ANPRM
Single IRB Review mandated for multi-site domestic research

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Life would be grand!
If I only had a single IRB!
Points to be made

• Proposed benefits of single/central IRB review
• Reminder of ‘review’ requirements
• Types of ‘central’ IRBs
• IRB versus institutional responsibilities
• Details of relying
• Experience with NeuroNEXT model
• Challenges that must be addressed
Proposed benefits
Specific to multi-site research

– More efficient IRB review
  • Multiple sites approved more quickly
  • Continuing review, amendments, changes to ICF
– Less duplication of review
– Potentially better IRB review
  • E.g., review of adverse events across the entire study
  • More consistent review
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May result in more successful study enrollment and completion
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Reminder of the Review Requirements

• Protocols require:
  – IRB review
    • Initial review
    • Continuing review
    • Amendments, adverse events, unanticipated problems, deviations…
  – Ancillary committee reviews
    • E.g., COI, Radiation safety, IBC,
  – Grants and contracts
  – Institutional sign-off and responsibility for the local conduct of the research
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Models of Central IRBs

• Non-share model
  – Central IRB fulfills all IRB-review requirements
  – Initial, continuing, adverse events amendments, etc.

• Share model
  – Central IRB and local IRB share review responsibilities
    • Most frequently re: amendments and adverse events
Proposed taxonomy of Central IRBs

Local IRBs alone  Non-share model

Share models
Proposed taxonomy of Central IRBs

Local IRBs
- Status quo
- IRBSShare
- NCI CIRB (original)
- VA CIRB
- Commercial

Non-share model
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IRB vs. Institution

Institutional Responsibilities
(including Federal Wide-Assurance details)
IRB vs. Institution

Institutional Responsibilities
(including Federal Wide-Assurance details)

IRB Review
IRB vs. Institution

Institutional Responsibilities
(including Federal Wide-Assurance details)

IRB Office Responsibilities

IRB Review

Scope of CIRB
Non-Share CIRB model

- **CIRB responsibility**
  - **All IRB review tasks**
    - Initial review
    - Continuing review
    - Amendments, deviations, AEs
  - **Possibly HIPAA determination**
    - Authorization
    - Waiver

- **Local Site responsibility** *
  - Site-specific context
    - E.g., Local laws
  - Ancillary review/s
    - E.g., Nursing, Rad’n safety
  - HIPAA implementation
  - Oversight of conduct of research
  - Required reporting

* Institutional NOT IRB review responsibility
The result: New system/s needed for local processes

- **Institutional**
  - Local protocol review to determine CIRB submission eligibility
    - Varying levels of formality
  - Process for ‘following’ the protocol in the local system
    - For the non-IRB review responsibilities
  - Capturing local context and policies
  - Dealing with site-specific adverse events, noncompliance
  - Determining Federal reporting responsibilities

- **Investigator**
  - Local requirements for using a central IRB
  - Understanding processes for:
    - Completing ancillary committee reviews
    - Completing sponsored research office sign-off
The result: New system/s needed for local processes

• Resources needed:
  – IT system integration – esp. important in terms of ancillary committees and contracts
    • Many institutions jerry-rig existing systems
  – Researcher training for use of a CIRB – and how it differs
    • Some have formal courses and designated educator
  – Initial negotiations - require much effort and time
    • But the more specific, the easier in the long run – need to specify
      – Who does what
      – How local policies will be respected and incorporated into the CIRB review
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Importance of the Reliance Agreement

• Delineates
  – Who is responsible for regulatory review/s
  – Assignation of legal, regulatory and contractual responsibilities
  – This is where the rubber meets the road
Reliance Agreement with whom?
Organizational Complexity

Primary Site

Affiliate A

Affiliate B

Affiliate C
Reliance Agreement with whom?
Organizational Complexity

Primary site

Affiliate A  Affiliate B  Affiliate C

Questions:
- What is the relationship between all entities?
- What is the HRPP structure?
  - How is/are IRB/s organized?
- What is the FWA status?
Organizational Complexity

- **Affiliate A**
- **Affiliate B**
- **Affiliate C**

**Primary Site**

**Straightforward scenarios:**

- Affiliates A, B and C all in same city/complex as Primary site
  - Same HRPP
  - Same IRB
  - One FWA

- Affiliates A, B and C and Primary site all in different cities
  - Separate HRPPs
  - Separate IRBs
  - Separate FWAs
Organizational Complexity

Less straightforward scenarios:

• Affiliates A, B and C and Primary site
  • Same HRPP
  • Same IRB
  • Separate FWAs

• Affiliates A, B and C and Primary site
  • Same HRPP
  • Separate IRBs
  • Separate FWAs
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NeuroNEXT CIRB

- NINDS Network of 25 Academic Medical Centers
  - CIRB situated at clinical coordinating site
- CIRB
  - Non-share model
  - CIRB conducts all IRB-reviews
Reliance Agreements

• Prior to any protocol, all network sites had to sign a reliance agreement with the CIRB
  – RA covers all NeuroNEXT studies
    • Process of CIRB review
    • Assignation of legal, regulatory and contractual responsibilities

• Non-member sites engaged in NN-research must sign a reliance agreement
  • The scope of the reliance agreement is limited to a single protocol
Protocol submitted via CCC

**cIRB**
- Initial assessment to determine 'IRB readiness'

**Sites**
- ‘IRB ready’ protocol sent to sites to identify ‘substantive’ and/or local issues

**cIRB**
- Receives ‘substantive’ and/or local issues from each site
- AND then reviews protocol

**cIRB**
- CCC sends approved protocol to sites

**Sites**
- Communicate decision to participate
- Sites participating submit as an amendment to the cIRB approved protocol

**Ancillary Reviews**
- cIRB receives ‘substantive’ and/or local issues from each site
- AND then reviews protocol

**The Basic Model**
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Anticipated Challenges

- Differentiating between institutional and IRB tasks
- Obtaining and addressing local context
- Simple logistics of communication
- Developing trust
- .....
Unanticipated Challenges

- The complexity of member sites
  - Multiple subsites at which research would be conducted
  - Myriad organizational structures

- Confusion of authority
  - Logos
  - Local IRB ‘stamps’ of approval

- Lack of consensus on some basic issues
  - E.g., Engagement in research
Challenges for the relying sites

• If and how to provide institutional review
  – Who should be involved?
    • The local IRB? The PI? Institutional Officials? Other?
  – What should that review include?

• Determining appropriate ongoing institutional oversight of the research.
  – Once the study is underway – what is their role?
  – Need to maintain HRPP responsibilities

• Supporting researchers’ compliance with the CIRB

• Confusion for those sites already using other single/central IRB models
General Concerns

• Requests/mandates for single IRB review do not adequately address the complexities involved and the resources required for:
  – Being the single/central IRB
  – Relying on a single/central IRB

• The many ‘models’ of single IRB review add confusion
  – For the institution
    • Local roles and responsibilities vary by model
  – For the investigators and their staffs
Being the central IRB

• Don’t under-estimate:
  – The time required for development
  – Start-up and long term costs of Central IRB infrastructure
  – The confusion resulting from institution-specific assignation of institutional responsibility and IRB-review responsibility
  – The critical role that trust and familiarity play in development and negotiation of IRB reliance relationships
Final slide

• Single IRB review may improve review of multi-site research – AND – increase the efficiency of many research protocols

• Single IRB review is not simple ‘out-sourcing’ of a task
  – It is a different way of completing that task that requires:
    • Investment in creation of a central IRB AND
    • Development of new ‘local site’ systems for meeting all other responsibilities for research oversight

• Development and use of a central/single IRB -- easier said than done
Questions?