

Local IRB Collaboration in Central IRB Reviews

By Joseph E. Andrews, Jr. and J. Brian Moore

Background

The lack of consistency between Institutional Review Board (IRB) reviews has been cited as a detriment to the conduct of research at multiple sites. The human research protection community is actively discussing ways in which multisite study review can be improved in terms of consistency, efficiency and economy.

A consensus approach has recently been suggested in which all local IRBs would have access to the concerns raised by other local IRBs and, through a mediator, all would ultimately agree to a single version of every multisite study protocol, consent form, and other study material. Such a process would solve the inconsistency issue arising from many separate IRB reviews requiring unique study materials at each site, but it does not address the efficiency or cost concerns.¹

As the community contemplates how best to move forward, study sponsors are increasingly reluctant to conduct multisite clinical research at sites that require local IRB review when other sites accept much faster, simpler and economical review by a single central IRB. Recent proposals for federal rule changes have included mandatory use of central IRBs in multisite research.² The value of central review in terms of speed, efficiency and consistency has been well documented.⁶ Yet, many sites have concerns about ceding IRB review authority to a central board.³ Some sites feel responsible for the protection of enrollees at their location and want to stay involved.⁴ According to Robert J. Levine, MD, "something of immeasurable value will be lost" in moving from local to central IRB review because local boards possess knowledge about the institution, investigators and culture that is hard to pass on to a central group.⁵ Different sites have different perspectives on study design: the importance of research objectives, standard of care, the risk of adverse events, the use of placebos, etc. Local board members know the history of research at the site, community sensitivities, any past litigation or regulatory activity, the research facilities and services, how research conduct varies across departments, and the track record of the individuals to be involved.

Since each site is responsible for the human research it conducts, each site must decide whether to participate in a particular multisite study. Some sites have reservations about conducting research that has not been vetted locally, at least to some degree. Without a voice in the review process, sites are in a take-it-or-leave-it situation.⁷ If local IRBs cede authority, is there an effective way to convey this information to the central IRB?

A Collaborative Review Process

A *collaborative* review process could respect the decision-making role of the central IRB but without abdicating the sites' responsibilities. By instituting a process with clear responsibilities and strict timelines, the benefits of both local and central review can be achieved with little or no cost in speed or efficiency.

The process we propose is simple:

1. A sponsor contracts with a central IRB to review and approve their study.
2. The central IRB conducts its review and, if appropriate, issues a "Preliminary Approval."

3. Each site has, say, a five-business-day window to assess the study, if it so wishes, and offer comments to the central IRB. This "Assessment" focuses on any necessary changes that the site would *require* to conduct the study, rather than on nice-to-have changes that the site would *prefer*. An Assessment is not a formal local IRB review; it might be performed by the Board, by a subgroup of Board members, or by an expert appointed by the Board. If the site does not have an IRB, site officials can appoint the reviewer(s). The number of required changes from a site should be very small and probably overlap with those from other sites. If a site sees any insurmountable obstacles, it can decline participation at this point.
4. Sites submit their Assessments to the central IRB.
5. The central IRB reviews the Assessments, makes any changes to the protocol that it deems worthwhile, in concert with the study sponsor, and, if appropriate, issues its "Final Approval" within, say, five business days, along with updated study documents, and the disposition of required changes from all the sites.
6. Each site then reviews the Final Approval, updated study documents, and disposition of proposed changes, and has, say, five business days to accept or decline the study as is, without modification, considering the history of research at the site, community sensitivities, any past litigation or regulatory activity, the research facilities and services, the processes followed in the various departments, and the track record of the individuals and departments to be involved.

Practical Considerations

According to metrics posted on the website of a large central IRB, it takes that IRB an average of 10 business days to complete its initial review, not including any time required to negotiate changes with the sponsor.⁸ Adding collaboration to the review process would add 10 to 15 business days or so to the process but offers the following benefits:

- Higher quality reviews because there are more eyes on the study
- All sites feel they have a voice
- More rapid startup by sites that would have required local IRB approval
- Shared learning about potential problems that can be addressed in future studies

However, given the time it typically takes sponsors and sites to negotiate contracts, 10 to 15 additional days for human subjects protection will have no effect on study start-up times for most sites.

The proposed process adds costs for the central IRB but reduces costs for sites that would have required local IRB approval, along with associated costs for the sponsor. Other sites, presumably, already have processes in place for deciding whether to accept a study approved by a central IRB. The number of costly and time-consuming protocol amendments should decline.

The proposed process does not require that all sites be identified at the same time. However, it does require an adequate initial number of sites to give legitimacy to the central IRB's approval. In addition, the disposition of required changes can guide review by sites that join the study later.

If a site has outsourced part or all of its IRB function to a central IRB, that IRB could participate in the collaborative review on its behalf. However, that central IRB would probably not have the local knowledge essential to the collaborative process. Instead, the site could assign responsibility to the local personnel best equipped for the task, be they IRB members, human subjects protection specialists, experienced investigators, or people specifically designated for such tasks.

Conclusion

Many local IRBs could improve their speed and efficiency with simple structural and process changes,¹⁰ but the trend is moving toward central IRB review of multisite studies. With a disciplined collaborative process, central IRBs can work with sites to achieve the speed, efficiency and consistency of central IRB reviews while improving quality with input from the sites — the best of both worlds.

With a shared learning process, the clinical research enterprise can improve the quality of initial protocol submissions, reach consensus on how to handle issues that continue to appear, and understand the requirements of different sites.

References

1. Ford, P. J., Stewart, D. O. & DeMarco, J. P. (2015) Increasing Common Rule protections: IRB consensus, black box warnings, and risk in Equipoise. *IRB: Ethics & Human Research* 37(3):7-11.
2. Wechsler, J. (2015). Pressure mounts for central IRBs. *Applied Clinical Trials*, 24(2), 10.
3. Flynn, K. E. , Hahn, C. L., Kramer, J. M., Check, D. K., Dombek, C. B., et al. (2013) Using Central IRBs for Multicenter Clinical Trials in the United States. *PLoS ONE*. 8(1): e54999. doi:10.1371/journal.pone.0054999
4. McNeil, C. (2005). Central IRBs: Why are some institutions reluctant to sign on? *Journal of the National Cancer Institute*, 97(13), 953-955.
5. Wechsler, J. (2007). Central vs. Local: Rethinking IRBs. *Applied Clinical Trials*, 16(2) 24-26.
6. Menikoff, J. (2010). The paradoxical problem with multiple-IRB review. *The New England Journal of Medicine*. 363(17), 1591-1593.
7. IRB Advisor (2015). Single IRB NIH guidance may leave more questions than answers. 15(3), 25-36.
8. Western IRB (WIRB) Turn-around time. Retrieved from <https://www.wirb.com/Pages/TAT.aspx> on 8 May, 2015.
9. Kiriakis, J., Gaich, N., Johnston, S. C., Kitterman, D., Rosenblum, D., Salberg, L., & Rifkind, A. (2013). Observational Study of Contracts Processing at 29 CTSA Sites. *Clinical and Translational Science*, 6(4), 279-285.
10. Andrews, J. E. & Moore, J. B. (2014). Overhauling an Academic Medical Center HRPP with Simple Process Changes. *Journal of Clinical Research Best Practices*. 10(9).

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