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Office of Clinical Research and Bioethics Policy
Office of Science Policy
National Institutes of Health
6705 Rockledge Drive, Suite 750
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RE: Draft NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research (Notice number NOT-OD-15-026)

The Association of American Medical Colleges ("AAMC"), a not-for-profit association representing all 141 accredited U.S. medical schools, nearly 400 major teaching hospitals and health systems, and 90 academic and scientific societies, appreciates the opportunity to submit comments on the draft policy on the use of a single Institutional Review Board (IRB) for multi-site research, released on December 3, 2014 by the National Institutes of Health ("NIH"). Through the AAMC's member institutions and organizations, the AAMC represents 128,000 faculty members, 83,000 medical students, 110,000 resident physicians, and thousands of graduate students and post-doctoral trainees.

In the draft policy, NIH has taken a sweeping approach to ensuring the increased use of single IRBs with the general rule that "all sites participating in a multi-site study will be expected to rely on a single IRB," and that compliance with the policy "will be a term and condition in the Notice of Award and a contract requirement in the Contract Award." The AAMC recognizes that increased use of single (or central) IRBs for certain multi-site trials has the potential to increase the efficiency of reviewing proposed and ongoing research and reduce burdens on institutions and investigators in what can be a redundant and inefficient process without commensurate increased protections to human subjects. As we expressed in our 2011 comments responding to the Department of Health and Human Services' (HHS) advance notice of proposed rulemaking (ANPRM)[1] that first suggested this approach:

> The use of a single IRB of record for multi-site studies has the potential to decrease burden, standardize protections, and reduce delays in approval processes. The ANPRM proposes that a single IRB of record be mandated for all multi-site, domestic trials. AAMC supports the establishment of a regulatory framework that promotes and

[1] Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators, 76 Fed. Reg. 44512, (notice published July 26, 2011).

> facilitates the adoption of single IRB review for multi-site studies. Regular use of a single IRB of record in large multi-site trials could accomplish both goals of the ANPRM if certain considerations, guidance, and clarifications are in place prior to the effective date of such a requirement.[2]

Despite our support for the increased use of single IRBs for multi-site trials, we believe that the implementation of this policy as drafted will not accomplish the NIH's laudable goals, but may instead increase costs, shift administrative burdens, and encourage the development of "shadow" IRB reviews to fill in the gaps left by insufficient guidance on how to create many simultaneous reliance agreements and relationships. We concur with many academic medical centers and research institutions that have commented on this issue, both in response to this draft policy and to the related section in the 2011 ANPRM, providing valuable information about the concerns and increased responsibilities of sites that function as single IRBs as well as sites that rely on others. We commend these thoughtful letters to your attention as well.

In these comments, we identify the primary concerns with the scope and structure of the policy and offer NIH recommendations for addressing these problems and alternative approaches that could accomplish similar results without unintended negative consequences.

Creating an effective inter-institutional reliance is not a rapid or simple process. The successful examples of single IRBs for large, complex multi-site studies are often the result of expensive and time-consuming development and negotiations. These relationships evolve over time and require the establishment of trust, a familiarity with processes, procedures, and personnel, and clear designation of roles and responsibilities for all aspects of managing the trials. An institution that has never served as an IRB for other sites will need to build the requisite infrastructure and expertise to allow it to play this role.

A single IRB will not be equally beneficial for all multi-site trials. This policy would be strengthened if NIH could use the experiences of institutions across the country to create a set of criteria identifying which types of trials would be most likely to realize the goals of efficiency and adherence to ethical principles. These criteria might include trials of a certain size, number of sites, or level of risk, or inclusion of a site with infrastructure in place to act as a single IRB. Using these guideposts, the NIH could implement a policy that had a more limited scope or implement a tiered or phased approach as we recommend below.

Roles and responsibilities of all sites must be clearly and explicitly defined before institutions will be confident in their ability to cede or take on IRB review for all NIH-funded multi-site studies. The roles that the responsible and the reliant institutions need to consider in the context of a multi-site trial are numerous, and should be better enumerated in the

[2] AAMC Comment Letter, October 25, 2011, (available at https://www.aamc.org/download/264544/data/aamccommentlettertohhsonproposedhumansubjectsresearchregulation.pdf).

policy or in related guidance. These would include issues related to cost, allocation of resources, liability, subject injury, investigator and subject records management, and the other institutional responsibilities now coordinated by many IRBs.

Institutions will need more guidance on how to choose a single IRB, and when this decision needs to be made. The draft policy indicates that NIH will have "final decisional authority for approving the selected single IRB," but does not include further information on the attributes that such an IRB must have or whether the selection of the single IRB must occur prior to the Notice of Award. It is not clear whether the appropriateness of the applicant's selection of the single IRB will affect the likelihood of a multi-site trial being funded. If the agreed-upon IRB must be identified at the time of application, applicants would need to have assurances that the selected IRB will meet established thresholds, such as accreditation by the Association for the Accreditation of Human Research Protection Programs (AAHRPP).

The exceptions to a mandate should be broader than currently proposed. If this policy is finalized with as expansive a scope as currently envisioned, the NIH should consider a policy of exceptions that goes beyond the inability of a designated single IRB "to meet the needs of specific populations or where local IRB review is required by federal, tribal, or state laws or regulations." There will undoubtedly be times when circumstances will warrant the local review to ensure the protection of human subjects, and the NIH policy should provide institutions with a clear mechanism for addressing these concerns without the fear of penalty from the funding entity.

Research the NIH has already agreed to fund should be used to determine the most effective way to draft and implement this policy. In a recent notice of funding opportunity, NIH has specifically solicited applications for grants to "explore two timely issues of significance for policy development" including "the principles and characteristics for central Institutional Review Boards (IRBs)."[3] As NIH states in the background to this notice, "the use of a single IRB for multi-site studies, which is permitted under current Federal human subjects research regulations (45 CFR part 46), was proposed as a requirement for domestic, multi-site studies in the 2011 Advanced Notice of Proposed Rulemaking on the Common Rule. While central IRBs have been used effectively in some contexts, research and analysis could inform the move to broader use of central IRBs." The application deadline for these grants is February 19, 2015, and we encourage NIH to consider how to promote "evidence-based policy" by using the information gained from this research to inform the current proposed move to a broader use of single IRBs.

NIH should consider alternatives to a broad mandate for all NIH-funded studies. There are many actions that the NIH could take in the interim to move toward the goal of increasing the

[3] NIH Funding Opportunity: Empirical Research on Ethical Issues Related to Central IRBs and Consent for Research Using Clinical Records and Data, RFA-OD-15-002 (available at http://grants.nih.gov/grants/guide/rfa-files/RFA-OD-15-002.html).

use of single IRBs beyond simply reminding institutions of the mechanism for the use of single IRBs and encouraging their wider use. We recommend that the NIH instead take one or more of the following approaches:

- Run a pilot program with a select group of institutions and studies to measure the true costs, benefits, and consequences of greater adoption of single IRBs.
- Issue a policy with incentives for voluntary adoption.
- As discussed above, determine the attributes of studies that are most readily adaptable to single IRB review and either limit the policy to those studies or begin a phased-in implementation of a broader mandate starting with these studies.
- Create or fund resources and tools that facilitate collaboration, cooperation and greater efficiencies, perhaps allowing the central review of multi-site studies through an online platform.

In the AAMC's comments to the 2011 HHS ANPRM, AAMC stated that "this is an area of great promise, but the process to move towards a mandated single IRB of record needs to be deliberate and thoughtful." The AAMC is appreciative of NIH's commitment to engaging the research community in ensuring that this policy is drafted and implemented in a manner that meets the NIH's stated goal to "enhance and streamline the process of IRB review and reduce inefficiencies so that research can proceed efficiently without compromising ethical principles and protections" and is also deliberate and thoughtful. We would be happy to provide any further assistance in this process. Please feel free to contact me or Heather Pierce, Senior Director for Science Policy and Regulatory Counsel at hpierce@aamc.org or (202) 478-9926 with any questions.

Sincerely,

Ann C. Bonham, Ph.D.
Chief Scientific Officer