Use of Central IRBs for Multicenter Clinical Trials

Kathryn Flynn1,2, Cynthia Hahn3, Devon Check1, Judith Kramer4, Lawrence Muhiha1, Jane Perlmutter5, Kevin Weinftur1,2
1 Duke Clinical Research Institute, Duke University School of Medicine, Durham, North Carolina; 2 Department of Psychiatry and Behavioral Sciences, Duke University School of Medicine, Durham, North Carolina; 3 Office of Research Compliance, Fox Chase Cancer Institute, Philadelphia, Pennsylvania; 4 Department of Medicine, Duke University School of Medicine, Durham, North Carolina; 5 Gemini Group, Ann Arbor, Michigan

Background
Maximizing the efficiency of multicenter clinical trials so they can provide high-quality evidence to answer important medical questions is an important public health interest.

To increase the efficiency of conducting multicenter clinical trials in the United States, the Food and Drug Administration (FDA), the Office of Human Research Protections (OHRP), and the Department of Health and Human Services (DHHS) support the use of central IRBs.

Despite this support, research institutions differ in their willingness to defer to centralized IRB review.

Objective
To facilitate the ethical and efficient conduct of multicenter trials, the Clinical Trials Transformation Initiative (CTTI) supported this project to:

• Determine the barriers to using central IRBs for multicenter clinical trials in the United States.
• Formulate solutions to overcome these barriers.
• Obtain feedback on the proposed solutions from stakeholders at diverse research institutions, and
• Develop recommendations for implementing these solutions.

Methods
1. Identify current perceptions of the barriers to central IRB review and formulate potential solutions to overcome these barriers (see Table).
2. Conduct standardized tests of IRBs to demonstrate quality of review, such as missing important information, redundant review, caliber/expertise of reviewers, outside IRB and the local IRB to compare results.
3. Conduct expert discussions to establish liability protections through a well-defined accountability plan and contracts with the outside IRB. CTTI has developed a guide to support communication and contractual relationships between institutions and central IRBs.

Results & Discussion

Barrier
Feasibility of working with multiple outside IRBs, each requiring different forms and/or electronic systems to submit a protocol

Potential Solutions
Identify standard data elements to facilitate review and reporting across disparate systems.

Concern about regulatory liability in the event of noncompliance

Establish liability protections through a well-defined accountability plan and contracts with the outside IRB. CTTI has developed a guide to support communication and contractual relationships between institutions and central IRBs.

Concern about legal liability in the event of litigation secondary to errors, omissions, or negligence of an IRB not directly affiliated with the institution conducting research

Quality of review, such as missing important human subject protections issues without redundant review, caliber/expertise of reviewers, and insufficient time spent on protocols

Potential loss of local context

Need to clarify terms

Confusion abounds about the term “central IRB.” We defined a central IRB as a properly constituted IRB to which sites cede all regulatory responsibility for scientific oversight and integrity of the protocol from initial review to termination of the research, including review of informed consent. Or, briefly, a single IRB of record for a multicenter clinical trial.

Decoupling institutional and ethical review responsibilities

Many of the perceived barriers to using central IRBs arise from institutional and ethical review responsibilities, thus protecting the institution from risk are often coordinated through the institutional IRB office, which seems to have altered perceptions of what is entailed in the ethical review of research.

This conflation of institutional responsibilities with the ethical responsibilities of the IRBs leads to confusion about how institutional responsibilities differ from the context of a central IRB review. There is need for concrete tools to help research institutions separate institutional responsibilities from ethical responsibilities required of the IRB. CTTI created one such tool, a document that delineates these responsibilities and how they might be assigned to each entity or both entities.

Level of comfort and trust with central IRB review

Many institutional stakeholders expressed discomfort with a central IRB model due to concerns with an external entity handling of clinical review and oversight of a multicenter protocol, which seemed to be related to previous experiences with outside IRBs. What is still needed is experience with, not just knowledge about, using the central IRB model.

Addressing concerns about local context

Institutions and central IRBs need a detailed communication plan that includes a way to share information about local issues (site, investigators, etc.). The regulatory posture of OHRP and FDA specify their position, that an outside, central IRB could reflect local context issues satisfactorily.

Recommendations
The Clinical Trials Transformation Initiative (CTTI) recommends that sponsors in a position to require a central IRB review for multisite clinical 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.

Contact
Cynthia Hahn at CHahn@nshu.edu

Kathryn Flynn at kflynn@mcw.edu

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