



June 3, 2009

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By E-mail: IRBaccountability@hhs.gov.

RE: "IRB Accountability RFI" Request for Information and Comments

On behalf of Public Responsibility in Medicine and Research (PRIM&R), we appreciate the opportunity to submit comments on whether OHRP should pursue a notice of proposed rulemaking (NPRM) to hold institutional review boards (IRBs) and the institutions or organizations operating the IRBs, hereafter referred to as the IRB organizations (IORGs), directly accountable for meeting certain regulatory requirements of the Department of Health and Human Services (HHS) regulations for the protection of human subjects.

PRIM&R is an international, non-profit organization dedicated to advancing the highest ethical standards in the conduct of research. Since 1974, PRIM&R has served the full array of individuals and organizations involved in biomedical, social science, behavioral and educational research. PRIM&R's membership community includes professionals representing human subjects protection, animal care and use, and institutional biosafety programs, as well as researchers, institutional officials, government personnel, subject advocates, ethicists, policy makers, pharmaceutical and biotechnology leaders, and attorneys. Via a wide variety of conferences and courses, PRIM&R provides balanced, well-researched, and accurate information on the range of ethical and regulatory issues affecting research, while also offering access to certification, networking, and professional development resources.

Overview

PRIM&R supports the general proposal to hold institutional review boards (IRB) and the institutions or organizations operating the IRBs, directly accountable for meeting regulatory requirements of the Department of Health and Human Services (HHS) regulations for the protection of human subjects. Moreover, PRIM&R supports any systemic changes that will enhance protections for human subjects. PRIM&R would not however, support a regulatory change primarily promulgated to reduce institutional administrative burdens, if they might diminish protections for human subjects. Cooperative review agreements should not be used to waive, transfer or weaken the responsibility of the institution or investigators conducting the research to protect human subjects and to comply with the federal regulations and ethical principles that govern

human subjects research. The institution engaged in human subjects research has a strict obligation to protect the rights and welfare of human subjects regardless of which IRB reviews the research protocol.

It is well accepted that the responsibility for protecting human subjects in research is shared by all elements of the human research protection program (HRPP) including the investigator/researcher, the institution engaged in research and the IRB that reviews the research. As stated in the advanced notice of proposed rulemaking (NPRM) concerning the Federalwide Assurance (FWA), “[a]n FWA commits the entire institution (including institutional officials, IRBs designated in the assurance, research investigators, and all other employees or agents) to compliance with the HHS regulations whenever the institution is engaged in HHS-conducted or -supported human subjects research.” This commitment cannot be undermined by agreements with external IRBs or investigators.

PRIM&R supports a clarification the regulations that reflects the shared responsibility of each component of the HRPP to engage in ethical research. Furthermore, PRIM&R supports regulatory revisions that would expand OHRP’s enforcement authority so that it may enforce compliance with its regulations through each component of the HRPP that is legally independent.¹ Finally, PRIM&R suggests that new regulations that clarify the obligations of the institution, the IRB, and investigators towards human subjects provide additional clarification that the obligations set forth in the FWA continue regardless of the terms of any cooperative review arrangements entered into by the institution.

Having said this, we recognize that there are procedural matters for which an institution that uses an external IRB has no control. For example, if an external IRB violates quorum or voting requirements, it would be unfair to hold the research institution responsible for these violations. However, the research institution must continue to be responsible for all aspects of the human subjects’ protection process that is in its control. For example, the fact that an external IRB approves a faulty consent process does not relieve the research institution and investigator from obtaining appropriate informed consent. The obtaining of proper consent should be deemed a non-delegable responsibility.

Specific Responses

OHRP seeks information and comments on several specific issues. PRIM&R addresses below, those issues which are relevant to the advancement of ethical research, and to the protection of human research subjects.

- 1. Is there sufficient need for HHS to pursue a regulatory change to enable OHRP to hold IRBs and IORGs directly accountable for meeting certain requirements of the HHS regulations at 45 CFR part 46? Please explain your response.*

It is not clear to us that the clarification of responsibility alone requires a new regulation. However, a regulation may be necessary if new sanctions are to be imposed for non-compliance with the regulations. We certainly agree that there is a need for a regulatory enforcement system that governs all parts of the HRRP regardless of location.

¹OHRP may not be able to hold an internal IRB liable for noncompliance, as it is not a legally independent entity, but rather a committee of the institution. It could, however, hold an external, independent IRB, liable for noncompliance.

5. *If HHS pursues a regulatory change to enable OHRP to hold IRBs and IORGs directly accountable for meeting certain requirements of the HHS regulations at 45 CFR part 46, what kinds of administrative actions would be appropriate for OHRP to take against IRBs that are found to be out of compliance with 45 CFR part 46? For a description of some of the corrective actions that OHRP has required when it has been determined that an institution was not in compliance with 45 CFR part 46, see OHRP's guidance document entitled, "OHRP's Compliance Oversight Procedures for Evaluating Institutions" at <http://frwebgate.access.gpo.gov/cgi-bin/leaving.cgi?from=leavingFR.html&log=linklog&to=http://www.dhhs.gov/ohrp/compliance/ohrpcomp.pdf>.*

In its document entitled "Compliance Oversight Procedures for Evaluating Institutions" OHRP sets forth its procedures for determining non-compliance and sanctions for noncompliance. Sanctions are properly imposed on the *institution* not on the institution's IRB. Sanctions include "suspending all research." The issue that independent IRBs raise is that they, themselves, must be subject to sanction since they are not part of the institution that conducts the research. Other sanctions are also clearly related to institutional failings (not IRB failings). For example, if an investigator fails to obtain required training, the imposition of a sanction on the independent IRB for this failure would not be appropriate.

We suggest that current sanctions that apply to research institutions are sufficient. The issue of sanctions for independent IRBs is more challenging. The sanctions related to IRB member training and the requirement for re-review of improperly reviewed protocols would certainly apply to independent IRBs. We think it would be proper for OHRP to consider the use of fines for non-compliance. If that is not within its statutory authority it should seek such authority

6. As described in Section VI of this notice, in order to facilitate public comment, OHRP has made a preliminary attempt to group some of the regulatory requirements under 45 CFR part 46 into the following three categories: (1) Responsibilities that may be unique to IRBs and IORGs; (2) responsibilities that may be unique to institutions engaged in human subjects research; and (3) responsibilities that may be fulfilled by either IRBs/IORGs or institutions engaged in human subjects research.

6a. Are these categories appropriate? If not, what other categories should there be?

As stated in our introduction, we think it would be reasonable to exclude the research institution from responsibility for the purely procedural failings of an external IRB. For example, if an external IRB does not meet the quorum requirements for a vote, and the research institution is unaware of that fact, the research institution should not be held responsible. The external IRB should bear total responsibility for that failure. However a failure to obtain adequate informed consent is a non-delegable responsibility borne by the research institution and researcher. The fact that an external IRB does a faulty job in this area should not absolve the institution and researcher from their responsibilities. Similarly the investigator and institution have the obligation to ensure that risks are minimized even if the IRB does a poor job of this. If an external IRB approves research

that includes unnecessary medical procedures that expose subjects to unnecessary risks, both the external IRB and the research institution should be held accountable for this example of non compliance. Without commenting on the specific categorization in the NPRM, we agree in principle that there are limited circumstances in which an external IRB can bear the entire responsibility for failure to comply with the procedural requirements for review.

7. With regard to the responsibilities that may be fulfilled by either IRBs or institutions, the IRB Authorization Agreement between an external IRB and an FWA-holding institution is often used to clarify which entity will be responsible for carrying out these regulatory requirements.

7c. If a regulatory change to 45 CFR part 46 is pursued, should the regulation describe which regulatory requirements would need to be met by external IRBs and which regulatory requirements would need to be met by institutions engaged in the research?

The new regulations should clarify that agreements between external IRBs and institutions may not be used to release the research institution from its ethical responsibilities to protect the rights and welfare of human subjects that participate in research conducted by employees or agents of the institution.

Thank you again for the opportunity to comment on this proposal.

Respectfully Submitted,



Leonard Glantz, JD
Chair, Board of Directors
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Cc: Board of Directors, Public Policy Committee