

Commentary on Diamond et al.: The efficiency of single institutional review board review in National Institute of Child Health and Human Development Cooperative Reproductive Medicine Network–initiated clinical trials

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Diamond et al.'s paper,¹ “The efficacy of single institutional review board review in National Institute for Child Health and Human Development Cooperative Reproductive Medicine Network–initiated clinical trials,” presents critical issues and makes important contributions to the literature, highlighting urgent needs for research on rapidly expanding single institutional review boards (sIRBs). The main findings of the study, that sIRB reviews for multicenter trials reduced the time for institutional review board (IRB) review and initial approval, but increased the total time to final local site approval, shed critical light on the complexities of human study participant protection, and of the social and institutional ecologies in which IRB reviews occur.

The study revealed that under the sIRB system, the total amount of time before the study could start almost doubled. Delays occurred because institutions differ in the language they used concerning areas such as the Health Insurance Portability and Accountability Act of 1996 (HIPAA), participant injury, indemnity, privacy and compensation, biosafety, radiation and chemical safety, local processes and approvals for adding or removing study personnel, conflicts of interest, and advertising of studies through print, TV, radio, or the Internet.

SIRB guidelines from the National Institutes of Health (NIH) and the proposed changes to the Common Rule² do not address these local issues. Researchers' understandable frustrations with unwarranted discrepancies among local IRBs in multisite studies fueled the push for sIRB policies, which were then drafted and are being implemented essentially in the absence of any data on how effective these new structures are or would be.

Local IRBs (LIRBs) have often claimed that discrepancies in their decisions reflected differences in local

community values, which turns out not to be the case.³ Rather, as Diamond et al. indicate, variations can result from local bureaucratic processes. State laws may occasionally prove to be barriers, but most differences appear to result from differences in individual institutions' wording concerning, for instance, personnel, advertising, privacy, compensation, and handling of dangerous substances. Many hospitals' lawyers compose their own boilerplate language without having to consider other institutions' equivalent text and how these might diverge from each other. When these documents were each drafted, before sIRB policies were implemented, no pressures existed to reduce these discrepancies. Little, if any need for such coordination existed. Now, however, given federal mandates for sIRBs, such inter-institutional variations generate significant problems and are no longer acceptable a priori. Rather, harmonization is critical, and lack of it can delay the start of important studies.

Diamond et al. highlight, too, how sIRB approval is only one aspect of much larger institutional and regulatory contexts in which human subject research approvals occur. Yet the guidelines concerning sIRBs have not addressed these other key components of protocol approval and need to coordinate these other institutional functions. Doing so is vital, however, to reduce these remaining barriers to optimal and efficient sIRB reviews. As Diamond et al. conclude, “Greater coordination with LIRBs is key,” regarding these functions.

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But, such standardization will require concerted efforts. Public Responsibility in Medicine and Research (PRIM&R), the Office for Human Resource Protection, NIH, and others can develop model templates of documents that research sites can share.

Yet obstacles need to be overcome. Various institutional factors may foster these inter-institutional differences. For example, in a multisite study, some institutions, but not others, may engage in certain other kinds of research that use particular radioactive substances. An institution that uses these substances may include relevant language in its patient safety documents as boilerplate, even though this text does not apply to all of that institution's studies. Yet that institution, when participating in a multisite study, may consequently have different safety documents and processes, which can delay the initiation of any protocol. Instead, institutions may need to become more flexible, adjusting such boilerplate text to include certain elements only when these apply. Similarly, institutions may vary in their language about conflicts of interest based on particular cases they have encountered. For instance, some institutions may have had to address investigators who hold patents that provide no remuneration now but may do so in the future. Such an institution may thus include language concerning such situations in its standard boilerplate conflict of interest forms, while other institutions do not do so. Again, such differences can, however, postpone the start of multisite studies.

These varying forms and processes can presumably all be addressed and harmonized, but these examples also underscore crucial needs for empirical research to examine the specific types, scope, and sources of these discrepancies.

Diamond et al. highlight the importance of collecting and analyzing ongoing data to help design, implement, and refine policies in this area, especially since sIRB policies were instituted without any data on how well they would work. Such data are thus critical.

Yet, unfortunately, many aspects of IRBs are not transparent to researchers, study participants, or scholars examining IRBs.⁴ Numerous IRBs have refused to participate in research on their processes, refusing to allow investigators to observe meetings or often interview chairs, members or staff in order to understand how these committees operate and might be improved. Although data on a few quantitative, logistical aspects of IRBs (e.g., length of time to approval) have been published, studies of these boards' decision-making processes have been stymied because many of these committees these committees refuse to be observed for research purposes. Recently, for instance, Paul Appelbaum, Chuck Lidz, and I, along with other colleagues, conducted a study of sIRBs.⁵ But all of the large for-profit sIRBs, along with several of the federally funded ones, refused

to participate. Several chairs of for-profit IRBs whom we had contacted expressed interest in possibly participating, but said that they first had to obtain permission from their companies' owners. The latter then refused, stating that they felt that there was nothing for them to gain from participating—that is, that doing so would not provide them any financial advantage. One CEO, for instance, insisted on the high quality of their reviews but refused to allow us to interview staff or members or observe meetings. Yet as Diamond et al. show, such data on sIRB operations are vital to illuminate where and how improvements can be made.

Currently, researchers involved with other multisite studies and sIRBs should thus also publish data on their processes—on how policies differ among the individual sites and why—to understand how the system can be enhanced. At the same time, data are needed on not only the form but also the *content* of multisite approval processes—that is, not only on the lengths of time to approval but also on the content of the specific obstacles that emerge regarding differences in interpretations of policies and guidelines regarding conflicts of interest, radiation and chemical safety, personnel changes, and other areas—how exactly institutions vary in their requirements and/or language, which terms in HIPAA or other regulations institutions define differently and why, what barriers to harmonization exist, and how these might best be overcome.

These examples underscore needs for qualitative, not just quantitative research to investigate these domains. Yet, many research funders, including some institutes within NIH, have been unfamiliar with, and hence less supportive of, such qualitative, as opposed to strictly quantitative research. Funding for such investigations will, however, be crucial to advance research on human subject protections. Reductions in the length of time before protocols can begin will require understandings of exactly how and why institutional documents and processes vary, and whether the reasons are justifiable or result merely from idiosyncratic historical path dependency.

This accompanying article by Diamond et al. has certain limitations, including the fact that the total number of studies and sites is relatively small. Nonetheless, the findings are important and suggestive, especially since data on the logistics and workings of sIRBs remain scant. Their article thus raises vital concerns and will hopefully serve as a model that will inspire others to continue to illuminate how to improve protocol review processes both centrally and at individual institutions.

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