Are you ready for Mandated Single IRB Review for Multicenter Clinical Trials?
Introduction to CTTI and CTTI Central IRB Projects

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CTTI Definition of Central IRB

CTTI's Definition of Central IRB: A single IRB of record for all sites involved in a multi-center protocol. A range of entities may serve as a central IRB:

- another institution’s IRB
- a federal IRB
- an independent IRB
Clinical Trials in Crisis

Discovery's 'First In Human' Calls Much-Needed Attention To Clinical Trials
Addressing This Need

Public-Private Partnership
Co-founded by Duke University & FDA
Involves all stakeholders
80+ members

MISSION: To develop and drive adoption of practices that will increase the quality and efficiency of clinical trials
Multi-Stakeholder

Everyone must have a seat at the table

- Clinical Investigators
- Government & Regulatory Agencies
- Industry (pharma, bio, device, CRO, & tech)
- IRBs
- Patients, Caregivers & Patient Advocacy Groups
- Academia
- Trade & Professional Orgs
- Patients, Caregivers & Patient Advocacy Groups
CTTI Membership

*Version: Sept. 26, 2017*
We use quantitative & qualitative research methods, selecting those best aligned with each project’s objectives, to:

- Identify/describe “what is going on” to gain a better understanding of a particular phenomenon
- Move beyond individual views to a more complete and objective understanding of the disincentives and motivators for change

Equipped with data, we then challenge assumptions, identify roadblocks, build tools and develop recommendations to change the way people think about and conduct clinical trials.
Real-World Impact within Organizations

- CTTI’s Central IRB tools & recommendations are used by:
  - Celgene Corporation
  - National Institute of Neurological Disorders and Stroke (NIH)
  - Northwell Health

- CTTI’s Quality by Design framework is used by:
  - AstraZeneca
  - DCRI
  - The Medicines Company
  - PCORNET
  - Pfizer
  - Seattle Genetics
  - Target Health Inc
  - University of Oxford
CTTI and its work have been cited in:

- A NIH draft Policy
- Several FDA guidance documents
- An EMA reflection paper
- HR 21st Century Cures & corresponding Senate effort
Project Methodology

1. State Problem
2. Gather Evidence
3. Explore Results
4. Finalize Solutions
5. Drive Adoption
6. Communicate

**Identify Research Impediments**
- Issue Statement & Project Plan

**Identify Gaps/Barriers**
- Literature Reviews, Surveys, & Interviews

**Analyze & Interpret Findings**
- Team Meetings

**Develop Recommendations/Tools**
- Team, Expert, & Ad Hoc Committee Meetings

**Disseminate & Implement**
- Pilot Studies, Measure Impact, & Implementation
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| **COMPLETE PORTFOLIO**  
| **September 2017**  |
|----------------------|----------------------|----------------------|----------------------|----------------------|
| **Complete Projects** | **Systematic Evidence Generation** | **Patients as Equal Partners** | **Efficient & Quality Trials** | **Public Health Concern** | **Safe & Ethical Trials** |
| Complete Projects | Large Simple Trials | GCP Training | ABDD Peds Trials | Central IRB |
| | MCT Novel Endpoints | Investigator Community | ABDD Trials | Central IRB Advancement |
| | Registry Trials | Monitoring | Streamlining HABP/VABP Trials | DMCs |
| | | Quality by Design | ABDD Unmet Need | Informed Consent |
| | | Recruitment | Long-Term Opioid Data | IND Safety |
| | | Site Metrics | | IND Safety Advancement |
| | | | | Pregnancy Testing |
| | | | | SAE Reporting |
| **Complete Collaborations** | **Clinical Trials for Comparative Effectiveness** | **Patient Engagement Survey** | **Clinical Trials Poll** | **Cardiovascular Endpoints** |
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CTTI Central IRB Projects

Use of Central IRBs for Multicenter Clinical Trials (2010-2013)

Advancing the Use of Central IRBs for Multicenter Clinical Trials (2013-2015)
Rationale for Central IRB Project

- Stakeholders frustrated by slow pace of research
- Separate local IRB review at each site adds delays and cost (Ravina, 2010; Wagner, 2010)
- In a multicenter clinical trial, full review by each site’s IRB may not enhance the protection of research participants
  - Distributed accountability; no IRB takes charge? (Meninkoff, 2010)
- The FDA, the Office of Human Research Protections, and Department of Health and Human Services support the use of central IRBs for multicenter trials
- However…it was not a common practice.
Goals of CTTI Central IRB Projects

Use of Central IRBs for MCTs

- Identify solutions to address barriers to the adoption of central IRBs for multicenter clinical trials

Central IRB Advancement

- Follow-on project
- To assess and propose solutions for remaining areas of concern for using single IRBs of record for multicenter clinical trials
Methods

- Literature Review
- Expert Advisory Panel
  - Institutional, federal, and commercial IRBs, industry, and regulatory agencies
- Semi-structured Interviews
  - Stakeholders at six research institutions that did not typically use central IRBs
- 2 Expert Meetings
  - FDA, OHRP, federal and industry sponsors, independent IRBs, research institutions, and patient advocates
- Webinar Series – Sponsor and Institutional Perspectives
- Collection of IRB Authorization Agreements to create template
- Creation of additional tools
Central IRB Team

Team Leaders:

▶ Colleen Gorman (Pfizer)
▶ Felix Gyi (Chesapeake Research Review)
▶ Jennifer Li (DCRI)

*Soo Bang (Pfizer), an initial team lead

CTTI Project Manager:

▶ Sara Calvert**

**Cheri Janning, initial project manager

Team Members:

▶ Judith Kramer (CTTI)
▶ Cynthia Hahn (Feinstein)
▶ Jane Perlmutter (Patient Representative)
▶ Cheryl Grandinetti (FDA)
▶ Patrick Archdeacon (FDA)

Research Team (DCRI):

▶ Kathryn Flynn
▶ Kevin Weinfurt
▶ Devon Check
▶ Carrie Dombeck
Central IRB Advancement Team

Team Leaders:
- Soo Bang (Celgene)
- Cynthia Hahn (Feinstein)
- Petra Kaufmann (NIH)

CTTI Project Manager:
- Sara Calvert

Team Members:
- John Buse (UNC)
- Cami Gearhart (Quorum IRB)
- Yvonne Higgins (WIRB-CG)
- Hallie Kassan (NS-LIJHS)
- Patrick McNeilley (FDA)
- Jane Perlmutter (Patient Representative)
- Andy Womack (Genentech)
Since 2015…

- Federal Policy for the Protection of Human Subjects; Final Rule
- SMART IRB Launched
- 21st Century Cures Act
- CTTI mission was changed to include “drive adoption”
- CTTI Steering Committee voted to conduct additional driving adoption activities for the Central IRB projects
  - Approved by CTTI Executive Committee
Meeting Objectives

- Review upcoming NIH policy and Common Rule changes regarding single IRB review as well as existing FDA Guidance on Centralized IRB Review Process in Multicenter Clinical Trials
- Discuss the remaining gaps in knowledge, guidance and tools for implementing a single IRB review model
- Propose solutions regarding implementation of single IRB model for federally funded (e.g., NIH-sponsored), and for FDA-regulated drug and device, multicenter clinical studies
Answer the question -

What can FDA, OHRP, NIH, and/or CTTI do to help transition to mandatory single IRB review for multisite research?
THANK YOU.