PRIM&R
PUBLIC RESPONSIBILITY IN MEDICINE AND RESEARCH

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December 23, 2022

Robert M. Califf, MD
Commissioner of Food and Drugs
Food and Drug Administration
19903 New Hampshire Avenue
Silver Spring, MD 20993

RE: Docket No. FDA–2019–N–2175 for "Institutional Review Boards; Cooperative Research."

Dear Dr. Califf,

Public Responsibility in Medicine and Research (PRIM&R) appreciates the opportunity to comment on the Food and Drug Administration (FDA)'s Proposed rule on "Institutional Review Boards; Cooperative Research," published in the *Federal Register* on September 28, 2022.

PRIM&R is a nonprofit organization dedicated to advancing the highest ethical standards in the conduct of research. Since 1974, PRIM&R has served as a professional home and trusted thought leader for the research protections community. Through educational programming, professional development opportunities, and public policy initiatives, PRIM&R seeks to ensure that all stakeholders in the research enterprise appreciate the central importance of ethics to the advancement of science.

PRIM&R appreciates FDA's efforts to reduce regulatory burden on the research community by harmonizing the FDA regulations with the provisions of the revised Common Rule regarding the use of a single IRB (sIRB) for multi-site or cooperative research studies. We applaud FDA for (1) acknowledging that implementing the sIRB rule will be burdensome and giving due consideration to whether those burdens will be offset by benefits accruing from streamlining of oversight processes and enhancement of subject protections; (2) recognizing and articulating exceptions to the sIRB rule either because it is inappropriate in a particular instance or because the associated increase in burdens is not accompanied by a commensurate increase in research protections; and (3) incorporating recommendations of the Secretary's Advisory Committee on Human Research Protections. **However, PRIM&R believes that it is premature for FDA to mandate the use of a sIRB**

and recommends a more thorough evaluation of the impact of this rule on the regulated community. We elaborate on our position below.

One major concern is that unlike the requirement for sIRB under the revised Common Rule and the National Institutes of Health (NIH) sIRB Policy, which has resulted in the creation of a variety of reliance arrangements among IRBs at universities or academic medical centers, the FDA mandate is likely to result in even greater use of commercial, for-profit IRBs for the review of industry-sponsored research. Given Congressional interest in how such IRBs work and the on-going investigation of commercial IRBs by the Government Accountability Office (GAO), the FDA should consider delaying the implementation of this rule, at least until GAO issues its report.

Other concerns include:

- **Lack of data to support the assumption that a sIRB model improves the efficiency of IRB review process and reduces burdens on both investigators and IRBs without undermining human subjects' protections**. The NPRM does not provide or cite data on the impact of the sIRB model on human research protections, the first-hand experience of investigators working with this model, and whether it has improved efficiencies, such as reducing delays in study start-up. Given that the Common Rule sIRB requirements as well as the NIH sIRB Policy have been in effect for a few years, we urge the FDA to gather data from the regulated community about their experience with the sIRB model to learn about the advantages and pitfalls of sIRB, before issuing a final rule.

- **The lack of FDA involvement in the identification of the designated IRB.** Unlike the Common Rule requirement that the IRB of record be identified or at least subject to the acceptance of the Federal department or agency supporting or conducting the research, this NPRM proposes a hands-off approach regarding FDA's role in identifying the sIRB. However, we believe to ensure public trust in the IRBs selected to serve in this critical capacity, it is essential for the FDA to have some role in ascertaining the appropriateness of the IRB of record. This might include, for example, establishing minimum criteria for an IRB to be eligible to serve in this capacity.

- **Underappreciation for the importance of taking into consideration local contexts, norms, and values.** Concerns related to the ability of the sIRB model to appropriately address local context and local considerations have persisted since the implementation of the revised Common Rule requirement and NIH policy for sIRB for cooperative research These concerns emerge from the recognition that community perspectives are often embedded in local review processes. No data are presented that the provision of local context information by the ceding IRB to the sIRB via existing administrative processes, or the NPRM proposed use of consultants to incorporate community perspectives are viable solutions to address these concerns. In addition, the designated IRB may not take into consideration

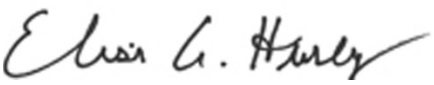
ethical best practices adopted by the ceding IRB, based on local norms and requirements. This, in turn might, require the ceding IRB to conduct its own review, thereby negating the purported reduction in burden on the local IRB. While these concerns emerged in response to the Common Rule requirement and the NIH policy for sIRB for cooperative research, neither the research community nor the regulatory and funding agencies have identified viable solutions.

- **Loss of opportunities for mentoring and relationship building between IRBs and investigators at the local level.** With the shift to a sIRB model, researchers may become increasingly disconnected from their own local IRBs and human research protection programs (HRPPs). Interactions are critical to ensuring that researchers are kept abreast of regulatory and policy requirements, and their own obligations and responsibilities to be in compliance with current federal, state, and local policies. It also serves to establish the local IRB as a resource for researchers to turn to with questions or concerns that might arise in the course of their research studies. PRIM&R recommends that FDA evaluate the impact of this lost opportunity on the overall human research protections program and consider ways to mitigate its effects.

- **The proposed compliance date of one year from the date the final rule is issued is too short.** While some institutions have gained experience with implementation of the HHS and NIH sIRB requirements, the shift to sIRB presented a tremendous burden for staff training and implementation of new processes to ensure compliance. The NPRM lists a number of exceptions to the sIRB mandate for FDA regulated research; the provisions of the proposed rule are complex and will require considerable training of researchers and oversight professionals to accurately identify which particular studies qualify for an exception. Therefore, PRIM&R requests that the effective date be extended to two years after the final rule is published, similar to the cooperative research mandate under the revised Common Rule.

Thank you again for the opportunity to comment on the proposed rule on single IRB review for cooperative research. We hope our comments will be useful to the FDA in its ongoing deliberations on this important issue. PRIM&R stands ready to provide any further assistance or input that might be of use. Please feel free to contact me at 617.303.1872 or ehurley@primr.org.

Sincerely,



Elisa A. Hurley, PhD
Executive Director

cc: PRIM&R Public Policy Committee, PRIM&R Board of Directors