institutional officials, the public, funding sources, government agencies, and clinical research organizations.

Partners in clinical research

Investigators and the OHRP are partners in developing and testing new medical products and in protecting research subjects. Maintaining the trust of the public is critical to making the process run smoothly in the long run.

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