“Use of Central IRBs for Multicenter Clinical Trials”

Origin of the Project

April 25, 2012

Jane Perlmutter, PhD
Patient Representative to CTTI Steering Committee

Alignment with CTTI's Mission

- Study Start-Up Activities
  - Identified by CTTI's Executive Committee (EC) as a priority area for research
- Input from CTTI Steering Committee (SC)
  - Identified promising new projects to improve quality and efficiency of clinical trials (brainstorming sessions)
  - One of 6 most promising project ideas: Why single central IRBs were not being utilized widely for multicenter clinical trials
- Workgroup formed on this topic; members included Felix Gyi, Chesapeake IRB, and Jane Perlmutter, patient representative
- Project plan developed and approved by CTTI EC in Dec. 2010

Background: Previous work

- **2005 Workshop sponsored by the NIH, VA, OHRP, AAMC, and ASCO**
  - Explored alternative models to local IRB review
- **2006: National conference in f/u to the 2005 workshop**
- **Concerns about review by a central IRB**
  - Review quality
    - Including local context, safety net of redundant review, consent forms
  - Regulatory liability
  - Legal liability
  - Potentially negative public relations
    - (Should a central IRB be found non-compliant)
  - Loss of income
    - generated from fees for IRB review of studies with commercial sponsors, which is often used to cover institutional costs

Background: Regulatory positions

- 2006 Food and Drug Administration Guidance[1]
  - "The Agency hopes that sponsors, institutions, Institutional Review Boards (IRB), and clinical investigators involved in multicenter clinical research will consider the use of a single central IRB (centralized IRB review process), especially if using centralized review could improve the efficiency of IRB review."
- 2010 Menikoff Commentary in NEJM[2]-Scientific Concerns
  - Multiple local IRBs can lead to a diffusion of responsibility and potentially expose trial participants to undue risks
  - Potential "authority vacuum" in which no IRB feels empowered to demand changes in the protocol
- Despite these stated positions, the willingness of institutions to defer to outside IRBs varies

1. Guidance for Industry - Using a Centralized IRB Review Process in Multicenter Clinical Trials; March 2006
2. Menikoff J. The paradoxical problem with multiple-IRB review. N Engl J Med. 2010; 363:1591-1593.

Use of Central IRBs for Multicenter Clinical Trials

- **Goal**

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

- **Objectives**
  - Solicit current perceptions of barriers
  - Develop a strategy to address the identified barriers
  - Assess reactions to proposed solutions to remove these barriers

Project Definition of "Central IRB"

- Context: Multicenter clinical trials
- **Central IRB = Single IRB-of-record for a given protocol**
  - Central IRB assumes all regulatory responsibility for scientific oversight and integrity of the protocol from initial review to termination of the research
    - including review of informed consent and protection of study participants
  - A range of entities may serve as a central IRB
    - e.g., independent IRBs, federal IRBs, another institution's IRB
  - Implies that an institution not choosing to use the single IRB-of-record would not participate in that protocol
  - Central IRB must assure compliance with regional, state, and local laws *for all sites*

Use of Central IRBs for Multicenter Clinical Trials: Organization

CTTI Staff

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Project Manager

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Cheryl Grandinetti
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Use of Central IRBs for Multicenter Clinical Trials

Colleen Gorman
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Jane Perlmutter
Patient Advocate

Team Members

Note: Soo Bang, Celgene, served as one of the initial team leaders; Cheri Janning, CTTI, served as the initial project manager

Thoughts from a Patient Advocate

- The International Council on Harmonization (ICH) defines an institutional review board (IRB) as a group formally designated to **protect the rights, safety and well-being of humans** involved in a clinical trial by reviewing all aspects of the trial and approving its startup. IRBs can also be called independent ethics committees (IECs).
- These rights, safety and well-being **do not** vary from site-to-site
- Thus **patients should be treated consistently** across sites—e.g., see identical informed consent documents

Thoughts from a Patient Advocate: Potential Consequences of Inconsistent Reviews Across Sites

- Patients at different sites may compare notes and be confused and/or disturbed by differences
- Informed consent documents may not be able to be translated with multiple versions

Thoughts from a Patient Advocate: Some Advantages of Using a Single IRB

- Reduces cost and time to open trials
  Note: this is important to patients who can't always afford the luxury of being patient
- Over-time, multi-site studies will be reviewed by IRBs with increased awareness of evolving ethical consensus (e.g., in regard to privacy, returning of genetic information)
- Reinforces that IRBs main function is to protect patients, not institutions