Approach to Central IRB: CTSA & PCORnet Collaboration

AGENDA

• Welcome and Introductions- Adrian Hernandez
• PCORnet Perspective – Rachael Fleurence
• CTSA Perspective- Petra Kaufmann
• What is IRBRel? - Sabune Winkler
• Collaboration – Madeleine Williams
• Concluding Remarks- Alan Green/Petra Kaufmann
• Q & A – Adrian Hernandez
PCORnet and Approach to Central IRB

Rachael Fleurence
March 2, 2016
Time for Implementation: Central IRB

- **1968**: OHRP (Office for Human Research Protections) formed
- **1991**: OHRP guidance: knowledge of local research context
- **1993**: NEJM Menikoff editorial
- **1994**: ANPRM: revision to common rule
- **1995**: NEURONext awarded
- **1997**: NIH Draft policy: single IRBS multisite research
- **2001**: VA CIRB
- **2003**: OIG sting: COAST IRB
- **2005**: NINDS Stroke network awarded
- **2009**: CTTI central IRB advancement recommendations
- **2014**: Use of central IRBs at the multi-CDRN level in PCORnet

**Timeline Events**:
- **1969**: First US independent IRB
- **1974**: FDA regulations
- **1975**: OPRR(OHRP) single project assurance
- **1982**: AAHRPP founded
- **1988**: NCI CIRB 881 enrolled institutions/affiliates
- **1990**: NCI CIRB formed
- **1991**: OHRP guidance: knowledge of local research context
- **1993**: AAHRPP founded
- **1994**: FDA guidance: use of central IRBS
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**Use of Central IRBs**

CTTI USE OF CIRBS RECOMMENDATIONS

NCI CIRB: 881 enroled institutions/affiliates

NEUMEx awarded

NINDS STROKE NETWORK AWARDE

NIH DRAFT POLICY: SINGLE IRBS MULTISITE RESEARCH

CTTI USE OF CIRBS RECOMMENDATIONS
PCORnet Workgroup

Adrian Hernandez & Pearl O’Rourke (co-leads)
Katherine Schuff, Jim Fischer, Todd Rice, Raffaella Hart, Nichelle Cobb, Jeremy Corisco, Joe Ali, Ivana Croghan, Jeffrey Krishner (Members)
**PCORnet Context**

- IRB review is only one component of research oversight
  - Myriad non-IRB institutional responsibilities that stay with the institution regardless of which IRB is used
- Increasing demand for single IRB review
  - NIH draft guidance → soon to be more than draft
  - NPRM
  - Condition of grant awards
  - Industry sponsors
- Increasing frustration as institutions are dealing with numerous models
  - There are too many ‘one-offs’
- PCORnet IRB Working Group Formed to Determine Approach
PCORnet Approach to cIRB Implementation

- Leverage an approach that can accommodate the majority of PCORnet studies
- Facilitate research across PCORnet
- Partner with CTSA
  - Agreement and SOPs
- Phased approach with studies and continuous evaluation
- Future Studies
  - Need to consider cIRB approach & integrate
Approach to Central IRB: CTSA & PCORnet Collaborations

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Division of Clinical Innovation
Office of Rare Diseases Research

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Associate Dean for Clinical and Translational Science, Geisel School of Medicine at Dartmouth

Madeleine Williams
Senior Director
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Sabune Winkler, J.D.
Co-Regulatory Lead, IRBRelY
Harvard Catalyst | The Harvard Clinical and Translational Science Center

March 2016
Overview of Presentations

- NCATS perspective (Petra)
- IRBrely (Sabune)
- Collaboration (Maddie)
- Next steps (Petra)
How do discoveries become health benefits?

- Scientists make discoveries in the lab
- Doctors and clinicians make observations in the clinic
- Patients and communities also make observations

How can this be translated to benefit others?
Why do we need to change the model for research review?

Under the current model of multiple Institutional Review Boards (IRBs) evaluating one protocol:

- Patients are frustrated with the slow pace of translational and clinical research (*comments on draft NIH policy available online*).
- Research teams spend too much time on bureaucratic tasks.
- Start-up time for NIH-funded trials often exceeds one year.
- Separate, local IRB reviews at each research site often result in:
  - Additional delays and cost (*Ravina et al, 2010*).
  - Inconsistencies in IRB assessments between sites (*Hirshon et al, 2002*).
  - Distributed accountability may paradoxically increase risk (*Menikoff, 2010*).
Signals suggest a shift away from the traditional, distributed IRB model:

- HHS NPRM for Revisions to the Common Rule (Sept. 2015)
- HHS ANPRM for Revisions to the Common Rule (July. 2011)
CTSA Program hubs are natural vanguard for using single IRBs in multisite research

- Builds on existing strength
  - Clinical research
  - IRB
- Success of regional reliance networks
- National reach
- Unique position at interface of clinical care and research
- Links local capacity with network collaboration
Regional CTSA IRB Agreement Networks

UC BRAID
U Texas
IRB SHARE/Choice
New England
Wisconsin/MARCH/GPC
Ohio Collaborative
U New Mexico
CTSA Program investigators chose to pilot a national IRB *reliance* model

**IRB**rely

- Fully streamlined implementation, beyond simply information sharing
- For maximum efficiency, a single IRB is selected. Local context is provided by the relying institution and is reviewed by the single IRB
- In smaller studies, institutions can flexibly rely on another IRB
- In larger studies or networks, the agreements and processes can be used by central IRBs
NCATS IRB Reliance Model: Toward a *national* IRB system

Together with Case Western, Dartmouth, Harvard, University of California, University of New Mexico, University of South Florida, UT Southwestern, University of Wisconsin and Vanderbilt; and Duke and all CARRA pilot sites:

<table>
<thead>
<tr>
<th>Role</th>
<th>Name and Institution</th>
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<tbody>
<tr>
<td>Principal Investigator</td>
<td>Alan I. Green (Dartmouth)</td>
</tr>
<tr>
<td>Sr. Reliance Advisor</td>
<td>Barbara Bierer (Harvard)</td>
</tr>
<tr>
<td>Regulatory Leads</td>
<td>Sabune Winkler (Harvard) Nichelle Cobb (University of Wisconsin)</td>
</tr>
<tr>
<td>Informatics Leads</td>
<td>Amarendra Das (Dartmouth) Doug MacFadden (Harvard)</td>
</tr>
<tr>
<td>Lead for single IRB in rare diseases networks</td>
<td>Jeff Krischer (U of South Florida)</td>
</tr>
<tr>
<td>Division of Clinical Innovation/NCATS</td>
<td>Michelle Culp, Mary Purucker, Todd Wilson, Monica Shah</td>
</tr>
<tr>
<td>Critical contributions</td>
<td>CTSA IRBs, investigators and teams</td>
</tr>
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IRBrely Components

Building on existing strength and successful regional reliance models, IRBrely is a large scale national solution:

<table>
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<tr>
<th><strong>IRB Master Reliance Agreement</strong></th>
<th>An umbrella single authorization form that all sites can sign once and use to cede review for any study</th>
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</table>
| **Standard Operating Procedures** | • Details roles and responsibilities delineated in the Agreement such as Reviewing IRB, Relying Institution, Overall PI, Site Investigators, and lead regulatory contacts  
  • IRBrely SOPs may be substituted when other SOPs are agreed upon or mandated |
| **Informatics** | • Website for information  
  • Joinder mechanism to join IRBrely  
  • In development, an end-to-end, workflow based, platform for study teams and site to communicate with each other about reliance (not an IRB review system) |
Iterative and Communal Development: History to Date

Phase 1
- **Concept and SOPs** developed by best practice gap analysis comparing agreement of the regional consortium

Phase 2
- **Agreement drafted and distributed**; feedback received and integrated.

Phase 3
- **Agreement redistributed**
- Current draft was created with input from 71 Institutions
- Agreement and SOPs distributed to 71 FWA institutions
  - Some asked for more time
  - More than 50% will accept in some form

Phase 4
- On February 24, 2016, **NCATS distributed to all CTSAs for review and comment**
- Currently welcoming and responding to questions and comments
## IRBrely Agreement:
Some key elements in the framework

<table>
<thead>
<tr>
<th>Summary Differences (not exhaustive)</th>
<th>IRBrely</th>
<th>Other reliance agreements</th>
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<tbody>
<tr>
<td><strong>Layout</strong></td>
<td>Follows a roles based delineation based on a division of responsibility – Reviewing IRB/Relying Institution/ PI or designee</td>
<td>Follows the lifecycle of a study</td>
</tr>
<tr>
<td><strong>Scope</strong></td>
<td>Universal agreement covering all kinds of studies and all kinds of phases of study</td>
<td>Generally limited to specific study or consortium; may be limited to level of risk</td>
</tr>
<tr>
<td><strong>Participation by independent IRBs?</strong></td>
<td>Yes-. FWA or IRB Registration institutions; Independent/commercial IRBs are allowed as long as they have an IRB Registration with OHRP</td>
<td>No</td>
</tr>
<tr>
<td><strong>Joinder Process</strong></td>
<td>Facilitated by IRBrely central administration; “Treaty” – any party can join if they meet basic criteria</td>
<td>None</td>
</tr>
<tr>
<td><strong>FWA</strong></td>
<td>Does not require unchecking the box</td>
<td>Not addressed or some explicitly require the box be “unchecked”</td>
</tr>
<tr>
<td><strong>Insurance</strong></td>
<td>Required but can be waived by agreement</td>
<td>Required and amounts specifically delineated</td>
</tr>
<tr>
<td><strong>Governing Law</strong></td>
<td>Silent</td>
<td>Specific to state of location</td>
</tr>
<tr>
<td><strong>SOPs</strong></td>
<td>IRBrely SOPs are provided; may be substituted by agreement</td>
<td>Best practice guidance</td>
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<tr>
<td><strong>Communication</strong></td>
<td>Under IRBrely SOPs, PI (or their designee) is functionally responsible for facilitating most communication with the Reviewing IRB and study teams</td>
<td>Same, or directly to Reviewing IRB</td>
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IRBrely Collaborations: National harmonization will be important to minimize burden on institutions

- Rare Disease Clinical Research Network
  - IRBrely is linking to an initiative led by Jeff Krischer of the U of South Florida (Tampa), which helps rare disease investigators build on the IRBrely platform

- CARRA
  - 14 Pilot sites for CARRA Registry with Duke as the Reviewing IRB

- PCORnet
  - IRBrely is coordinating with PCORnet investigators so:
    - COMBINE STUDY
    - INVESTED STUDY
Lessons Learned from our Pilot: With Duke, CARRA study helped to test agreement, SOPs, and inform informatics infrastructure needs

• Lessons learned:
  - Reviewing IRB needs infrastructure/processes to support serving as a central IRB (“one to many relationship”)
    - May need tweaks to eIRB system and/or processes
  - Lead Study Team has significant role in facilitating communication between Reviewing IRB and relying sites
  - Study specific workflows and forms may need to be created
  - Reviewing IRB required information for review needs to be communicated to relying sites
PCORnet & IRBrely Collaboration: Testing the IRBrely model

**COMBINE STUDY:**
Will evaluate low dose oral methotrexate in children with Crohn’s Disease who are initiating anti-TNF therapy

- Overall PI at University of North Carolina
- PEDSnet CDRN
- Reviewing IRB (Cincinnati Childrens Hospital Medical Center) plans to follow IRBrely SOPs (IRB review began before IRBrely master agreement ready)

**INVESTED STUDY:**
Will compare high dose influenza vaccine to standard dose vaccine in adult individuals at high risk for cardiovascular events

- Study is a collaboration between University of Wisconsin-Madison (UW) and Harvard University researchers
- UW will serve as single IRB for sites across multiple PCORnet CDRNs
- Plan to use IRBrely master agreement and SOPs
- Expected to start process late spring
IRBrely: What’s next?

• Agreement and SOPs
  ➢ CTSA institutions agree to IRBrely model
  ➢ Continued distribution to non-CTSA sites

• Informatics
  ➢ User acceptance testing for prototype joinder and cede request/review demonstration

• Develop and refine “entry points” for networks, small and large studies

• Promote partnerships
  (PCORNNet, NIH ICs, others)

• Convene training meeting
  (TIC Liaison, IRB Administrator, CT Lead)

• Plan for future multi-site studies using IRBrely

Streamlined IRB review will help accelerate the path from discovery to health benefit.
Questions