ANPRM

Single IRB Review mandated for multi-site domestic research

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Partners Health Care

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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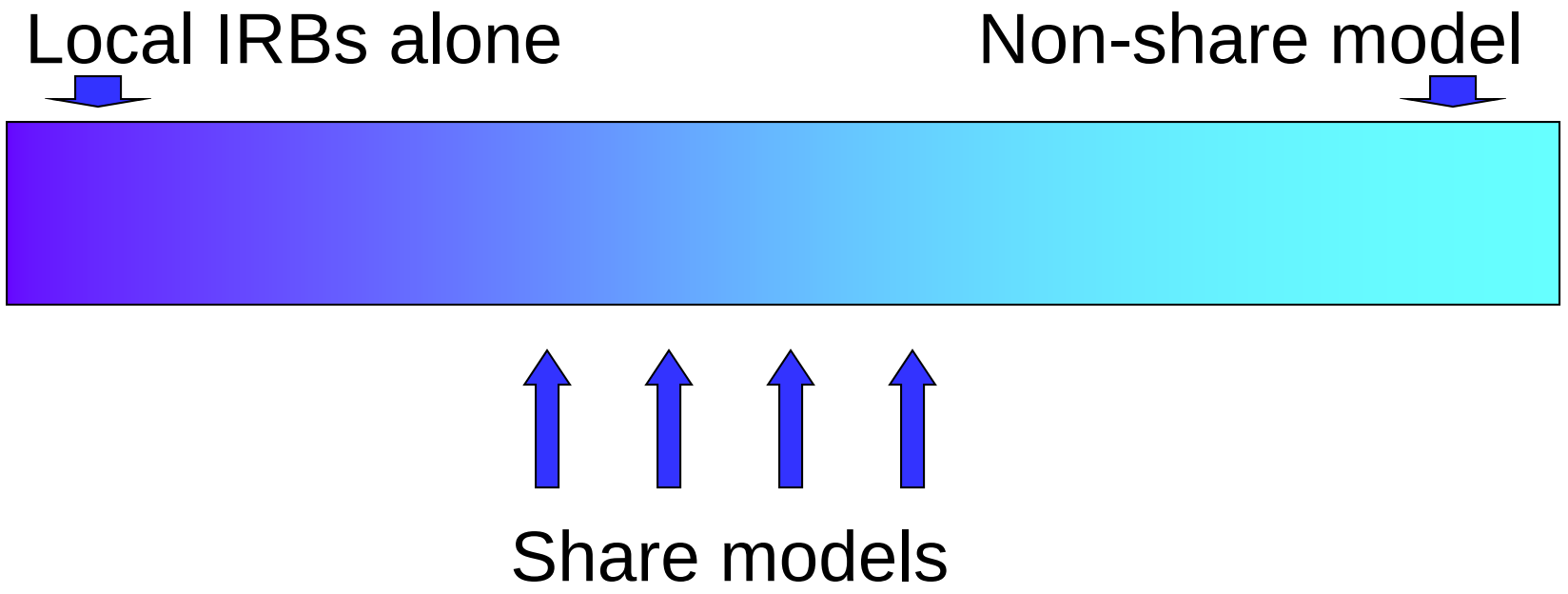
Models of Central IRBs

- 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



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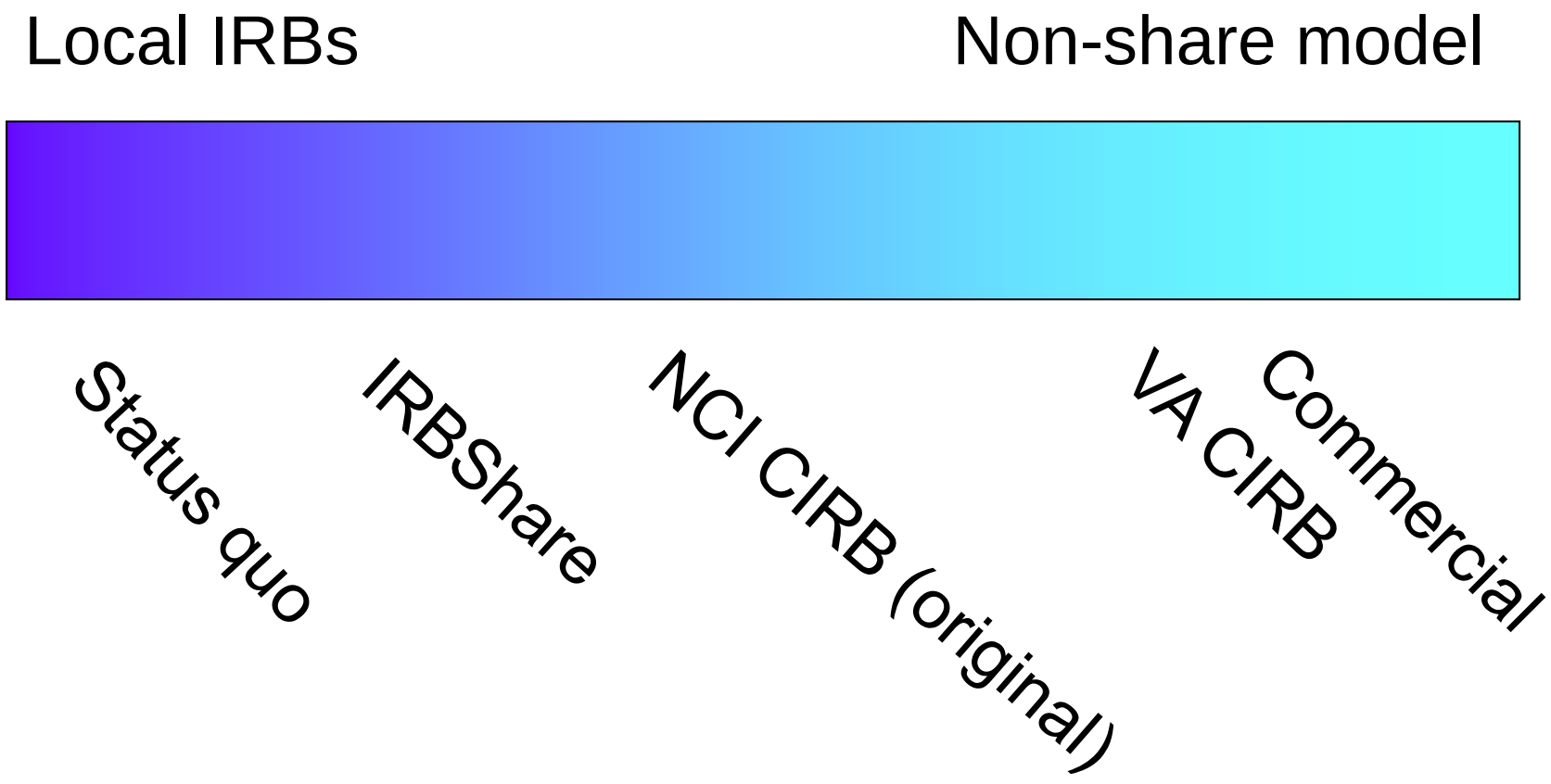

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IRB vs. Institution

Institutional Responsibilities
(including Federal Wide-Assurance details)

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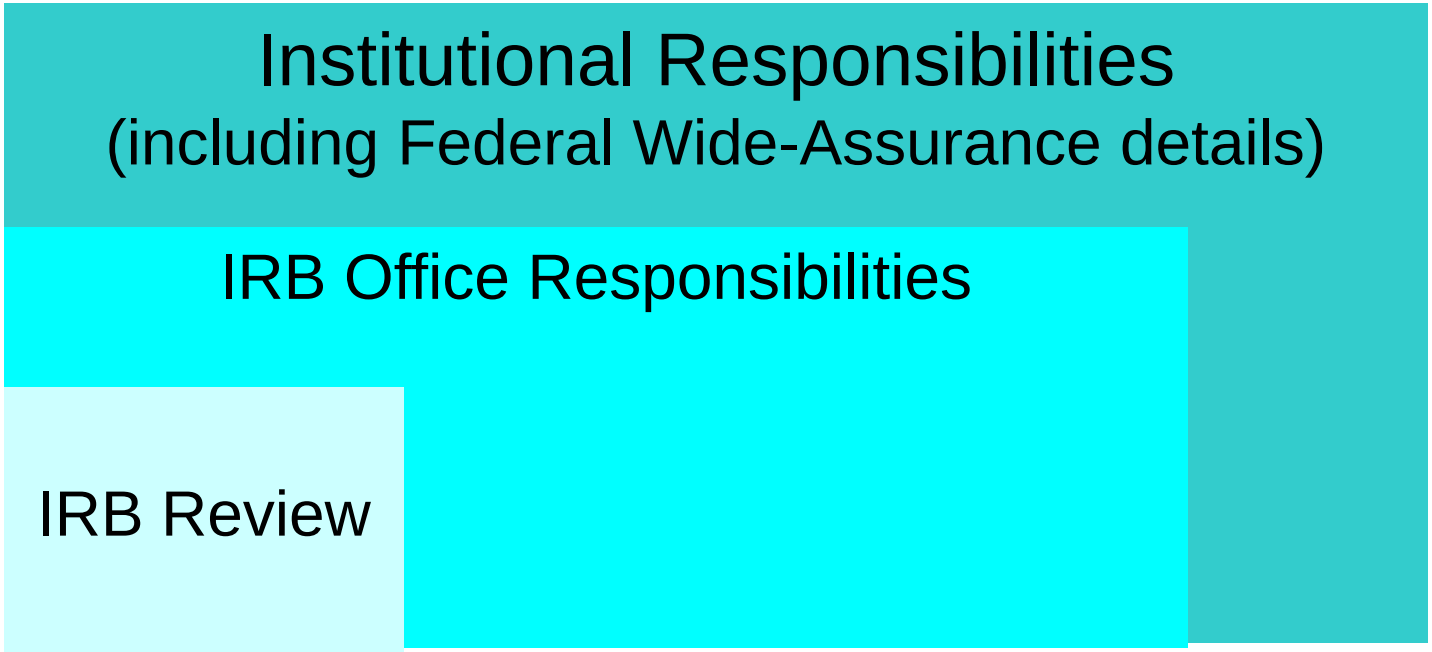
IRB Review

IRB vs. Institution



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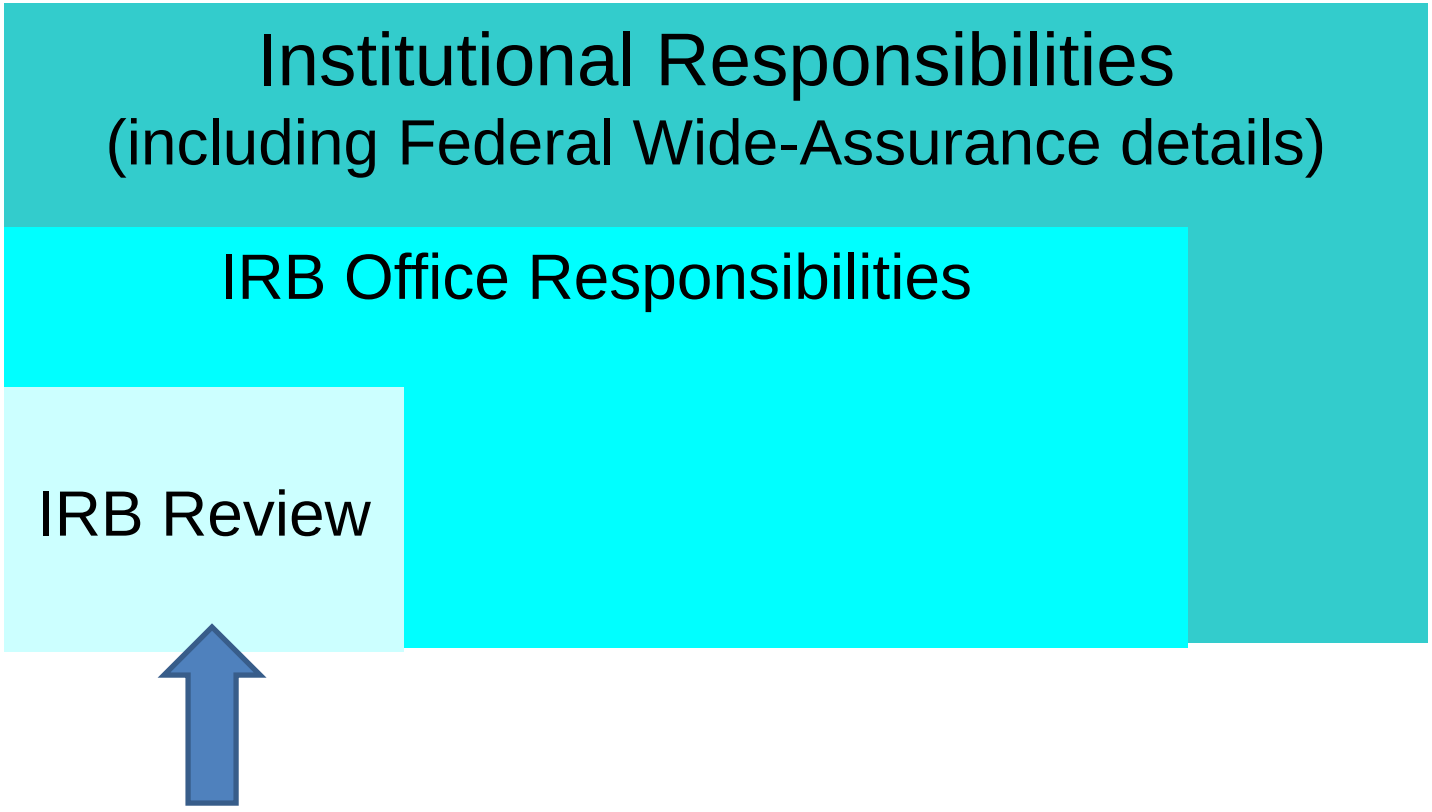

Non-Share CIRB model

- 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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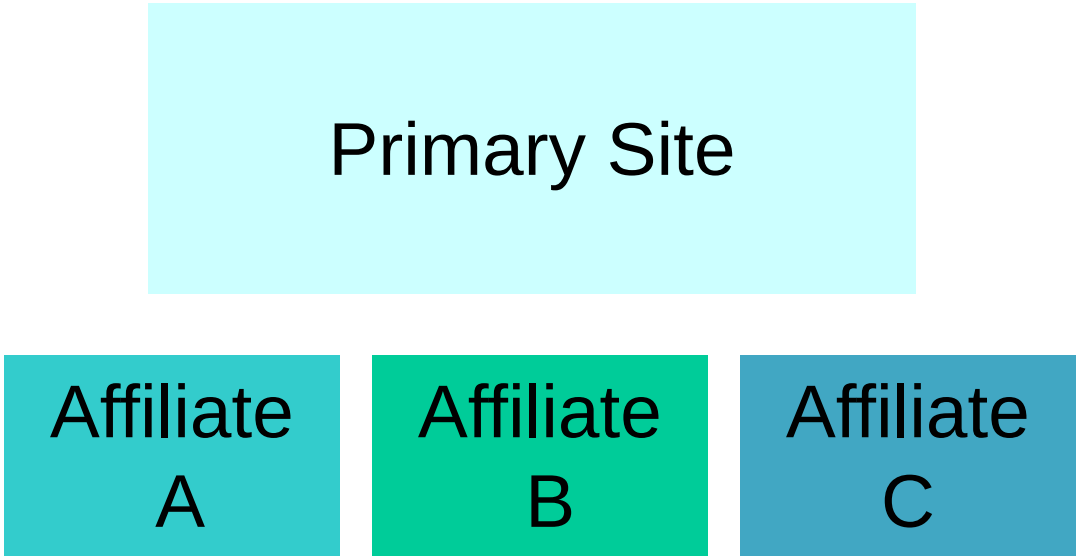
Importance of the Reliance Agreement

- Delineates
  - Who is responsible for regulatory review/s
  - Assignation of legal, regulatory and contractual responsibilities
  - This is where the rubber meets the road

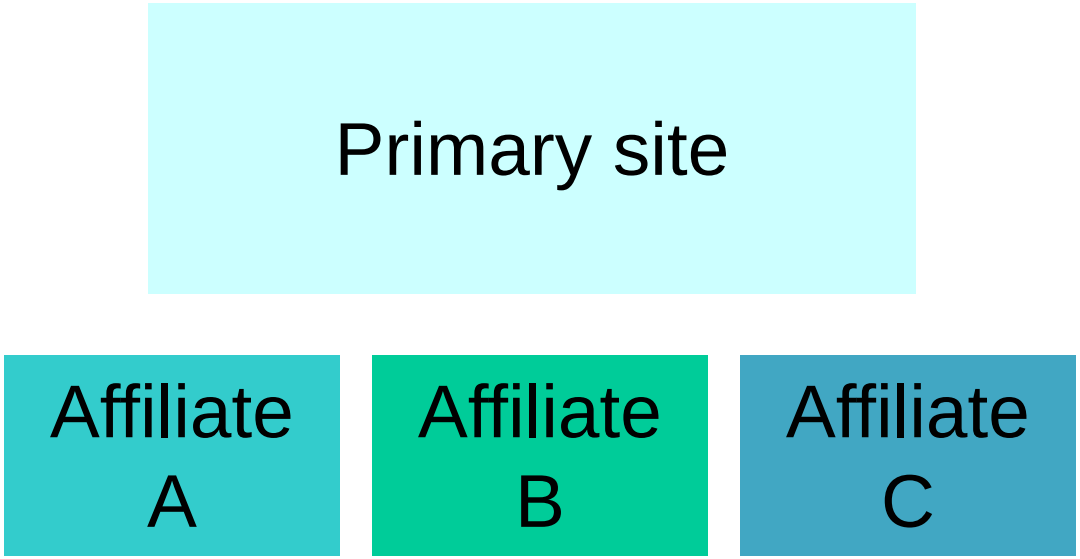
Reliance Agreement with whom?

Organizational Complexity



Reliance Agreement with whom?

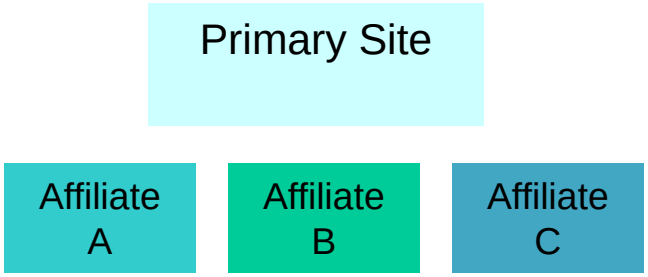
Organizational Complexity



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

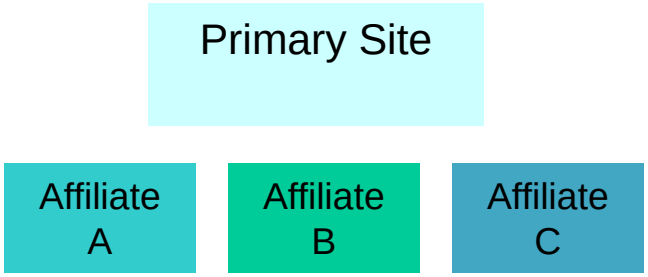


Straightforward scenarios:

- 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
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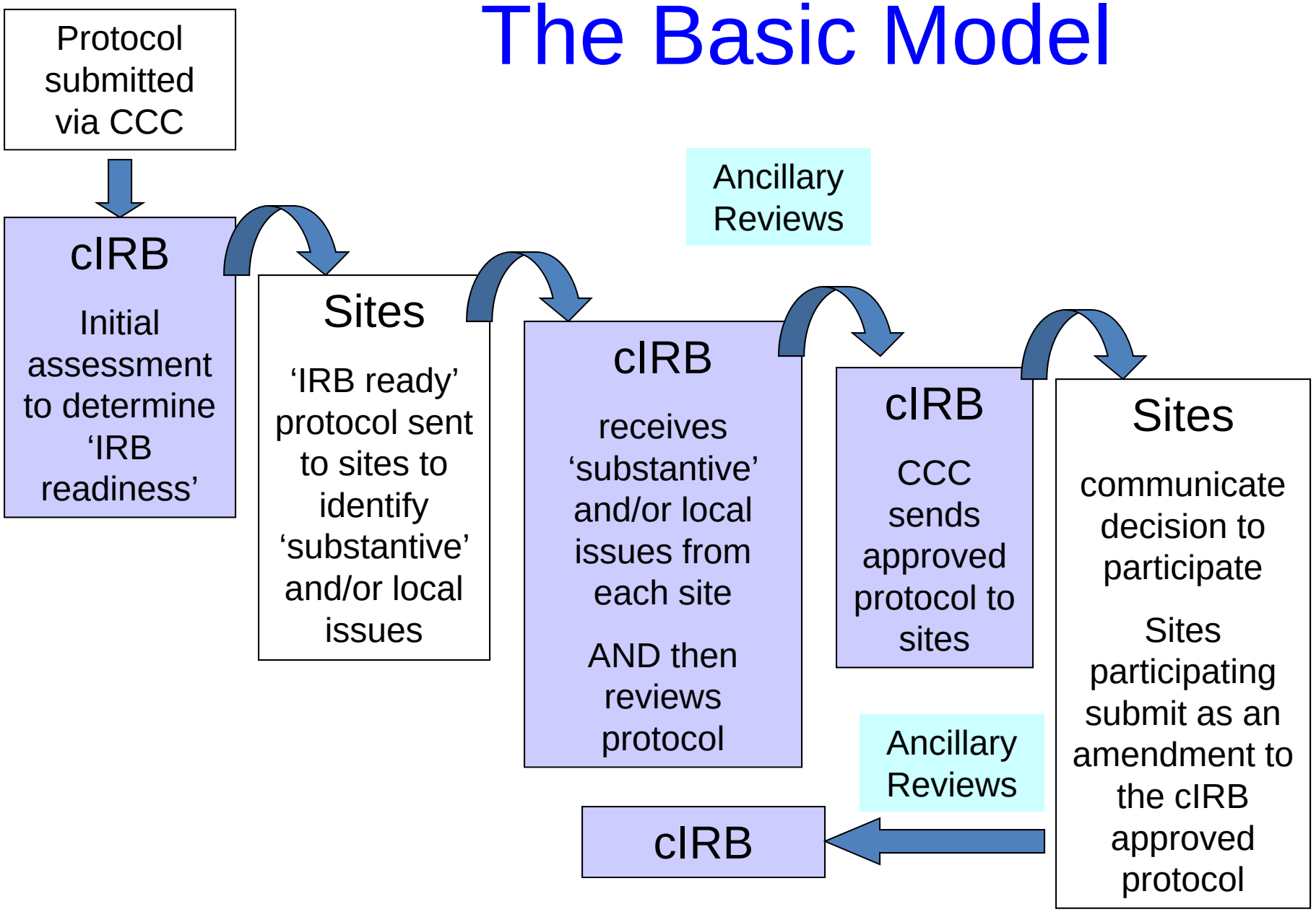
NeuroNEXT CIRB

- 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

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?