

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 central IRBs for multicenter trials to meet the requirements of existing IRB regulations.<sup>4,5</sup> The Department of Health and Human Services (DHHS) has proposed a change the Common Rule, and the National Institutes of Health (NIH) issued a draft policy, requiring centralized review for most multicenter trials.<sup>6,7</sup>

CTTI began a project in 2010 to determine the barriers to using central IRBs for multicenter clinical trials in the United States. A summary of CTTI's findings was published in January 2013.<sup>6</sup> The following recommendations were issued.

1. CTTI recommends using a central IRB (defined as a single IRB 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 central IRB.
3. CTTI recommends that sponsors in a position to require the use of central IRB review for multisite trial networks should do so in order for relevant stakeholders to gain experience with central IRB review. The resulting experiences may foster greater comfort and trust with the central IRB model.

CTTI conducted a follow-on project from 2013-2015 to encourage adoption of the recommendations and address remaining barriers. The project team frequently encountered questions about how to implement a single/central IRB model for multicenter clinical trials. To address these questions CTTI conducted webinars with implementation examples from sponsors and research institutions. Also, additional tools were developed 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 Central IRB (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 Central IRBs 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.

## CTTI TOOLS FOR FACILITATING THE USE OF A CENTRAL/SINGLE IRB FOR MULTICENTER CLINICAL TRIALS

Considerations Document: <http://bit.ly/2kIHHTm>

Evaluation Checklist: <http://bit.ly/2kIFlyd>

IRB Authorization Agreement Template: <http://bit.ly/2m5bgie>

Webinars:

- Research Institution Perspectives on Advancing the Use of Central IRBs for Multi-center Clinical Trials in the United States: <http://bit.ly/2lk0in7>
- Sponsors' Perspectives on Advancing the Use of Central IRBs for Multi-center Clinical Trials in the United States: <http://bit.ly/2m9p8Ve>

Quicklink to CTTI's Central IRB Project: <http://bit.ly/2lDqt92>

## REFERENCES

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