

In a multicenter clinical trial, full review by each site's institutional review board (IRB) may not enhance the protection of research participants, may cause differential treatment of patients across research sites, and can lead to significant delays in study start-up.<sup>1-3</sup> The Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP) support the use of single IRBs (sIRB) for multicenter trials to meet the requirements of existing IRB regulations.<sup>4,5</sup> The Department of Health and Human Services (DHHS) has issued a change to the Common Rule effective in 2020, and the National Institutes of Health (NIH) issued a final policy effective as of Jan. 2018, requiring sIRB review for most multicenter trials.<sup>6,7</sup>

Concurrently, CTTI has championed the adoption of single IRBs (sIRBs) for multicenter clinical trials for the past decade. We began a project in 2010 to determine the barriers to using sIRBs for multicenter clinical trials in the United States, resulting in a summary of findings<sup>8</sup> and the following recommendations:

1. CTTI recommends using a sIRB of record for all sites to improve the quality and efficiency of multicenter clinical trials.
2. To address blurred distinctions between responsibilities for ethics review and other institutional obligations, CTTI recommends that sites and IRBs use a CTTI-developed guide, also known as the Considerations Document, to support communication and contractual relationships between institutions and a sIRB.
3. CTTI recommends that sponsors in a position to require the use of sIRB review for multisite trial networks should do so in order for relevant stakeholders to gain experience with sIRB review. The resulting experiences may foster greater comfort and trust with the sIRB model.

CTTI then conducted a follow-on project from 2013-2015 to encourage adoption of the recommendations and address remaining barriers. We frequently encountered questions about how to implement a sIRB model for multicenter clinical trials. To address these questions, CTTI conducted webinars with implementation examples from sponsors and research institutions. We also developed additional tools through a collection of existing IRB authorization agreements/templates/policies and a June 2014 multi-stakeholder meeting. The following recommendations were issued:

1. CTTI recommends use of the CTTI-developed Evaluation Checklists:
  - ▶ For institutions to determine their readiness to use a sIRB (federal, academic, or independent IRB) for multicenter clinical trials,
  - ▶ For institutions/sponsors when selecting a particular IRB to serve as the single IRB of record, and
  - ▶ For sIRBs when deciding whether to work with a specific institution during a multicenter clinical trial.
2. To address administrative and legal concerns and to reduce time when first executing a reliance (authorization) agreement, CTTI recommends that institutions and IRBs adopt or begin negotiations with the CTTI-developed IRB authorization agreement template.
3. To address local context concerns, CTTI recommends that IRBs and institutions follow the Secretary's Advisory Committee on Human Research Protections (SACHRP) Recommendations on Consideration of Local Context with Respect to Increasing Use of Single IRB Review (January 2013).
4. CTTI recommends additional research be conducted to further define quality in IRB review.

5. CTTI recommends research be conducted to develop data and technology standards across electronic IRB application systems to facilitate communication and efficacious and transparent review.

In 2017, CTTI started driving adoption activities to determine what additional resources are needed for the research community to implement a single IRB model for multicenter clinical trials. An expert meeting was held in November 2017, additional expert interviews are being conducted, and a multistakeholder committee was formed to address the remaining needs. Additionally, we are collaborating with an NIH workgroup to develop a comprehensive plan for [assessing the NIH's sIRB policy](#).

## CTTI RESOURCES FOR FACILITATING THE USE OF A SIRB FOR MULTICENTER CLINICAL TRIALS

- ▶ **Webinars:** <http://www.ctti-clinicaltrials.org/webinar-series>
- ▶ **Considerations Document:** [https://www.ctti-clinicaltrials.org/sites/www.ctti-clinicaltrials.org/files/ctti\\_sirb\\_considerations\\_one-pager\\_2018\\_0.pdf](https://www.ctti-clinicaltrials.org/sites/www.ctti-clinicaltrials.org/files/ctti_sirb_considerations_one-pager_2018_0.pdf)
- ▶ **Evaluation Checklists and IRB Authorization Agreement Template:** <http://www.ctti-clinicaltrials.org/what-we-do/ctti-projects/central-irb-advancement/products>

## REFERENCES

1. Menikoff J. The paradoxical problem with multiple-IRB review. *N Engl J Med* 363: 1591–1593.
2. Wagner TH, Murray C, Goldberg J, et al. Costs and benefits of the national cancer institute central institutional review board. *J Clin Oncol* 28: 662–666.
3. Abbott D, Califf R, Morrison BW, et al. Cycle time metrics for multisite clinical trials in the US. *Ther Innov Reg Sci*, 00 (2013), pp. 1–9.
4. US Food and Drug Administration. Guidance for industry: using a centralized IRB review process in multicenter clinical trials. 2006(July 31, 2012).
5. Menikoff J. Office of Human Research Protections Public Correspondence on Central IRBs. 2010; <http://www.hhs.gov/ohrp/policy/Correspondence/mcdeavitt20100430letter.html>. Accessed August 6, 2012.
6. Department of Homeland Security, Department of Agriculture, Department of Energy, et al. Federal Policy for the Protection of Human Subjects. *Fed Regist*. 2017;82(12):7149-7274. Available at: <https://www.federalregister.gov/documents/2017/01/19/2017-01058/federal-policy-for-the-protection-of-human-subjects>
7. National Institutes of Health. Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research. <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html>.
8. Flynn KE, Hahn CL, Kramer JM, et al. Using central IRBs for multicenter clinical trials in the United States. *PLoS One* 2013; 8(1): e54999.