

January 29, 2015

Office of Clinical Research and Bioethics Policy
Office of Science Policy
National Institutes of Health (NIH)
6705 Rockledge Drive, Suite 750
Bethesda, MD 20892
SingleIRBpolicy@mail.nih.gov

RE: NOT-OD-15-026: Draft NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research

Dear Sir/Madam:

The Association of Clinical Research Organizations (ACRO) represents the world's leading, global clinical research organizations (CROs). Our member companies provide a wide range of specialized services across the entire spectrum of development for new drugs, biologics and medical devices, from discovery, pre-clinical, proof of concept and first-in-man studies through post-approval and pharmacovigilance research. With more than 110,000 employees engaged in research activities around the world, ACRO advances clinical outsourcing to improve the quality, efficiency and safety of biomedical research.

Each year, ACRO member companies conduct more than 11,000 clinical trials involving nearly two million research participants in 115 countries. On average, each of our member companies works with more than 500 research sponsors annually, including as sub-contractors to NIH grantees, and we have a broad and unique understanding of the roles, responsibilities and behavior of all the stakeholders – research sponsors, investigators, Institutional Review Boards (IRBs,) clinical trial participants and ancillary providers of all types – that are part of the research enterprise.

ACRO thanks the NIH (the Agency) for issuing this Draft Policy and is pleased to support the use of a single IRB for multi-site research projects in the comments to follow.

Duplicative IRB Review Delays the Initiation of Multi-Site Studies

As the Agency points out in the Background section of the draft policy, “there is no evidence that multiple IRB reviews enhance protections for human subjects.” The FDA (2006) and the Office for Human Research Protections (OHRP) in 2010 have issued guidance to allow institutions participating in multi-site studies to use joint review, rely on the review of another qualified IRB (besides the institution’s own,) or establish other arrangements for avoiding duplication of effort. Notwithstanding the encouragement provided by the FDA and NIH and longstanding examples of successful implementation, such as the Central Institutional Review Board (CIRB) utilized for the review of NCI-sponsored clinical trials, adoption of single (or central or lead) IRB review models has occurred in only a small percentage of multi-site research projects.

Some institutions express concerns about a potential lack of clarity concerning regulatory and legal liability of cooperative IRB review arrangements. But the practical result of this is that multi-site research studies are delayed. Data provided by several of our member companies suggests that in commercially-sponsored research duplicative IRB review results in significant delays; for example, from initiating a multi-site study in less than 50 days with a central IRB model to well over 100 days with duplicative local reviews. We believe the magnitude of delay is worse for NIH-sponsored multi-site studies. The time savings of a single IRB model has a meaningful impact, not only on the costs and time to develop a new product or treatment, but on the ultimate availability of drugs, device and treatments for the patients who are waiting.

The Draft Policy moves from “May” to “Should” and relevant Guidances Must Catch Up

Beyond the institutional turf and lack of trust issues that may underlie resistance to the use of a single IRB model, it is certainly possible that the overlapping and potentially contradictory requirements of Common Rule and FDA regulations make a complicated situation even more so. For example, the Common Rule (45 CFR Part 46) at 46.114 states, “In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy [emphasis added.] With the approval of the department or agency head, 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 to avoid duplication of effort.” By contrast, FDA regulation (21 CFR Part 56) at 56.114 says, “In complying with these regulations, institutions involved in multi-institutional studies may use joint review, reliance upon the review of another qualified IRB, or similar arrangements aimed at avoidance of duplication of effort.” It seems to us that this emphasis on the responsibility of “each institution” has exacerbated institutional concerns about the potential liability of shared review arrangements, and we believe it would be helpful for OHRP to issue an interpretation of 46.114 that aligns with the straightforward and unambiguous encouragement of avoidance of duplication of 56.114 in order to facilitate acceptance of this Draft Policy.

The Draft Policy distinguishes between the accountability of the single IRB for a multi-site project as the IRB of record, and the responsibility of participating sites to meet other regulatory obligations, such as obtaining informed consent, overseeing the implementation of approved protocols, reporting adverse events to the single IRB, etc. Further to the question of needed guidance, we believe it would be useful for OHRP to issue, prior to implementation of the Draft Policy, guidance discussing the kinds of “mechanisms” that should be established for the consideration of local issues, involvement of vulnerable populations, and the like.

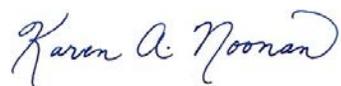
The Draft Policy stipulates exceptions to the use of a single IRB, including as required by federal, tribal, or state laws or regulations, which makes sense. However, the Policy indicates that the NIH will not “prohibit any participating site from carrying out its own IRB review” if it chooses to. While the Draft Policy says that the cost of such duplicative review must be borne by the site, we would suggest that the Agency reinforce the importance of not delaying multi-site studies by stipulating that any additional review, beyond that of the single IRB of record, must be completed within 10 days of the institution’s agreement to participate as a research site.

Concluding Remarks

By proposing to make compliance with the use of a single IRB for multi-site research a term and condition of NIH awards and contracts, the Agency is committing to achieving greater efficiencies of review and speeding the initiation of studies across the NIH’s clinical research portfolio. ACRO salutes this bold stroke, which we believe will have a significant and salutary impact on FDA-regulated, multi-site studies, as well.

Please do not hesitate to contact ACRO if we can provide further information (knoonan@acrohealth.org or 202-464-9340). We look forward to opportunities to collaborate with the Agency in implementing this needed change in order to facilitate the timely initiation of multi-site research projects.

Respectfully submitted,



Karen Noonan
Vice President, Global Regulatory Policy