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NIH Policy on Single-IRB Review — A New Era in Multicenter Studies

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Review of the ethics of multi-center clinical studies is typically conducted by the institutional review board (IRB) of each participating center. Extensive evidence suggests that the current practice is costly, is unnecessarily duplicative, and delays commencement of research.[1] The U.S. government has permitted single-IRB review and other streamlined review models since 1991, but few investigators have taken advantage of those options.[2]

In June 2016, the National Institutes of Health (NIH) issued new guidance on single-IRB review of multicenter studies.[3] The policy was introduced as a means to increase the efficiency of multicenter studies, reduce the time to study initiation, promote consistency of ethics review, alleviate the burden on investigators and administrators, and eventually reduce research costs. Under the new policy, U.S. centers participating in NIH-funded multi-center studies must use a single IRB for initial and ongoing ethics review. As of May 25, 2017, this policy will apply to investigators submitting applications for non-exempt multicenter studies involving human participants and using a common study protocol. The policy does not apply if it is prohibited by "federal, tribal, or state law, regulation or policy."[3] The NIH will consider other exceptions with appropriate justification.

The single-IRB policy ushers in new and important responsibilities for investigators. A proposal for use of a single IRB must be included with the initial application, and at that time all involved U.S. institutions must agree to use the selected IRB. If funding is awarded, federal guidance requires a signed IRB-authorization agreement between each participating institution and the single IRB outlining the roles and responsibilities of investigators, institutions, and the IRB. The principal investigator must ensure that the selected IRB is qualified to serve as the single IRB and that all authorization agreements and communication plans among the various centers and the selected IRB are in place. Even though in practice institutional counsel and IRB administrators will probably negotiate and execute IRB-authorization agreements, investigators must understand their responsibilities under such agreements.

Although the response to the policy has been very positive overall, public comments highlight several challenges to streamlining ethics review.[3] The first challenge relates to the

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costs of single-IRB review. The NIH has released guidance on allocation of costs for single-IRB activities.[4] When the single IRB is affiliated with an institution that is receiving funds for conduct of the study in question, ethics and consent-form review must be covered as "indirect costs." Review of local materials and investigator credentials and communications with the participating centers may be included as "direct costs." If the single IRB is unaffiliated with the participating institutions — is, for instance, an independent IRB that operates on a fee-for-service basis — all review activities may be included as direct costs. NIH intramural IRBs may serve as a study's single IRB but are prohibited from receiving funding.

> The NIH expects that the benefits of this transition will be realized as use of single IRBs increases, but it will monitor outcomes such as time to research initiation and threats to the protection of participants.

Many established academic IRB consortia are well placed to conduct single-IRB review, but some academic IRBs may require extensive modifications to information systems and standard operating procedures to accommodate the new approach.[3,5] Institutions will need to allocate substantial resources before May 2017, and it is unclear whether and how these costs will be recovered. Resources required for single-IRB review may well exceed available indirect funds.[3] As a result, academic institutions may be reluctant to assume the costs of single-IRB review in the absence of explicit reimbursement. These institutions may also not yet have enough data to appropriately estimate the direct costs. Surely, decisions regarding the application of direct and indirect costs will weigh heavily in the selection of the single IRB.

Given the barriers to single-IRB review for some academic institutions, investigators may consider, or institutions may suggest, relying on independent IRBs. Such IRBs were initially established to provide single-center and multi-center study ethics reviews for investigators who lacked an IRB affiliation, but they have also served as the single IRB for multi-center studies that include both academic institutions and investigators without IRB affiliation. Independent IRBs have standard operating procedures specific to single-IRB review, the infrastructure to manage and monitor administrative functions, and a fee schedule for the activities outlined in the NIH policy. Although independent IRBs may therefore have an advantage in the new single-IRB era, academic IRBs should also participate in reviewing NIH-funded multicenter studies. Without a critical mass of both academic and independent IRBs prepared to serve in this capacity, the expected gains in efficiency may be delayed or unrealized.

A second challenge lies in the uncertainty regarding the regulatory and legal liability of investigators and institutions when an unaffiliated IRB reviews their study — uncertainty that will remain until a new federal liability policy is developed.[3] A proposed modification to the federal policy on the protection of human participants includes an assurance that the single IRB would be held responsible if there are deficiencies in ethics review. Unfortunately, final approval of that policy may not occur before the single-IRB requirement becomes effective.

A third concern is the efficiency of the IRB review process. The need to interact with only one IRB is clearly an advantage, since it eliminates the delays associated with duplicative IRB review, but there are two provisions that may extend the time to study commencement. First, executing the required IRB-authorization agreements will take a variable amount of time, potentially up to several months. These agreements must be negotiated with the selected single IRB each time a study is funded, unless otherwise specified. This requirement may at least initially counteract the expected gains in efficiency. The NIH hopes that use of existing IRB-agreement templates will expedite this process. It appears prudent for institutions to also discuss roles and responsibilities prior to the notice of award. Second, the NIH discourages but does not prohibit duplicative ethics review by local IRBs. Institutions might therefore impose local-IRB review under certain conditions and before study enrollment at their center. Since IRB agreements are often negotiated individually, this provision may affect some but not all participating centers and may result in considerable delay of study commencement.

The NIH expects that the benefits of this transition will be realized as use of single IRBs increases, but it will monitor outcomes such as time to research initiation and threats to the protection of participants. Since utilization of single-IRB review has been limited, data on long-term outcomes have not been available or have not been published. We do not yet know whether streamlining IRB review will affect an IRB's ability to protect the welfare of human participants. Widespread adoption of single-IRB review will provide a wealth of empirical data for assessing the utility of this practice in the United States. IRBs do not typically divulge information regarding deliberations or administrative metrics, although metrics may be examined internally. These data need to be accessible, collected, analyzed, and reported systematically.[1]

We anticipate that with time, angst over this new policy will lessen, as evidence is collected to confirm the prophesied advantages. Implementation of the policy should be seen as a work in progress, and modifications and clarifications may be required as outcomes data are analyzed. Ultimately, a high-quality, efficient ethics-review process is a public health good.

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