Establishing a NIH-Funded Central IRB: The NIH StrokeNet Experience

Michael Linke, PhD, CIP
Health Science Officer, Department of Veterans Affairs Medical Center-Cincinnati
Associate Professor, UC Department of Internal Medicine
Chair, UC Institutional Review Board
About Schulman IRB

- Established in 1983
- Superior audit history with FDA—five consecutive audits with no findings
- 21 CFR Part 11 compliant electronic systems
- Compliant with FDA, OHRP and Health Canada requirements
- Full Board meetings **five days a week**
- Dedicated **daily expedited review** of qualifying minimal risk protocols
About Schulman IRB

- Review outcome provided within **one business day** of new study review
- **One business day** turnaround for complete new site submissions
- Dedicated streamlined processes tailored to **Phase I timelines**
- **Expert oncology IRB members** experienced in all phases of oncology research
  - National IRB for **Cancer MoonShot 2020** initiative
- Customized services for **institutions**
- **Experienced primary points of contact** for sponsors, CROs, institutions and sites
About Schulman IRB

- Clinical Quality Assurance (CQA) and Human Research Protection (HRP) consulting services provided by Provision Research Compliance Services

Provision is a joint venture between Schulman IRB and Falcon Consulting Group
The industry’s choice for central and local IRB services.

- Get Started
  - Begin the initial review process.
  - GO

- Forms
  - Download the latest forms for your study.
  - GO

- Contact Us
  - Request more info & send feedback.
  - GO
About Today’s Presenter

Michael Linke, PhD, CIP
• Health Science Officer, Department of Veterans Affairs Medical Center-Cincinnati
• Associate Professor, UC Department of Internal Medicine
• Chair, UC Institutional Review Board

➤ University of Cincinnati IRB member for over 20 years
➤ Chair of the UC IRB since 2004
➤ Awarded the Greater Cincinnati Health Council’s first ever Servant Leadership Award for his efforts in creating and leading the Consortium of Greater Cincinnati IRBs
➤ Led the formation of the NIH StrokeNet Central IRB
➤ Serves as a consultant on a NIH RO1 Award to Vanderbilt University to study the implementation of Central IRBs
Establishing a NIH-Funded Central IRB: The NIH StrokeNet Experience

Michael Linke, PhD, CIP

Health Science Officer,
Department of Veterans Affairs Medical Center-Cincinnati

Volunteer Associate Professor
Department of Internal Medicine
University of Cincinnati College of Medicine

Chair, University of Cincinnati Institutional Review Board
Disclosure

• Serves as consultant on:

5R01HL126492-02
USING REAL WORLD DECISIONS TO DEVELOP A MODIFIED CENTRAL IRB MODEL
PI: Todd Rice   Institution: VANDERBILT UNIVERSITY

• The content is solely the responsibility of the presenter and does not necessarily represent the official views of the National Institutes of Health or the Department of Veterans Affairs
Learning Objectives

1. Describe the proposed requirements of single IRB review of multi-site studies funded by the NIH
2. Outline how a university-based IRB established a central IRB
3. Describe running a central IRB through a university-based IRB
4. Identify obstacles and solutions to operating a central IRB at a university
5. Recommend ways to improve interactions with central IRBs
I believe this proposed policy is a step forward to reducing burdens associated with NIH-funded clinical research and enhancing the efficiency of the process while still ensuring protections of all the volunteers who generously participate in human subjects research for the betterment of us all.

• Sally Rockey, PhD, NIH’s deputy director for extramural research

• Purpose
  • Increase the use of single IRBs for multi-site studies funded by the NIH.

• Goal
  • To enhance and streamline the process of IRB review
  • Reduce inefficiencies
  • Improve efficiently without compromising ethical principles and protections
• Responsibilities
  • All sites participating in a multi-site study will be expected to rely on a single IRB
  • The single IRB will be the IRB of record for the other participating sites
  • The single IRB will be accountable for compliance with regulatory requirements for IRBs
  • Relying sites responsible for meeting other regulatory obligations

• Responsibilities
  • IRB Authorization Agreements
  • Participating sites rely on the IRB of record to satisfy all regulatory requirements
  • Consider local context issues during IRB deliberations
  • Does not prohibit any participating site from carrying out its own IRB review
Responsibilities

- Identification of the single IRB of record is the responsibility of the principal investigator
- NIH has final decisional authority for approving the selected single IRB
- Use of the designated single IRB will be a term and condition of award
- IRB costs will be included in the Notice of Award as a direct cost
• Exceptions
  • May only be made with appropriate justification
What Is NIH StrokeNet?

- Funded by NINDS/NIH to conduct clinical trials for stroke prevention, treatment, and recovery.


What Is NIH StrokeNet?

The University of Cincinnati serves as the National Coordinating Center and provides national leadership for StrokeNet.

- Joseph P Broderick, MD Principal Investigator
- Pooja Khatri, MD, MSc, FAHA Co-Investigator
- Dawn Kleindorfer, MD Co-Investigator – Educational Core Chair
- Arthur Pancioli, MD Co-Investigator
- Judith Spilker, RN, BSN Administrative Director
- Jamey Frasure, PhD, RN Director
- Diane L. Sparks, RN, BS Contracts Manager, Legal Liaison
- Rose Beckmann, CCRP Administrative Specialist
- Katherine Carey, BA Financial Manager
- Jeanne Sester Educational Coordinator

NIH StrokeNet
Prevention | Treatment | Recovery
What Is NIH StrokeNet?

The National Data Management Center at the Medical University of South Carolina oversees all aspects of data management and provides full statistical support for StrokeNet research.

- Yuko Y. Palesch, PhD, Co-Principal Investigator
- Wenle Zhao, PhD, Co-Principal Investigator
- Catherine Dillon, Director of Operations
- Jessica Simons, Data Manager
What Is NIH StrokeNet?

- The network includes 25 Regional Coordinating Centers

1. CASE WESTERN RESERVE UNIVERSITY
2. COLUMBIA UNIVERSITY HEALTH SCIENCES
3. EMORY UNIVERSITY
4. MASSACHUSETTS GENERAL HOSPITAL
5. MEDICAL UNIVERSITY OF SOUTH CAROLINA
6. MEDSTAR RESEARCH INSTITUTE
7. MOUNT SINAI SCHOOL OF MEDICINE
8. NORTHWESTERN UNIVERSITY AT CHICAGO
9. OHIO STATE UNIVERSITY
10. STANFORD UNIVERSITY
11. UNIVERSITY OF CALIFORNIA LOS ANGELES
12. UNIVERSITY OF CALIFORNIA SAN DIEGO
13. UNIVERSITY OF CALIFORNIA SAN FRANCISCO
14. UNIVERSITY OF CINCINNATI
15. UNIVERSITY OF IOWA
16. UNIVERSITY OF MIAMI SCHOOL OF MEDICINE
17. UNIVERSITY OF MICHIGAN
18. UNIVERSITY OF MINNESOTA
19. UNIVERSITY OF PENNSYLVANIA
20. UNIVERSITY OF PITTSBURGH AT PITTSBURGH
21. UNIVERSITY OF TEXAS HLTH SCI CTR HOUSTON
22. UNIVERSITY OF UTAH
23. UNIVERSITY OF WASHINGTON
24. UNIVERSITY OF WISCONSIN-MADISON
25. VANDERBILT UNIVERSITY MED CTR
RCC Management of Satellites and Clinical Performance Sites

- Regional Coordinating Center (RCC)
- Clinical Trial Performance Sites (CTPS)
- RCC Clinical Performance Sites (RCC-CPS)
- RCC Satellite Site (RCC-SS)
What Is NIH StrokeNet?

The University of Cincinnati IRB serves as the Central IRB (CIRB) for StrokeNet

- Michael Linke, PhD, CIP, Chair CIRB
- Susan K. Roll, RN, BSN, CCRP Central IRB Liaison
- Angela Braggs-Brown, RAC, CIP, MA, UC HRPP Director
The Introduction and Implementation of Stroke Trials within National Institutes of Health StrokeNet. “cIRB” indicates Central Institutional Review Board; “NINDS” is National Institute of Neurological Disorders and Stroke.

Building the NIH StrokeNet Central IRB Process

• “Non-share model” CIRB developed by Partners for Network for the Excellence in Neuroscience Clinical Trials (NeuroNEXT)*

• Single IRB of record for NIH StrokeNet affiliated research as designated by NINDS

• Central IRB fulfills all IRB-review requirements including initial and continuing review, adverse events and amendments

How a University-Based IRB Established a Central IRB
How Do We Get There?

• Reliance Agreement
  • NIH and OHRP templates*
  • Draft reviewed by selected RCCs
  • Revised per comments
  • 2nd draft reviewed by RCCs
  • Final document distributed to RCCs for execution
  • Distributed to RCC SSs and Satellite CPSs

* [http://www.hhs.gov/ohrp/assurances/forms/irbauthorizpdf.pdf](http://www.hhs.gov/ohrp/assurances/forms/irbauthorizpdf.pdf)  
Reliance Agreement

Request:

• A signed copy of the site’s Federalwide Assurance (FWA)
• Require the IO listed on the FWA agreement to sign
• A contact name from the site who can help to facilitate the signing of the Reliance Agreement
Reliance Agreement

- Partially executed RA sent to the site contact to facilitate the signing of the RA by the site’s IO

- Site contact obtains IO’s signature and sends fully executed RA back to the Contracts Manager/Legal Liaison
## StrokeNet Reliance Agreements

<table>
<thead>
<tr>
<th></th>
<th># of RAs</th>
<th>median TAT (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCCs</td>
<td>24</td>
<td>30</td>
</tr>
<tr>
<td>RCC CPSs</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>RCC Satellites</td>
<td>112</td>
<td>20</td>
</tr>
<tr>
<td>RCC Satellite CPSs</td>
<td>32</td>
<td>43.5</td>
</tr>
</tbody>
</table>

Total 185 CIRB Reliance Agreements fully executed
Running a Central IRB through a University-Based IRB
StrokeNet CIRB-Related SOPs*

- ADM 11 Central Institutional Review Board Reliance
- ADM 12 Central Institutional Review Board Reporting
- ADM 2 Reporting Conflict of Interest And Financial Disclosure

*network administrative SOPs available on the NIHSTROKENET.org
ADM 11 Central Institutional Review Board Reliance

- Defines the process for an Institution engaged in NIH StrokeNet affiliated research to transfer human subjects review to the CIRB
- Provides an overview of the protocol review
- Describes the information flow between the Institution and the CIRB throughout the lifecycle of the protocol
ADM 12 Central Institutional Review Board Reporting

- Defines the process for required reporting by sites
- Describes the types of required reports
- Defines the standards, time frames, and procedures for these reports
ADM 2 Reporting Conflict of Interest And Financial Disclosure

- Document the process by which the NIH StrokeNet will assure compliance with HHS and FDA financial COI regulatory requirements
- Details the NIH StrokeNet Network efforts to manage individual COI in a manner that is both ethical and practical
Running a CIRB through a University-Based IRB

*How does it really work?*
Running a CIRB through a University-Based IRB

• UC IRB acts as the StrokeNet CIRB
• CIRB Liaison
• Dedicated HRPP Office Staff
• Use UC HRPP electronic Protocol Administration System (ePAS)
  • Huron’s Click® IRB software platform
  • CIRB Liaison enters site information
StrokeNet CIRB Administration

NCC
- New studies
- Site Approvals,
- Amendments,
- Continuing reviews

CIRB

Liaison
- Regulatory Documents
- Reportable Events

RCCs

NDMC

WebDCUTM

WebDCUTM
## How Do We Work Together?

<table>
<thead>
<tr>
<th>CIRB Responsibility</th>
<th>Local Site Responsibility</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IRB review tasks</strong></td>
<td><strong>Site specific context</strong></td>
</tr>
<tr>
<td>▶ Initial review</td>
<td>▶ Local laws</td>
</tr>
<tr>
<td>▶ Continuing review</td>
<td>▶ Institutional policies</td>
</tr>
<tr>
<td>▶ Amendments, deviations, etc.</td>
<td>▶ Local context</td>
</tr>
<tr>
<td>▶ COI</td>
<td>▶ COI</td>
</tr>
<tr>
<td><strong>HIPAA determinations of:</strong></td>
<td><strong>Ancillary reviews</strong></td>
</tr>
<tr>
<td>▶ Authorization forms and any accompanying request for alterations when authorization is combined with informed consent</td>
<td>▶ Nursing</td>
</tr>
<tr>
<td>▶ Requests for waivers of authorization</td>
<td>▶ Radiation</td>
</tr>
<tr>
<td><strong>Local context review</strong></td>
<td>▶ Safety</td>
</tr>
<tr>
<td>▶ Collect local information required for IRB review</td>
<td></td>
</tr>
<tr>
<td>▶ Distribute a high-level protocol synopsis and highlights sheet</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Other compliance areas</strong></td>
</tr>
<tr>
<td></td>
<td>▶ HIPAA requirements outside those expressly covered by CIRB</td>
</tr>
<tr>
<td></td>
<td>▶ Oversight of research conduct</td>
</tr>
<tr>
<td></td>
<td>▶ Other required reporting and actions under federal, local, or institutional laws, regulations or policies</td>
</tr>
</tbody>
</table>
Efficiency of CIRB Review?

CREST-2 is designed to compare three different methods of stroke prevention to find the safest and most effective treatment.

<table>
<thead>
<tr>
<th># of Sites</th>
<th>Median turn around time from submission to approval</th>
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<tbody>
<tr>
<td>48</td>
<td>8.5 days</td>
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</tbody>
</table>
Obstacles and Solutions
Obstacles and Solutions

• **Obstacle**
  • Cultural resistance*

• **Solutions**
  • Communication
  • Transparency
  • Education/guidance

Obstacles and Solutions

- **Obstacle**
  - Lack of universal electronic IRB application platforms

- **Solution**
  - Develop data and technology standards across electronic IRB application systems to facilitate communication and efficacious and transparent review*
    - IRBrely
    - IRBchoice
    - Commercial products**

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*CTTI RECOMMENDATIONS: ADVANCING THE USE OF CENTRAL IRBS FOR MULTICENTER CLINICAL* Released April 2015  
Obstacles and Solutions

• Obstacle
  • Administrative and legal concerns
    • Complicated Reliance Agreements

• Solution
  • Develop template agreements
    • IRBchoice
    • IRBrely
    • CTTI
Obstacles and Solutions

• Obstacle
  • Administrative and legal concerns
    • Enforcing compliance with 45 CFR part 46 through the institutions that are engaged in human subjects research

• Solution
  • NPRM
  • Proposal on IRB accountability released by OHRP in 2009
Obstacles and Solutions

- **Obstacle**
  - Roles in ensuring IRB review

- **Solutions**
  - FDA Guidance on Centralized IRB Review Process in Multicenter Clinical Trials (March 2006)
  - CONSIDERATIONS to Support Communication Between Institutions and Outside IRBs When Responsibilities are Being Assigned for Multicenter Clinical Trial Protocols

*CTTI RECOMMENDATIONS: ADVANCING THE USE OF CENTRAL IRBS FOR MULTICENTER CLINICAL* Released April 2015
Obstacles and Solutions

• **Obstacle**
  • Cost sharing

• **Solutions**
  • Include costs in grant budgets
    • “If the agreed-upon single IRB is a fee-based IRB, these costs will be included in the Notice of Award as a direct cost”
Obstacles and Solutions

• Obstacle
  • Consideration of Local Context

• Solutions
  • SACHRP Recommendations on Consideration of Local Context With Respect to Increasing Use of Single IRB Review (Revised by SACHRP October 2012)
    • Applicable Law and Local Standards
    • Knowledge of Institutional Policies and Capacity
    • Investigator and Study Staff Capability
    • Community and Subject Considerations
Ways to Improve Interactions with Central IRBs

• Develop internal SOPs
• Define your organizational structure
• Understand the process
• Good communications
• Develop relationships/networking
Support and Disclosure

- Supported by the National Institute of Neurological Disorders And Stroke of the National Institutes of Health under Award Numbers:
  - National Coordinating Center: University of Cincinnati U01NS086872;
  - National Data Management Center: Medical University of South Carolina U01NS087748.

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