# Toward a National IRB System: IRBrely

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National Issue

• Ethical-regulatory review by IRBs for multisite studies has been constrained by process-related inefficiencies and questions about the value of redundant reviews.

• These delay or prevent initiation of multisite studies, and may not provide adequate protection for human subjects.

• Thus need for collaborative IRB review models for multisite studies.

• **December 3, 2014**: NIH issues draft policy to promote the use of single IRBs in multi-site clinical research studies.
NIH takes step to speed the initiation of clinical research by ensuring use of single IRB

The National Institutes of Health issued a draft policy today to promote the use of single institutional review boards or IRBs, in multi-site clinical research studies. IRBs play a critical role in assuring the ethical conduct of clinical research, and studies must be reviewed and approved by an IRB before they can begin.

“Maintaining the highest ethical standards in the research we fund is of utmost importance,” said NIH Director Francis S. Collins, M.D., Ph.D. “By using single IRBs in multi-site studies, we reduce duplication of effort, speed the initiation of important research, and save time and taxpayer funds.”
Challenges

Some reasons for reluctance to defer IRB review:

– liability
– administrative challenges
– possible confusion of responsibilities
– quality of review by other IRBs (trust)
– ensuring local requirements are addressed
– additional burden of changing internal processes to accommodate different methods of review
Toward a National CTSA IRB Initiative

PROJECT / ACTIVITY CONCEPT

PROPOSAL TITLE: DEVELOPMENT OF A CROSS-CTSA IRB RELIANCE AGREEMENT

DATE: February 22, 2014

DESCRIPTION OF PROPOSED PROJECT/ACTIVITY

1. Describe the project. What will be done?
   a. Launch project following discussion with PIs of CTSA sites.
   b. Engage leaders of existing consortial reliance (“sentinel consortia”) agreements toward development of a more inclusive CTSA IRB process to facilitate multicenter clinical trials.
   c. Conduct a quick cost/benefit analysis of reliance model vs. use of a commercial IRB model.
   d. Decide on optimal model for use.
   e. Identify needed resources: staffing, informatics capability, common language, costs, etc to expand existing sentinel consortia towards an inclusive CTSA model – likely a reliance model – among these existing “sentinel” sites.
   f. Build a harmonized IRB reliance agreement.
   g. Identify a single multicenter trial to pilot across sites using the agreed-upon CTSA reliance IRB model. The trial PI would serve as IRB of record for the trial.
   h. Invite non-affiliated CTSA sites to join the national CTSA IRB model.
Proposed Solutions

• **Central IRB (cIRB):** One IRB as IRB of record for all sites involved in multi-center protocols. cIRBs generally focus on particular topic or disease (e.g., NeuroNext, NCI CIRB)

• **Commercial IRB:** Often used for industry-sponsored multi-center trials; also called “independent IRBs”

• **IRB Share:** A joint review model and “Shared Review Process” in which a Lead IRB approves a study, but the Local Oversight IRB verifies agreement with the determination of the Lead IRB, and reviews local context issues.

• **Reliance model:** A single or consolidated IRB of record, chosen on a study-by-study basis, for the life of a study, involving a “reviewing IRB” and “relying institutions”
Major IRB Agreement Networks

UC BRAID
U Texas
IRB SHARE
New England
Wisconsin/MARCH/GPC
Ohio Collaborative
U New Mexico
While there are barriers to IRB reliance, there are current regional models that are working. And, there is increasing willingness across the CTSA consortium to trust and test a national IRB reliance model.

Create – “IRBrly”
Two Examples

Harvard Catalyst – New England Reliance

From January 2010 – November 20, 2014
32 FWA signatories (22 Catalyst institutions; 10 non-Catalyst institutions)
1,413 applications requesting reliance
1230 applications (87%) represent a reduction of duplicative review
78% of the time the Reviewing IRB is that of the PI’s primary employer

Wisconsin IRB Consortium (WIC)

Includes 4 major research institutions across the state
Since January 2008 > 150 studies ceded for single IRB review
Expanding model across state lines to MARCH (6 institutions) & GPC
(10 institutions focused on PCORI research), so far -
* MARCH: 1 study involving 3 sites
* GPC: 2 studies involving up to 10 sites each
Value of Reliance Agreement and Network: Boston Marathon Bombing

• Doctors at Mass Eye and Ear wanted to quickly study outcome of blast-related ear injuries

• Harvard CTSA already had an IRB reliance network in place.
  ➢ With 7 other hospitals, rapid IRB approval was obtained to study ear injuries, and to observe patients as they healed
Specific Aims

• Create a national IRB reliance agreement, building on the expertise of existing regional IRB models
• Identify and build the informatics infrastructure to support a national IRB reliance model
• Implement and utilize the new IRB reliance national model to support multi-site clinical trials
• Identify a low-risk multi-center clinical trial to demonstrate feasibility of national IRB reliance model
• Evaluate the processes developed and the infrastructure created
Nature of Initiative

• Starting with CTSA sites, but expected to expand beyond these institutions

• Based on reliance model
  – Distinct from “NeuroNext-type” and “commercial” central IRB models, as well as “IRBShare-type” model
  – Respecting the legal autonomy of each participating institution, reliance is determined in a case-by-case basis
  – Supported by the Agreement, ceding IRB review, and serving as Reviewing IRB is voluntary
  – Can be used for any multi-site, human subjects research involving institutions that have signed the Agreement
Implementation Plan—Year 1

- **NCATS Funding**  September 2014 -- August 2015
- **Staffing**  Project Director (Bechert), Project Manager (Oranski)
- **Executive Committee**, including CTSA PIs from regional IRB consortial programs:  **Decision-Making Body**
- **Regulatory Subcommittee** to propose harmonized language for national IRB agreement and SOP framework to manage reliance
- **Informatics Subcommittee** to develop and build informatics infrastructure to support national IRB program
- **Evaluation Group** to assess the processes developed and infrastructure created to support the national IRB reliance model
- **Operations Committee** meets weekly to ensure initiative meets timelines
Executive Committee

- Alan I. Green – Dartmouth College
- John N. Clore – Virginia Commonwealth
- Lars Bergland – U California – Davis (BRAID)
- Gordon Bernard – Vanderbilt University
- Philip Cola – Case Western Reserve
- Marc Drezner – U Wisconsin-Madison
- Richard Larson – U New Mexico
- Lee Nadler – Harvard Medical School
- Robert Toto – U Texas Southwestern
Regulatory Subcommittee

• Sabune Winkler, Harvard Medical School
• Nichelle Cobb, University of Wisconsin – Madison
• Barbara Bierer, Harvard Medical School

• Carol Pech, University of Wisconsin – Madison
• Kathy Lawry, Case Western Reserve University
• Carson Reider, The Ohio State University
• Ginger Pomiecko, MetroHealth Med. Center Cleveland
• Cynthia Gates, University of California, Davis
• Eric Mah, University of California, San Francisco
• Kate Marusina, University of California, Davis
• Rachael Sak, University of California, Davis
• Elizabeth Bankert, Dartmouth College
• Jeremy vanHoff, Dartmouth College
Regulatory Committee Cont.

- Julie Ozier, Vanderbilt University
- Emily Sheffer, Vanderbilt University
- Terri Edwards, Vanderbilt University
- Todd Rice, Vanderbilt University
- Lynn Baker, University of Texas Southwestern
- Diane Sheppard, University of Texas Southwestern
- Agela Wishon, University of Texas Southwestern
- Corey Ford, University of New Mexico
- Marguerite Valenca-Reed, University of New Mexico
- Emily Ringo, University of New Mexico
- Michelle Stickler, Virginia Commonwealth University
- Elizabeth Witte, Harvard Medical School
Informatics Subcommittee

• Amarenda Das, Dartmouth College
• Kristen Carvaines, Case Western Reserve University
• David Fenstermacher, Virginia Commonwealth Univ.
• David Pilasky, Case Western Reserve University
• Dipti Ranganathan, UT Southwestern
• Ruben Amarasingham, UT Southwestern
• Doug MacFadden, Harvard Medical School
• Kent Anderson, University of California, Davis
• Tom Tuckerman, MetroHealth Medical Center Cleveland
• Matt Hall, University of Wisconsin – Madison
• Umberto Tachinardi, University of Wisconsin - Madison
• Paul Harris, Vanderbilt University
• Ross Davis, Vanderbilt University
• Brian Levin, Dartmouth College
• Steven Andrews, Dartmouth College
Operations Committee

- Alan I. Green, Dartmouth College
- John Clore, Virginia Commonwealth Univ.
- Barbara Bierer, Harvard Medical School
- Amarenda Das, Dartmouth College
- Nichelle Cobb, University of Wisconsin – Madison
- Sabune Winkler, Harvard Medical School
- Tom Bechert, Dartmouth/Huron
- Lydia Oranski, Dartmouth College
Timeline—Year 1

- **October – December, 2014**
  - Regulatory Subcommittee
    - First meeting October 6-7
      - Began drafting Master IRB Reliance Agreement
      - COI, Metrics Subcommittees formed
      - Initiated engagement with PCORI to harmonize efforts
    - Second meeting of subgroup at PRIM&R, December 5
      - Distributed agreement to institutions and attorneys post PRIMR
  - Informatics Subcommittee
    - Initial meeting, October 6-7
    - Face-to-face meeting -- December 3
  - Operations Committee
    - Weekly meetings
Timeline—Year 1

• January–April 2015
  – Review of agreement by consortial sites; additional agreement modification; Draft SOPs
  – Face-to-face Regulatory and Informatics Subcommittee meetings  
  – Goal: Final agreement by March, 2015
  – Establishment of informatics solution and long-term support structure
  – Visits to project sites; development of near-final agreement
  – Identify low-risk multi-center study as a demonstration project

• May–August 2015
  – Expand agreement to other CTSA sites
  – Implement multi-center study

• July–August 2015: Executive Committee -- review and future planning for sustainability
Informatics Subcommittee

- Need scope of work that matches the overall timeline
- Solution needs to be sustainable
- Cost needs to be reasonable
- < 1-year timeline to fully develop a robust system is not realistic.
- Focus on project management, requirements gathering, workflow development.
- Pilot project may potentially use a prototype, “proof of concept” solution.
Additional Components

• **Develop governance structure:**
  – Provide leadership for effort and support to sites
  – Address issues that arise
  – Identify resources needed to support
  – Help to ensure sustainability

• **Create workflows:**
  – Application process
  – Communicating determinations

• **Setting up website to house:**
  – Information about initiative and joining the agreement,
  – SOPs and other supporting documents

• **Work toward best practices/harmonization:**
  – Requirements for IRBs of record, particularly for larger studies
  – Universal consent form template
  – Reportable event requirements
Determining Eligibility to Use the Agreement

**Proposed Solution:** Institutions must meet some minimum requirements to be eligible to use the agreement, including:

- Having a current FWA
- Ability to assure a certain level of HRPP standards:
  - Accreditation or OHRP’s Quality Assurance Program
  - Quality assurance program ability to conduct study audits
- Following Standard Operating Procedures (SOPs) developed in support of agreement
Communication

Proposed Solutions:

• Developing a centralized system for communicating and reviewing requests to cede review/serve as Reviewing IRB

• Requiring institutional Lead Regulatory Contact (LRC) for Reviewing IRB and Relying Institution to:
  – serve as resources for process
  – ensure communication across institutions and with study teams
  – make decisions regarding accepting or ceding IRB review

• Requiring identification of a Lead Study Team responsible for most communication with the Reviewing IRB and disseminating information to/collecting information from participating study teams
Addressing “local context” issues

Proposed Solution:

- LRCs at Relying Institutions provide “local context” information to the Reviewing IRB, such as
  - State Law
  - Other institutional requirements that affect the study (e.g., local populations, limited consent form language)
Proposed Solution:

- **Relying Institutions** required to:
  - Manage their study teams’ conflicts of interest (COI) and communicate relevant COIs and management plans to the Reviewing IRB
  - Ensure that:
    - their study teams are trained
    - their study teams conduct the research in compliance with applicable federal regulations and IRB determinations
    - institutionally-required ancillary reviews are completed
Proposed Solution (Continued):

- **Reviewing IRB** required to:
  - Oversee studies across their lifespan (i.e., conduct review of new application, continuing review, changes, and reportable events)
  - Serve as HIPAA Privacy Boards
  - Conduct grant congruency reviews

- **Study teams** required to:
  - Comply with the policies of the Reviewing IRB
Collaboration -- NCATS & PCORnet?

• NCATS Reliance Initiative can be leveraged for a PCORnet trial across the IRBs
  – Agreement will eliminate need for per study negotiation across sites
  – SOPs and informatics solutions will be broadly useful

• NCATS/PCORI IRB reliance partnership can serve as a demonstration project for testing agreement beyond CTSA sites – and as a prototype for NIH
PCORI “task forces” can help tackle key issues related to ceding IRB review

- Developing best practices for:
  - Comparative effectiveness research, especially in regard to informed consent and risk disclosure
- Developing strategies for including entities not routinely engaged in human subjects research
  - e.g., How to train personnel, address local context & state law issues, ensure compliance with study protocol
• Finalize agreement language – by March
• Develop/finalize SOPs – by March
• Agree on workflow – by mid-February
• Develop informatics strategy – by mid-February
• Develop metrics listing
• Create communication strategy through IRBrelly
• Spread agreement throughout consortial subsites
• Identify pilot study – by April
• Create sustainability platform -- by May
• Implement agreement and processes within pilot study
• Add Wave II sites to agreement -- begin June