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Jerry Menikoff, MD, JD
Director
Office for Human Research Protections
Department of Health and Human Services

Robert M. Califf, MD
Commissioner
Food and Drug Administration

(81 Federal Register 50711)

Dear Dr. Menikoff and Dr. Califf:


Since 1974, PRIM&R has been dedicated to advancing the highest ethical standards in the conduct of research. We accomplish this goal by serving individuals and organizations involved in biomedical, behavioral, and social science research, particularly the members and staff of IRB and human research protection programs (HRPPs). With respect to this core group, we pursue two goals: (1) creating a strong and vibrant community of ethics-minded individuals involved in research administration and oversight, and (2) providing educational and professional development to promote the highest ethical standards in research.

PRIM&R agrees with the agencies that additional guidance regarding IRB written procedures will benefit the research community, and that
careful attention to input received through this public consultation will serve to enhance the value of the final product. We also strongly believe that such efforts to harmonize OHRP and FDA guidance eliminate unintended inconsistencies and simplify compliance by IRBs who are answerable to both the DHHS and FDA rules.

Furthermore, PRIM&R agrees that documentation requirements can support human subjects protections by helping focus attention on critical aspects of human subjects research review. We also recognize that the checklist format may be particularly useful to institutions that currently have little in the way of written procedures in place and are looking to strengthen their research oversight infrastructure. More generally, we acknowledge that a checklist that meaningfully engages the user with regulatory requirements can be helpful.

However, we would like to share some concerns about the draft guidance. First, as we have suggested in the past, excessive attention to documentation will lead to the unnecessary expenditure of time and effort by both the IRB and investigators at the expense of more meaningful efforts to promote human subject protections by educating reviewers and enhancing review. If satisfying the requirements of the checklist becomes a compliance goal in and of itself, more valuable opportunities to promote protections may be lost. It is important for the checklist to contribute to improved understanding of regulatory requirements and how these can be translated into practice.

Furthermore, we note that the stated purpose of the checklist is “to assist IRBs in preparing and maintaining detailed written procedures,” and “help regulators understand how the IRB operates and fulfills its regulatory responsibilities.” To meet this goal, the guidance should provide additional direction. Consider for example, item 5, bullet 4:

“How the IRB assesses any potential benefits to subjects or others that may be reasonably expected to result, and whether this provides a reasonable basis for assuming the risks of the research.”

Certainly the question of how an IRB assesses benefits and risks is interesting, important, and complex. However, the intent of this checklist prompt is uncertain. Is the prompt seeking a description in written procedures of the deliberative process by which IRBs assess the balance of risk and benefit? If so, it’s not clear how IRBs would document in procedural terms the judgement-based process that is at the heart of IRB review. Or is the “correct” answer to ensure that IRB written procedures require an investigator to describe benefits in the IRB application and that this information is considered during review and deliberation about how those benefits weigh against foreseeable risks? Regardless, we believe it would be helpful to provide specific examples of responsive answers.

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1 We note, too, that the clause “and whether this provides a reasonable basis for assuming the risks of the research” requires clarification. We suggest rewriting this as, “and whether the balance of risk and benefit is reasonable.”
The same point can be made about several prompts under items 5, 6, and 7, which call for written procedures about other activities at the core of IRB review and deliberation, namely, the application of the criteria for review, the review and approval of informed consent processes, and the decision to ask for additional safeguards for vulnerable subjects. The risk is that, without examples of acceptable practices that will “help regulators understand how the IRB operates,” the prompts may do little more than result in documentation that merely reiterates the prompt itself.

It is also unclear whether the draft guidance is in fact strictly for IRBs. Consider the following three items in the checklist

- Item 47: “Training and education of the IRB chairperson, IRB members, alternates, administrative support staff, and investigators (including any orientation, continuing education, and a list of any reference materials provided as a resource)”
- Item 50: “Any additional IRB considerations or requirements when reviewing sponsor-investigator research.”
- Item 51: “Keeping the IRB informed of study completion and close out.”

While responsibility for these and other activities mentioned in the checklist may often fall to the IRB committee, they are not strictly IRB committee functions, but rather administrative functions that instead might be carried out by an IRB administrator or administrative office, or by another entity within a larger HRPP. We request that the guidance clarify exactly who the guidance is for, and ensure that the content matches the intended audience. Without this clarification, the checklist could perpetuate IRB “mission creep,” threatening to divert IRB resources and attention from the core of its work of protecting human subjects.

We hope that you will find our input on this matter useful as you finalize this guidance. If you have any questions or require any further information, please feel free to contact me at (617) 423-4112 or ehurley@primr.org, or the chair of PRIM&R’s Public Policy Committee, Dr. David H. Strauss at strauss@nyspi.columbia.edu.

Sincerely,

Elisa A. Hurley, PhD
Executive Director

cc: Board of Directors