Centralized IRB Models

NWABR / OHRP Conference
July 31, 2014

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Outline

• Central IRB’s – Why Now?
• Some Terms and Refresher
• Different Central IRB Models
• Reliance Agreements
• Discussion and Questions
Why Now? – OHRP ANPRM

“…Public comment is requested on the feasibility, advantages, and disadvantages of mandating that all domestic sites in a multi-site study rely upon a single IRB as their IRB of record for that study. (This would apply regardless of whether the study underwent convened review or expedited review.) This proposal would only affect which IRB would be designated as the IRB of record for institutional compliance with the IRB review requirements of the Common Rule.”

Federal Register / Vol. 76, No. 143 / Tuesday, July 26, 2011 / Proposed Rules
Why Now? – NIH Mandates

NIDDK: Type 1 Diabetes TrialNet Clinical Centers (U01)
Posted June 18, 2013


Central Institutional Review Board (IRB)
NIDDK will give preference to Clinical Centers agreeing to use a central IRB of record to accelerate IRB approval in multi-center trials. To that effect, the network will use a “federated” IRB model. This model gives participating institutions the option to choose one of three tiers of IRB review:

• Tier 1 indicates reliance on a central IRB as IRB of record;
• Tier 2 indicates designation of a central IRB as IRB of record in addition to involvement of a local IRB;
• Tier 3 indicates reliance on a local IRB.

The concurrent review and selection of the Clinical Network Hub will provide an opportunity to coordinate a central IRB of record and manage all required IRB communication and documentation including, but not limited to, tracking approval, maintaining regulatory documents, communicating with local IRBs, and handling adverse event reporting and notifications.
Outline

• Central IRB’s – Why Now?
• Some Terms and Refresher
• Different Central IRB Models
• Reliance Agreements
• Discussion and Questions
Central IRB – Defined

- **Central IRB** – According to the Clinical Trials Transformational Initiative (CTTI) a “Central IRB is a single IRB of record for a given protocol. The Central IRB assumes all of the usual IRB responsibilities including all reviews of all relevant documents”

*Does this cover it?*
Other Key Terms

- Reviewing IRB
- Relying Institution
- Internal IRB
- External IRB
- Independent IRB
- Reliance Agreement
“So I thought we were relying on the Central IRB, why are we still doing so much work!”
Refresher - What is *really* Centralized?

Institutional Human Research Protection Program (HRPP) Oversight Responsibilities

IRB Office Responsibilities

The IRB Review
Types of Reviewing IRBs

- Independent commercial IRB
- Collaborative or Community IRB
- Another hospital, academic center, or research institution’s IRB
Scope of Review

• Single Protocol

• Multiple Protocols
  – By type of research (e.g. HVTN)
  – Specific group of institutions (Cancer Consortium)
  – By funding (e.g. all U54 projects)

• All Protocols
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Models of Reliance

• Non-share model
  – Central IRB fulfills *all* IRB review requirements

• Share model
  – Central IRB and local IRB share review responsibilities
Share Model vs Non-Share

Local IRB Review vs All Centralized

All Local vs Non-Share

Traditional Local IRB vs Commercial

IRB Share vs CIRB

Facilitated Review vs Lead IRB

Old NCI vs New NCI

FHCRC vs IRB
Strategies Vary by Scale and Need
Case Study 1 – FHCRC Central IRB for Regional SCCA Network

Fred Hutchinson Cancer Research Center
UW Medicine
Seattle Children’s

Working together to cure cancer
SCCA Network IRB Services

• FHCRC serves as the IRB of record for all locations conducting cancer trials through the SCCA network

• IRB authorization agreements allow for one deferral to FHCRC to cover multiple protocols within a specific scope

• Centralized IRB management for SCCA Network Regulatory Support Office
SCCA Network - IRB Agreements

IRB Authorization Agreement

Institution A - Name of Institution or Organization Providing IRB Review: Fred Hutchinson Cancer Research Center (FHCRC)
IRB Registration #: Com A (00000021), Com B (00000022), Com C (00005619)
Federalwide Assurance (FWA) #: FWA00001920

Institution B - Name of Institution Relying on the Designated IRB: SCCA Network Location

Federalwide Assurance (FWA) #: 

The Officials signing below agree that all SCCA Network Location review and continuing oversight of its human subject research described in the enclosed protocol(s) is to be performed by the designated IRB.

This agreement is limited to the following specific protocol(s):

Title of Research Project: All protocols covered by research agreements with the Seattle Cancer Care Alliance (i.e. Fred Hutchinson Cancer Research Center, University of Washington Medicine, and Children’s Hospital) and made available through the Seattle Cancer Care Alliance Network as “Affiliate Protocols” and include: Affiliate Protocols approved by the Fred Hutchinson Cancer Research Center Institutional Review Board.

Individual Investigator Agreement

Name of Institution with the Federalwide Assurance (FWA): Fred Hutchinson Cancer Research Center

Applicable FWA #: FWA00001920

Individual Investigator’s Name

Specify Research Covered by this Agreement: Protocols covered by research agreements with members of the Seattle Cancer Care Alliance (i.e. Fred Hutchinson Cancer Research Center, University of Washington Medicine and Seattle Children’s Hospital) and made available through the Seattle Cancer Care Alliance Network as “Affiliate Protocols” and include: Affiliate Protocols approved by the Fred Hutchinson Cancer Research Center Institutional Review Board.

(1) The above-named Individual Investigator has reviewed: 1) The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research (or other internationally recognized equivalent; see section B.1. of the Terms of the Federalwide Assurance (FWA) for International (Non-U.S.) Institutions); 2) the U.S. Department of Health and Human Services (HHS) regulations for the protection of human subjects at 45 CFR part 46 (or other procedural standards; see section B.3. of the Terms of the FWA for International (Non-U.S.) Institutions); 3) the FWA and applicable Terms of the FWA for the institution referenced above; and 4) the relevant institutional policies and procedures for the protection of human subjects.

(2) The Investigator understands and hereby accepts the responsibility to comply with the standards and requirements stipulated in the above documents and to protect the rights and welfare of human subjects involved in research conducted under this Agreement.

(3) The Investigator will comply with all other applicable federal, international, state, and local laws.
FHCRC IRB Policies on Multi-Center Research and Lead IRB
Case Study 2 – Lead IRB for National Vaccine Trial Network
What did it take to make it work?

• Notifying DAIDS/NIH (annual report)
• Memo to site PIs laying the foundation
• Setting up calls with each site’s institutional review office director
• Setting up calls with the HVTN population (especially CABs) to explain how it would work: “Hot topic” and GCAB calls
• When final sites were on board, held call for CAB review—submitted minutes as part of the IRB application
More on what was done...

- Set up IRB authorization agreements
- Obtained grant application from sites; CVs of PIs, training records; how they intend to recruit & consent
- Drafted a WPG on how HVTN would communicate with the Lead IRB and sites
- Had sites identify “consultative reviewer” at each institution; someone who knew the research environment and local requirements
- Worked with each site on it’s consent and application
Lead IRB – Mechanics

- Infrastructure changes:
  - Programming
  - Filing system
  - Protocol level versus site level records
- Education of the IRB on how to be a Lead IRB
- Local consulting reviewers to satisfy OHRP guidance
  IRB knowledge of local research context
- IRB authorization agreements with each institution to defer IRB oversight
Lead IRB - Local Research Context Questionnaire

<table>
<thead>
<tr>
<th>Principal Investigator</th>
<th>Insert Local PI name</th>
<th>Date of Report:</th>
</tr>
</thead>
<tbody>
<tr>
<td>FHCRC IR File #</td>
<td>6944</td>
<td>Protocol #</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HVTN 505</td>
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| Title of Protocol if applicable | HVTN 505 - Phase 2, Randomized, Placebo-Controlled Trial to Evaluate the Safety and Effect on Post-HIV Acquisition VIRGINIA of a Multiclaude HIV-1 DNA Plasmid Vaccine Followed by a Multiclaude HIV-1 Recombinant Adenoviral Vector Vaccine in HIV-Uninfected, Adenovirus Type 5 Neutralizing Antibody Negative, Circumcised Men |

| Institution relying on FHCRC for Lead IRB review: | University Name Here |
| Local Context Representative: | Local Contact Name Here |

To assist the Fred Hutchinson Cancer Research Center (FHCRC) IRB in its Lead IRB review of HVTN 505, please provide a written response to the following questions relating to local research context.

1. Section 3 of the attached application describes the selection and recruitment of subjects for HVTN 505. Does this section adequately describe the activity to occur at your institution? Is there any additional data you would like to provide relevant to your institution?

2. Section 4 of the application describes the consenting process and compensation for research participants. Does the master application adequately describe the consent process to be used at your institution, specifically the plans to compensate subjects?

3. Does the consenting process outlined in the application, as well as the attached local consent form, comply with all of your local institutional consent policies and local law? Are there any issues you would like to specifically highlight for the FHCRC IRB which would help the Committee in their evaluation of the local consent process form?
Dear xxxx,

Thank you for agreeing to allow Fred Hutchinson Cancer Research Center (FHCRC) IRB to serve as your lead IRB for the HVTN 505 multi-center trial.

To facilitate the FHCRC lead IRB review of HVTN 505 for insert institution’s name please review the attached material and complete the associated Local Research Context Questionnaire, Local consultant Conflict of Interest Form, and the IRB Authorization Agreement:

Materials attached for local context review:
- FHCRC IRB application for HVTN 505
- Consent forms, and other local documents relating to the research being conducted at your institution

- Local Research Context Questionnaire (please complete and return)
- Local Consultant Conflict of Interest Form (please complete and return)
- IRB Authorization Agreement between insert institution and Fred Hutchinson Cancer Research Center (please sign and return)

Supporting Materials already approved by FHCRC IRB for HVTN 505:
- Reference B - HVTN 505 Protocol – Amendment 4.0 dated 3-4-2010
- Reference C - HVTN 505 Investigator Brochure
- Reference D - HVTN 505 Consent – Assessment of Understanding
- Reference E - HVTN 505 Questions and Answers
- Reference F - HVTN 505 Behavioral Risk Questionnaire
- Reference G - HVTN 505 Main Recruitment Package for All Sites

Return the completed and signed Local Research Context Questionnaire, Conflict of Interest Form, and IRB Authorization Agreement by May 18, 2010. The FHCRC IRB will be meeting on May 26th at 2:30pm pacific time to review your site for HVTN 505. Please let me know if you are available to be reached by phone should the IRB have questions about the local research context at your institution.

Completed forms should be returned to:

[Address]
# Authorization Agreement

**Institution A** - Name of Institution or Organization Providing IRB Review:
Fred Hutchinson Cancer Research Center

IRB Registration #:  IRB00000021, IRB00000022, IRB 00005619
Assurance #: (e.g. Federalwide Assurance (FWA), Multiple Project Assurance (MPA), Single Project Assurance (SPA))  FWA00001920

**Institution B** - Name of Institution Relying on the Designated IRB: Insert University

Federalwide Assurance (FWA) #: Insert FWA number here

The Officials signing below agree that **Institution Name Here** may rely on the designated IRB for review and continuing oversight of its human subject research described below: (check one)

- This agreement applies to all human subject research covered by Fred Hutchinson Cancer Research Center’s FWA.
- This agreement is limited to the following specific protocol(s):

  Title of Research Project: HTN 193 - Phase 2, Randomized, Placebo-Controlled Trial to Evaluate the Safety and Effect on Post-HIV Acquisition Uptake of a Multiclade HIV-1 DNA Plasmid Vaccine Followed by a Multiclade HIV-1 Recombinant Adenoviral Vector vaccine in HIV-Uninfected, Adenovirus Type 5 Neutralizing Antibody Negative, Circumcised Men

FHCRC Principal Investigator: Dr. Lawrence Corey, MD

Institution B’s Principal Investigator: Insert name here

The review performed by the designated IRB will meet the human subjects protection requirements of Institution B’s OHRP-approved FWA. The IRB at Institution Organization A will follow written procedures for reporting its findings and actions to appropriate officials at Institution B. Relevant minutes of IRB meetings will be made available to Institution B upon request. Institution B remains responsible for ensuring compliance with the IRB’s determinations and with the Terms of its OHRP-approved FWA. The term of this Agreement shall be for a period of three (3) years, which term shall renew automatically for additional one-year periods unless terminated by either party.
FHCRC Lead IRB Instructions for Researchers and Network

Multicenter Studies: Required Documents for IRB Review

Relevant IRB policies/procedures:
- Multi-Center Study Coordination - IRB Review and Oversight (Policy 2.14) [pdf]
- Cooperative Review Agreements (Policy 2.3) [pdf]

[all IRB policies/procedures]

- What is a definition of a multi-center study?
- Engaging in research with institutions with whom FHCRC has a Cooperative Review Agreement
- For performance sites where FHCRC does not have a Cooperative Review Agreement. What are the three (3) types of documentation that may be used by the FHCRC IRB?
  - IRB Certification of Approval for performance sites
  - Mutual Institutional Agreement
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Regulation

- Common Rule and FDA regulations provide for Central IRBs and other cooperative IRB review arrangements (45 CFR § 46.114, 21 CFR § 56.114)

- Must document arrangement in “a written agreement…that outlines [the] relationship and includes a commitment that the IRB will adhere to the requirements of the institution’s FWA” (OHRP’s Terms of FWA #6)
Basics

• Required by OHRP, recommended by FDA
• Serves as roadmap for the life of the study and the IRB reliance relationship
• Agreements cover:
  – Central IRB responsibilities
  – Relying institution responsibilities

*But what to cover??*
What to Cover?

• Regulatory criteria used by reviewing IRB for Initial and Continuing Review
  – HHS and FDA only?
  – DoD, EPA, DOE, DOJ?
  – ICH/GCP?

• If “Share Model” what part is the local IRB’s responsibility for completing the IRB
What to Cover?

- Unanticipated Problems, Noncompliance, Suspensions and Terminations:
  - In Share model, which IRB reviews the event(s)
  - Who is responsible for reporting findings to OHRP/FDA
  - Will drafts of OHRP/FDA letters be shared in advance
  - Who is responsible to conduct investigations, interviews with PIs, and determine corrective actions
  - What confidential information may be shared
What to Cover?

• HIPAA:
  – Does central IRB serve as a Privacy Board
  – Will the central IRB review authorizations
  – Special considerations for relying institution maintaining its obligations as a covered entity which cannot be delegated
What to Cover?

• Communications:
  – How are approval documents distributed
  – Who is authorized to communicate important issues and changes
  – Can PI’s communicate directly with central IRB or only through the relying institution IRB office
  – How are issues tracked and resolved between organizations which problems arise
What to Cover?

• Compliance with state and local law
• Investigator and Institutional Conflict of Interest standards and review
• Relying institution ancillary reviews:
  – Departmental
  – Scientific
  – Radiation Safety
• Other Local Context issues
Resources

AAHRPP Tip Sheet 24 on External IRB Review
http://www.aahrpp.org/SPFileDownload.ashx?fileName=Tip_Sheet_24_Relying_on_An_External_IRB.PDF

FHCRC Template IRB Authorization Agreement
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Contact Information

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