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What's New in GCP?
SACHRP Contends NIH Is "Premature" in Mandating Single IRB

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The Secretary's Advisory Committee on Human Research Protections (SACHRP) concluded it is "premature" for the National Institutes of Health to require single institutional review board review of multi-site studies.

SACHRP was responding to an NIH proposed policy released in December 2014. "The comments were due by the end of January, but we were able to get permission to bring this to SACHRP because we felt this was an important enough issue that SACHRP should weigh in on it," said Michele Russell-Einhorn, co-chair of SACHRP's Subpart A subcommittee.

"SACHRP maintains at this time that a uniform mandate of single IRB review for all domestic multi-site studies is premature," the committee said in comments approved March 25. "SACHRP supports the use of single IRBs but takes the position that a more measured and careful process of encouraging single IRB use, accompanied in a step-wise way by issuing guidance on critical issues involved in the use of single IRB review, would result in less disruption of the research enterprise, and eventual improvements in a single IRB process that is anchored in deep collective experience."

The committee added that "mandating single IRB review for domestic multi-site studies alone is not a sufficient solution to improve turn-around time for human subject's research." SACHRP noted that "requiring a single IRB to review a multi-site research protocol may well result in new procedures and policies being created by the relying institutions and the reviewing institution that will undermine the goals of this policy change and create a host of new challenges for research institutions."

"The tone to this document is to recognize that there is promise with the single IRB approach, but the basic criticism remains the same, that none of us have the data to suggest when it is most useful" to have single IRB review and when it is not, SACRHP chair Jeff Botkin said. "In order to make a fundamental change in the system, it seems to me that the onus is on NIH to present the data to say, 'Here is why we think this is going to work and we think the benefits are greater than the burdens.'"

Investigators Requested the Change

Valerie Gordon, NIH's acting director of clinical research policy, told the committee the reason NIH proposed the policy was because it was "a long-standing request and demand from the research community." She noted the comments NIH received on the proposed policy are "tremendously in favor" of the change. However, most of the comments are from "investigators, who are really, really frustrated with the IRB process for multi-site studies" and not IRB or institutional officials, Gordon said.

"We understand that the investigator community is interested in this, but we also understand that they don't understand the complexities," Botkin said. "This is a call for more dialogue, rather than specific conclusions about when this is going to work and when it is not."

SACHRP suggested that "rather than mandating review by a single IRB, NIH find mechanisms to encourage investigators and institutions to voluntarily utilize single IRBs as part of their grant submissions. This could be accomplished by providing incentives, such as additional dollars to those grants that agree to utilize single IRB arrangements."

SACHRP also recommended that NIH:

- Collect and disseminate data regarding experiences to date with single IRB review, including its own experiences, experiences of independent IRBs, and experiences of industry sponsors;
- Fund research evaluating the advantages and disadvantages of single IRB use in domestic IRB multisite research;
- Evaluate the cost issues and provide a proposal that would cover the cost of both single IRB review and local review without reducing dollars to the researchers. "Budgets for grants should increase where single IRB review is an integral part of the proposal and take into consideration the additional costs to both the reviewing and relying institutions," SACHRP said; and
- Support meetings with the research community where issues regarding the use of a single IRB can be discussed in a public forum.

SACHRP said "comprehensive data is needed to assess: the advantages and disadvantages of single IRB review on the reviewing IRB and the relying institutions; the impact on local review concerns; the cost of a single IRB system on various institutions; and the categories of research that are most appropriate for single IRB review."

How Many Studies in a Multi-Center Study?

SACHRP member Gary Chadwick said the draft policy does not define multi-site studies. "That could be a small collaboration between two sites," he said. "Quite often, to get one of the two IRBs to recognize the other IRB as its IRB for this particular study requires more effort than to just have both IRBs review the project and approve it. And that is often true for three or even four sites. If the intent is to improve the efficiency of getting research up and running for small collaborations, this doesn't make a lot of sense."

However, SACHRP member Thomas Eissenberg noted that, while "it may take a lot of trouble for one of the sites to agree to be the IRB of record, if they would it would be great. I don't understand why we are precluding a particular group of studies because some IRBs may be recalcitrant in some way. I think that if that is the issue — we ought to speak to that."

Chadwick said the "problem is the policy says for all multi-site studies and sometimes it doesn't make sense."

SACHRP said a "significant barrier" to institutional adoption of the single IRB model "is the information technology required to ensure adequate review, communication and oversight" as institutions' systems "differ from one another, are complex and expensive, and are not interoperable… Changing existing technology to incorporate communication and management of research being conducted at numerous outside sites is a considerable obstacle that has to be acknowledged and addressed," the recommendations said.

In addition, "investigator conflicts of interest and institutional conflicts of interest are two significant reviews that are often tied to the IRB review because conflicts of interest may well result in IRB determinations regarding additional information that should be included in the consent, additional monitoring by an independent DMC or DSMB, or removal of an individual as the primary investigator."

Local and regional variations also have to be considered, such as:

- State laws governing human subjects and/or research data, such as genetic testing, genetic privacy, health information laws that go beyond HIPAA, mental health information, mental retardation information, developmental disabilities information, surrogate consent, inclusion of children in research, age of majority, age of consent to certain medical treatment such as substance abuse, and investigator licensing requirements;
- Emergency research undertaken without subject consent, for which the FDA requires local community consultation;
- Disparate cultural norms among populations targeted for recruitment;
- Varying investigator and research team experience, which may require more or less oversight during the conduct of the research; and
- Varying institutional policies regarding availability of compensation for subject injury.

SACHRP said NIH also needs to consider a process for qualifying a single IRB and identified several issues that need to be addressed:

- Adequate record keeping systems with written standard operating procedures for tracking each site independently, including the ability to manage site-specific emergency care, conflicts of interest, sub-studies, unique consent forms, subject complaints, compliance issues, and unanticipated problems;
- Process to adequately obtain knowledge of state laws when the single IRB reviews research sites in other states to assure compliance;
- Written standard operating procedures describing how local cultural and resource context information will be gathered, both at initial and continuing review;
- Capacity to conduct site visits;
- Written standard operating procedures describing how the single IRB and institutions will coordinate issues, such as review by other committees, such as radiation and institutional biosafety, and unique institutional policies;
- Accreditation of its human research protection program; and
- Appropriate oversight by the HHS Office for Human Research Protections and the FDA.

SACHRP noted "reliance arrangements require complex coordination and communication to manage issues, such as how the single IRB will interact on an ongoing basis with local IRBs to, for example, the emergence of risks that might be unique to a site, the local investigator or its study population, and the implementation of uniform or site-specific measures to mitigate those risks." SACHRP said that single IRBs "should be expected, as part of their initial review and approval, to establish formal written standard operating procedures for accomplishing this in an ongoing way during the course of the approved studies.

Yet, this may be so complicated that, without careful planning and implementation, such a system coupling local review with a single IRB would, in the end, be less efficient than the current practice of each IRB performing its own separate review."

SACHRP added "a significant challenge to single IRB systems is the development and management of inter-institutional agreements and processes" and that tools are needed for developing and managing these agreements. SACHRP recommended that NIH "evaluate and work with institutions and the larger research community to fully develop a single IRB review model that addresses the issues faced by all of the involved parties."

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