What’s New in GCP?

**NIH Mandates Single-IRB Review for U.S. Multi-Site Research**

Starting next May, the National Institutes of Health (NIH) will require the use of a single institutional review board (IRB) for multi-site research in the United States funded by NIH.

“The NIH recognizes that the policy will begin a paradigm shift in IRB review. As such, the final policy will not take effect until May 25, 2017. In the interim, the NIH will issue guidance and provide resources to assist awardees in adapting to the shift,” NIH said in announcing the final policy.

“Eliminating duplicative IRB review is expected to reduce unnecessary administrative burdens and systemic inefficiencies, without diminishing human subjects protections,” NIH said. “The shift in workload away from conducting redundant reviews is also expected to allow IRBs to concentrate more time and attention on the review of single-site protocols, thereby enhancing research oversight.”

**NIH Finds “No Compelling Reason” To Narrow Scope from December Proposal**

NIH said that, after reviewing the comments, it “found no compelling reason to narrow the essential scope of the final policy — it will cover all domestic sites of NIH-funded, non-exempt, multi-site studies, as was proposed” — however, the agency clarified the policy intent and modified several provisions.

“The final policy is intended to apply only to studies where the same research protocol is being conducted at more than one site; it does not apply to studies that involve more than one site but the sites have different roles in carrying out the research,” NIH said.

Applicants/offerors will be expected to submit a plan identifying the single IRB that will serve as the IRB of record for all study sites. “It will be the responsibility of the applicant/offeror to assure that the single IRB is qualified to serve; the applicant’s plan will not be evaluated in peer review.”

NIH said the additional costs associated with single IRB review may be charged to grants or contracts as direct costs, provided “such costs are well-justified and consistently treated as either direct or indirect costs according to applicable cost principles in the NIH Grants Policy Statement and the FAR 31.202 (Direct Costs) and FAR 31.203 (Indirect Costs).”

NIH said the exceptions to the policy remain the same as in the proposed policy if federal, state or tribal laws, or regulations prohibit the use of a single IRB. The NIH also will grant exceptions where the federal, state or tribal prohibition on the use of a single IRB is established by policy and will consider granting an exception if a request is made and a compelling justification is provided. “Such justifications could be for reasons other than that the single IRB is unable to meet the needs of a specific population, as was proposed in the draft policy. The final policy also clarifies that multi-site studies within ongoing, non-competing awards will not be expected to comply with the policy until a competing renewal application is submitted.”

Many research institutions have concerns about mandating single IRB review and contend the federal government should encourage rather than mandate single IRB review. A major concern is increased administrative burden as institutions develop IRB authorization agreements between research entities and reviewing IRBs. There are also concerns about a loss of accountability at local sites and an inability to understand local concerns and conditions.
NIH proposed the policy in December 2014 and received 167 comments on it. NIH said most of the comments supported the agency’s goal of “enhancing and streamlining IRB review in multi-site research. Commenters, especially individual researchers, scientific and professional societies, and patient advocacy organizations, generally agreed that the use of a single IRB for multi-site studies involving the same protocol would help streamline IRB review, and would not undermine and might even enhance protections for research participants.”

The agency added that most of the comments also favored NIH’s approach of “making reliance on a single IRB an expectation for all non-exempt multi-site studies carried out at U.S. sites.” However, academic institutions “did not agree with the scope of the proposed policy or that it should become a term and condition of funding, and suggested the NIH incentivize, not mandate, reliance on a single IRB.”

**Researchers Support the Change**

NIH noted researchers supporting the policy “described unnecessary delays and additional costs caused by duplicative IRB reviews. They noted that IRB submission requirements at each site differ and take time to navigate and manage. They also indicated that review of the same protocol by multiple IRBs can sometimes lead to protocol and consent document changes that can introduce inconsistencies in the execution of the protocol across sites, lead to enrollment imbalances, and skew the analysis of the aggregated data.”

In addition, “multiple IRB reviews result in changes to consent documents that are merely stylistic and not substantive, or changes that focus on institutional interests (e.g., liability management) rather than human research protections.”

The comments also “raised the concern that the current practice...may actually contribute to some researchers’ reluctance to participate in rigorous, multi-site research and may incentivize smaller and simpler study designs.”

The NIH said scientific and professional societies generally favored the proposed policy, contending it “would decrease administrative burdens on clinical research staff, speed up participant recruitment, and streamline the research process, and that these changes would result in enhancements to the efficiency of research and acceleration of research progress. They also suggested that the benefits of such a policy include enhanced adverse event monitoring and improvements to the quality and consistency of IRB reviews.”

Patient advocacy groups and participant representatives supported the new policy, saying it would “lead to enhanced protections through increased accountability and improved efficiency.”

**Academic Institutions, IRBs Are Not Happy**

Academic institutions, IRBs and organizations that represent them contended the scope of the policy was “too broad and that the NIH should not make the policy a term and condition of award. They said that decisions about whether to use a single IRB should be voluntary and that the NIH should offer incentives to promote change.”

They suggested NIH encourage investigators and institutions to use single IRBs in grant applications by providing additional funding to those grants that agree to use a single IRB. Others recommended that, before issuing a broad policy, the NIH pilot and evaluate a narrower use of single IRBs and provide appropriate resources to support the participating awardees.
Others suggested NIH fund research on existing central IRB models to evaluate potential benefits and costs before mandating single IRB review.

There were also concerns about the timing of the policy in relation to the revisions of the Common Rule, contending the NIH should not adopt a single IRB policy until the Common Rule revisions are completed.

Academic institutions also were concerned that the membership of any single IRB “would not be able to achieve the level of local support for a particular research study or its acceptability in terms of all the participating sites’ institutional commitments and regulations, applicable laws, and standards of professional conduct and practice. Some commenters contended that only a local IRB is able to understand the specific protections required for a vulnerable population that comprises their research participant base.”

Others suggested site-specific practices for recruitment and retention, especially for vulnerable populations, would pose challenges for a single IRB. “A number of commenters stated that their institutional IRBs are in the best position to know and understand competencies of and potential conflicts of interest of specific investigators. Others stressed the importance of the relationship between an investigator and the local IRB and noted that IRB members can serve as mentors to investigators whose protocols they oversee.”

Some comments asserted the new policy did not “recognize the time and effort needed to identify and establish a single IRB of record, including negotiating and executing authorization agreements and standard operating procedures, conducting study initiation meetings, creating account activities, and modifying information technology systems. They suggested that the policy would result in the formation of hundreds of different ‘single IRBs of record’ with which institutions and investigators will need to interact.” Some comments questioned whether a single IRB could ensure local compliance at a relying institution and were concerned that a compliance problem for a single IRB would lead to compliance actions against the sites relying on that IRB.

Several comments that supported the use of single IRBs recommended that, rather than having participating sites identify a single IRB for each protocol, NIH should establish a central IRB to review all multi-site research studies, akin to the National Cancer Institute’s Central Institutional Review Board. “They suggested that this approach would create an even ‘playing field’ for every institution, big or small, regardless of whether their own IRB has the resources to act as a single IRB of record.”

Many comments, regardless of their position on the new policy, “noted that, over the past several decades, the IRB’s role has been expanded to include functions that go beyond ethical review of proposed research” and now include reviewing compliance with institutional policies, such as conflict of interest and investigator training. NIH noted that comments in favor of the new policy “thought that greater use of single IRBs would help to return IRB review to its primary mission of ensuring appropriate protections for human subjects rather than protecting the institution from legal liability or damage to its reputation. They also suggested that when institutions rely on a single IRB of record for multi-site research studies, IRB responsibilities are clearer, which helps institutions develop policies and provide resources beyond IRB review (e.g., human research protections experts) to facilitate compliance with the institutional human research protections program.

However, comments opposed to the new policy contended “the ancillary responsibilities of IRBs are so intertwined with the research oversight responsibilities that using a single IRB would disrupt the existing system of ‘checks and balances’ at institutions. They also argued that the opportunity for the IRB to recommend protocol changes for reasons unrelated to ethical review (e.g., scientific improvements, changes to study design) would be lost.”
One comment said HHS’s Office for Human Research Protections (OHRP) should provide guidance to support the policy’s stance on duplicative IRB review.

NIH Promises Guidance Before Next May

NIH said that, before the policy’s effective date next May, the agency plans to issue guidance on:

- how costs associated with single IRBs may be charged as direct versus indirect costs;
- considerations in the selection of the single IRB;
- the content of the single IRB plan that must be submitted with applications and proposals;
- the process for applicants/offerors to submit a request for an exception and process for NIH review of the request for exception;
- roles and responsibilities of the single IRB and participating sites;
- model authorization agreement that lays out the roles and responsibilities of each signatory;
- models for gathering and evaluating information from all the reliant sites about community attitudes and the acceptability of proposed research;
- and a model communication plan that identifies when and which documents are to be completed and shared with those involved so each may fulfill their responsibilities.

The guidance will be posted here when completed.

“While the NIH anticipates that that there will be challenges associated with implementation, we expect these to be short-lived. Once the transition to the new way of operating is made, the benefits of widespread use of single IRBs will outweigh any costs and, ultimately, reduce burdens to the research process. At the same time, the NIH will also closely monitor the implementation of the policy, consider its impact on research like improvements in time to initiation of research and reduction of unnecessary burden, and be vigilant about any diminution in the protection of human subjects,” the agency said.


Other Recent Developments in the Guide to Good Clinical Practice

Panel Calls for New “Belmont” Group”; Common Rule Revision Halt

FDA Provides Guidance on Expanded Access

FDA Issues Draft Guidance on Evaluating and Reporting Age, Race, Ethnicity Data for Device Trials