DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Announcement of a Draft NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research

SUMMARY: On December 3, 2014, the National Institutes of Health (NIH) published a request for public comments in the NIH Guide for Grants and Contracts on a draft policy to promote the use of a single Institutional Review Board of record for domestic sites of multi-site studies funded by the NIH. See Guide notice NOT–OD–15–026 at *http://grants.nih.gov/grants/guide/notice-files/NOT–OD–15–026.html.* NIH is publishing this notice in order to inform readers of the **Federal Register** about the draft policy and the opportunity to comment.

DATES: The deadline for receiving comments on the draft policy is no later than 5:00 p.m. on January 29, 2015.

ADDRESSES: Comments may be submitted by any of the following methods:

- Email: *SingleIRBpolicy@mail.nih.gov*
- Fax: 301–496–9839
- Mail/Hand delivery/Courier: Office of Clinical Research and Bioethics Policy, Office of Science Policy, National Institutes of Health, 6705 Rockledge Drive, Suite 750, Bethesda, MD 20892.

FOR FURTHER INFORMATION CONTACT: Office of Clinical Research and Bioethics Policy, Office of Science Policy, National Institutes of Health, 6705 Rockledge Drive, Suite 750, Bethesda, MD 20892, 301–496–9838, *OCRBP–OSP@od.nih.gov.*

SUPPLEMENTARY INFORMATION:

Background

The National Institutes of Health (NIH) is dedicated to improving the health of Americans by conducting and funding biomedical research through an extensive portfolio of human subjects research. While NIH-funded investigators must adhere to regulations for the protection of human subjects, the agency also looks for ways to reduce procedural inefficiencies so that human subjects research can proceed efficiently without compromising ethical principles and protections.

The Department of Health and Human Services (HHS) regulations for the Protection of Human Subjects at 45 CFR part 46 requires Institutional Review Board (IRB) review of non-exempt HHS conducted or supported human subjects research. IRBs are responsible for performing an ethical review of studies involving human subjects. Research protocols and informed consent documents must be approved by an IRB prior to the commencement of human subjects research. In 1975, when the HHS regulations for protection of human subjects were first published,[1] most clinical research was conducted primarily at a single institution. Since then, the research landscape has evolved, and many studies are carried out at multiple sites.

In order to avoid duplication of the effort, both the HHS regulations at 45 CFR part 46 and the IRB regulations of the Food and Drug Administration (FDA) at 21 CFR part 56 allow institutions that participate in multi-site studies to use joint review, rely on the review of another qualified IRB, or establish other arrangements.[2] FDA and the Office for Human Research Protections (OHRP) have also issued guidance on this topic.[3] [4] However, too few institutions involved in multi-site studies are taking advantage of the option.[5]

Proponents of the single IRB model maintain that review of a multi-site study by the IRB of each participating site involves significant administrative burden in terms of IRB staff and members' time to perform duplicative reviews. When each participating institution's IRB conducts a review, the process can take many months and significantly delay the initiation of research projects and recruitment of human subjects into research studies. Use of single IRBs in multi-site studies, on the other hand, has been shown to decrease approval times for clinical protocols and may be more cost effective than local IRB review.[6]

Importantly, there is no evidence that multiple IRB reviews enhance protections for human subjects. In fact, the use of single IRBs may lead to enhanced protections for research participants by eliminating the problem of distributed accountability, minimizing institutional conflicts of interest, and refocusing IRB time and resources toward review of other studies.[7] [8] With regard to assuring that local perspectives are addressed, the assessment of a study's risks and benefits and the adequacy of the informed consent should not generally require the perspective of a local IRB. Local contextual issues relevant to most studies (*e.g.,* investigator competence and site suitability) can be addressed through mechanisms other than local IRB review, such as the involvement of ad hoc members or consultants with the necessary specialized knowledge or expertise or by submission of information by the individual site(s). Even when certain vulnerable populations are targeted for recruitment, such alternative approaches may be appropriate.

Several extramural NIH programs already support the use of a single IRB for multi-sites studies. For example, the National Cancer Institute has had a Central Institutional Review Board (CIRB) in place for the review of NCI-sponsored clinical trials since 1999. The National Institute of Neurological Disorders and Stroke has incorporated the use of a single IRB for its Network for Excellence in Neuroscience Clinical Trials (NeuroNEXT) and Network for Stroke Research (NIHStrokeNet).[9] [10]

The draft Policy proposes that NIH funded institutions will be expected to use a single IRB of record for domestic sites of multi-site studies unless there is justification for an exception (see exceptions below). The draft Policy applies to all domestic sites participating in NIH conducted or supported multi-site studies, whether supported through grants, contracts, or the NIH intramural program. By expecting all domestic multi-site studies to use a single IRB, this Policy should help achieve greater efficiencies and speed the initiation of studies across NIH's entire clinical research portfolio. This Policy is also in keeping with one of the proposed changes being considered to the Common Rule.[11]

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[1] 40 FR 11854 (March 13, 1975)

[2] 45 CFR part 46.114 and 21 CFR part 56.114

[3] See *http://www.fda.gov/RegulatoryInformation/Guidances/ucm127004.htm*

[4] See *http://www.hhs.gov/ohrp/policy/protocol/cirb20100430.html*

[5] Flynn KE, et al. Using central IRBs for multicenter clinical trials in the United States. PLoS ONE. 2013; 8(1):e54999.

[6] Wagner TH, et al. Costs and benefits of the National Cancer Institute Central Institutional Review Board. J Clin Oncol. 2010; 28:662–666.

[7] Emanuel EJ et al. Oversight of human participants research: identifying problems to evaluate reform proposals. Ann Intern Med. 2004; 141(4): 282–291.

[8] Menikoff J. The paradoxical problem with multiple-IRB review. N Engl J Med. 2010; 367:1591–1593.

[9] See http://www.neuronext.org/researchers and *h*ttp://www.nihstrokenet.org/research

[10] Kaufmann P et al. Central institutional review board review for an academic trial network. Acad Med. 2014; doi: 10.1097/ACM.0000000000000562.

[11] An Advance Notice of Proposed Rulemaking issued in 2011 sought public comment on proposed changes to seven regulatory areas, including requiring the use of a single IRB for domestic sites in multi-site studies. Most commenters supported the idea of requiring the use of a single IRB for review of multi-site studies, especially for cooperative clinical trials, and agree that such a mandate would help speed the initiation of multi-site studies. Some commenters were concerned that

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Request for Comments

NIH encourages the public to provide comments on any aspect of the draft policy outlined below. Comments should be submitted electronically by January 29, 2015, to the Office of Clinical Research and Bioethics Policy, Office of Science Policy, NIH, via email at *SingleIRBpolicy@mail.nih.gov;* mail to 6705 Rockledge Drive, Suite 750, Bethesda, MD 20892; or fax at 301–496–9839. Submitted comments are considered public information; private or confidential information should not be submitted. Comments may be posted along with the submitter's name and affiliation on the OCRBP Web site after the public comment period closes.

Draft NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research

Purpose. The purpose of this Policy is to increase the use of single Institutional Review Boards (IRB) for multi-site studies funded by the National Institutes of Health (NIH). Its goal is to enhance and streamline the process of IRB review and reduce inefficiencies so that research can proceed efficiently without compromising ethical principles and protections.

Scope. NIH generally expects all domestic sites of multi-site NIH-funded studies to use a single IRB of record. The Policy applies to all domestic sites participating in NIH conducted or supported multi-site studies, whether supported through grants, contracts, or the NIH intramural program. While foreign sites in multi-site studies will not be expected to follow this Policy, they may elect to do so.

Responsibilities. All sites participating in a multi-site study will be expected to rely on a single IRB to carry out the functions that are required for institutional compliance with IRB review set forth in the HHS regulations for the Protection of Human Subjects. The single IRB will be the IRB of record for the other participating sites. The single IRB will be accountable for compliance with regulatory requirements for IRBs specified under the HHS regulations at 45 CFR part 46, such as providing initial and continuing review of the research.[12] All participating sites will be responsible for meeting other regulatory obligations, such as obtaining informed consent, overseeing the implementation of approved protocols, and, reporting unanticipated problems and adverse events to the single IRB of record.

Agreements between the single IRB of record and other participating sites will be needed in accordance with 45 CFR part 46. IRB Authorization Agreements will document the delegation of responsibilities of IRB review to the designated IRB of record and that IRB site's acceptance of the responsibilities. The agreement will set forth the specific responsibilities of each participating site. Participating sites will then rely on the IRB of record to satisfy the regulatory requirements relevant to the IRB review. The awardee or lead site for an NIH-funded, multi-site study will be responsible for maintaining authorization agreements and should be prepared to provide copies of the authorization agreements and other necessary documentation to the NIH funding Institute or Center upon request. As necessary, mechanisms should be established to enable the single IRB of record to consider local context issues during its deliberations. A duplicate IRB review at a participating site would be counter to the intent and goal of the Policy, but the Policy does not prohibit any participating site from carrying out its own IRB review. If this approach is taken, the participating site should expect to bear the cost of the additional review.

Identification of the IRB that will serve as the single IRB of record will be the responsibility of the extramural applicant or offerer, or the intramural principal investigator. The funding NIH Institute or Center has final decisional authority for approving the selected single IRB. Use of the designated single IRB will be a term and condition of award. If the agreed-upon single IRB is a fee-based IRB, these costs will be included in the Notice of Award as a direct cost.

Compliance with this Policy will be a term and condition in the Notice of Award and a contract requirement in the Contract Award.

Exceptions. Exceptions to the expectation to use a single IRB may be made with appropriate justification. Exceptions will be allowed only if the designated single IRB is unable to meet the needs of specific populations or where local IRB review is required by federal, tribal, or state laws or regulations.[13]

Effective Date. The Policy applies to all new grant applications (Type 1 and 2) and contract proposals with receipt dates after [date to be determined]. It will also apply to intramural multi-site studies submitted for initial review after that date.[14]

Dated: December 24, 2014.

Lawrence Tabak,

Principal Deputy Director,

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the use of a single IRB could lead to increased liability and diminished accountability for participating sites, and decreased consideration of local context. See *http://www.gpo.gov/fdsys/pkg/FR–2011–07–26/html/2011–18792.htm*

[12] On March 5, 2009, OHRP published an ANPRM requesting public comments on whether OHRP should pursue rulemaking to hold institutional review boards and institutions or organizations operating them directly accountable for compliance with the provisions of 45 CFR part 46 that relate to IRB responsibilities. In the ANPRM, OHRP identified: Responsibilities that may be unique to IRBs and the institutions operating them; responsibilities that may be unique to institutions engaged in human subjects research; and, responsibilities that may be fulfilled by either IRBs/IORGs or institutions engaged in human subjects research. See *http://www.gpo.gov/fdsys/pkg/FR–2009–03–05/pdf/E9–4628.pdf.*

[13] For example, FDA-regulated research involving a device is required to have local IRB review under 21 U.S.C. 360j(g)(3)(A)).

[14] When a final policy is issued, NIH will also provide more specific procedural guidance to facilitate implementation.

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National Cancer Institute; Amended Notice of Meeting

Notice is hereby given of a change in the meeting of the National Cancer Institute Special Emphasis Panel, January 29, 2015 10:30 a.m. to January 30, 2015, 04:00 p.m., National Cancer Institute Shady Grove, 9609 Medical Center Drive, Rockville, MD 20850 which was published in the **Federal Register** on November 26, 2014, 79FR70537.

The meeting notice is amended to change the date and start time to be held on January 29, 2015 at 10:00 a.m. The meeting is closed to the public.

Dated: December 30, 2014.

David Clary,

Program Analyst, Office of Federal Advisory Committee Policy.

[FR Doc. 2014–30883 Filed 1–5–15; 8:45 am]

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National Institute of Allergy and Infectious Diseases; Notice of Closed Meetings

Pursuant to section 10(d) of the Federal Advisory Committee Act, as