Central IRB 101: An Introductory Guide to Working with External IRBs for the First Time

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Manager, Institutional Services, Schulman IRB

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About Schulman IRB

- Established in 1983
- Superior audit history with FDA—six 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
- Review outcome provided within **one business day** of new study review
- **One business day** turnaround for complete new site submissions
About Schulman IRB

- Dedicated streamlined processes tailored to **Phase I timelines**
- **Therapeutically specialized** IRB panels in oncology and neurology with robust understanding of latest techniques, methodologies and discoveries
- Customized services for **institutions**
- **Experienced primary points of contact** for sponsors, CROs, institutions and sites
- **Institutional biosafety committee (IBC) services** for clinical, pre-clinical and non-clinical research
About Schulman IRB

Clinical Quality Assurance (CQA) and Human Research Protection (HRP) consulting services provided by:

www.provisionrcs.com

www.falconnest.com
The industry’s choice for central and local IRB services.

- Get Started: Begin the initial review process.
- Forms: Download the latest forms for your study.
- Contact Us: Request more info & send feedback.
About Today’s Presenter

Maria Stivers, CIP
Manager, Institutional Services, Schulman IRB
- With Schulman IRB since 2015
- Primary point of contact for institutional clients, providing initial training and ongoing support for all aspects of the working relationship
- Previously oversaw research compliance program at Northern Kentucky University, including all aspects of IRB, IACUC, IBC, research safety and sponsored program activities
- Previously served as community IRB member at University of Cincinnati and alternate IRB member at NKU
- Healthcare and neurology clinical research experience
Objectives

- Explain roles and responsibilities for the central IRB and relying institutions
- Describe typical steps in establishing working relationship with the central IRB
- Define common submission scenarios with the central IRB
“Single IRB” vs. “Central IRB”

They mean the same thing: a single IRB of record overseeing all clinical trial sites participating in a multisite study

- **IRB of Record**: the IRB that is responsible for the review, approval and regulatory oversight of a research study
  - Term used most consistently in federal guidance, correspondence and other documentation
  - Term focuses on IRB’s responsibilities
    - More important than IRB’s location or organizational relationship
  - Single IRB relationship can be established in a variety of ways
Why Centralized IRB Review?

- Multiple federal agencies endorse centralized IRB review for multisite research
  - NIH, FDA, OHRP
- Centralized review = more efficient process
  - Removes duplicative reviews
- Single IRB overseeing all participating sites = consistent oversight
  - Uniform protocol and informed consent template for all sites
  - Consistent subject protections
  - More reliable study data
Central IRB Review vs. Local IRB Review for Multisite Studies

Local IRB: oversees research at just one location
- Reviews the protocol-level information and investigator/site qualifications as a single unit

Central IRB: oversees research being conducted at many locations
- Reviews the protocol once on behalf of all sites
- Reviews each investigator/site submission in the context of the protocol
- cIRB may ask investigators/sites to only submit site-specific material
  - Study sponsor or coordinating site may have already submitted protocol material and study-wide informed consent for cIRB review
  - Check with cIRB and sponsor for specific instructions
Central IRBs have the same regulatory responsibilities as local IRBs.

- cIRBs audited regularly by FDA and relying sites

- AAHRPP accreditation
  - Shows above-and-beyond commitment to quality HRPP

21 CFR 50, 56
45 CFR 46
Getting Started with a cIRB
Communications

- Find out who the institution will work with at the cIRB
  - Possible cIRB contact scenarios: primary point of contact, dedicated team, etc.
- Consider designating someone at the institution as primary liaison with cIRB

- Possible types of communication scenarios
  - Study-specific
  - Global/over-arching issues

Communication is key!
Case Study: Getting Started with a cIRB

1. **Relationship Initiated**
   - Introductory Call
   - Visit

2. **Reliance Agreement**
   - Defines relationship
   - Reduces administrative burden

3. **Unique Profile Development**
   - Start-up call
   - IC language
   - Submission process

4. **Training**
   - eTools
   - Education
   - Resources
Reliance Agreement

Study-by-Study Agreement

- This agreement establishes a reliance relationship between the central IRB and relying institution for a single study (or set of related studies) only
  - Any other studies would require a separate reliance agreement
  - Allows institutions to make a study-by-study determination of which IRB to use

Global Agreement

- More proactive—establishes expectations and processes up front so review process can begin immediately when a new study is submitted
- Outlines roles and responsibilities of relying institution and central IRB being relied upon as IRB of record
- A global agreement generally allows review by the central IRB of all research submitted by the relying institution
  - Relying institution retains authority to determine which studies to submit to the central IRB
  - Having a global agreement in place streamlines the process for these reviews
# Responsibilities

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<tr>
<th>cIRB Responsibilities</th>
<th>Institution Responsibilities</th>
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<tr>
<td>Assess investigator qualifications as part of submitted material</td>
<td>Assess investigator qualifications prior to submission to IRB and report any changes to qualifications that negatively impact subject safety</td>
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<td>Assess research education and training documentation for investigators and research staff</td>
<td>Require and document research education and training for investigators and appropriate study staff</td>
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<td>Maintain registration with FDA and OHRP</td>
<td>Provide appropriate credentialing of staff</td>
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<td>Notify designated institutional officials of accreditation changes</td>
<td>Maintain the institution’s approved FWA(s)</td>
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<td>Ensure compliance with ethical standards and regulations in approved research</td>
<td>Conduct security and privacy review of protocol and informed consent as required for HIPAA (unless cIRB is responsible)</td>
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<td>Assume regulatory responsibility for IRB’s actions as IRB of record</td>
<td>Ensure investigator compliance and conflict of interest is managed in accordance with IRB requirements</td>
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<td>Manage necessary site-specific information for inclusion in the informed consent</td>
<td>Decide whether to participate in a study or to limit an investigator’s involvement prior to submitting research to IRB</td>
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<td>Approve informed consents that meet the IRB’s requirements and maintain review of revisions</td>
<td>Indicate any relevant state laws or institutional concerns regarding the research in IRB’s submission material</td>
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<td>Provide copies of IRB decisions and rosters</td>
<td>Include assessment of local context in IRB submission material to be considered during review of research proposals</td>
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<td>Notify institution of serious or continuing noncompliance determinations, unanticipated problems in research, and suspension or termination of IRB approval</td>
<td>Report to the IRB any serious or continuing noncompliance, unanticipated problems in research, and other compliance issues potentially impacting human subject protections</td>
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For more information, see [FDA Guidance for Industry – Using a Centralized IRB Review Process in Multicenter Clinical Trials](https://www.fda.gov/regulatoryinformation/guidances#multicenterclinicaltrials)
Local Context

- Evaluate how the local review process will impact the cIRB review process
- Examples
  - Must cIRB receive a completed cover sheet before proceeding with review?
  - Does the institution have required IC language?
- Identify any other local context requirements cIRB should be aware of, such as:
  - State law
  - Institutional policies/procedures
  - Ancillary committee requirements
  - Unique community features/needs

Examples of Institution’s Required ICF Content
- Compensation for research-related injury
- Institutional contact information
- Institution’s HIPAA language
- Ethical religious directives
- Costs of participation

AKA: unique institutional/local/regional requirements or items the reviewing IRB should know
Case Study: Informed Consent

**Institutional IC Language**
- Most institutions have required language to be inserted into a sponsor template
  - This is only the required language
- This is different than the institutional IC template
  - Institutional IC template is the entire consent form template

**Negotiate Language**
- IRB reviews language, approves it and keeps it on file
  - IRB can insert language into the sponsor template for institution with each submission
  - OR
  - Institution provides language with each submission in tracked changes, and IRB double checks that it matches the approved language

**IRB does not need to review institution’s separate HIPAA document**
- IRB will review HIPAA if it is inserted into institution’s IC
- Let IRB know if institution will use sponsor’s HIPAA language
Training with Researchers and Research Staff

- Ensure everyone at institution understands cIRB relationship and any associated institutional requirements
  - Local administrative review requirements
  - Communicate requirements and policies to all stakeholders

- Possible cIRB training topics
  - cIRB online portal
  - cIRB submission process
  - “New to cIRB” overview
Institutional Process for cIRB Submissions

What studies will the institution send to the cIRB?

- Answer(s) may vary based on source of research funding
- Sample scenarios:
  - Industry-funded research goes to cIRB; investigator-initiated research stays with local IRB
  - Research in certain therapeutic areas (e.g., oncology, neurology, etc.) goes to cIRB
  - Late phase research goes to cIRB; early phase remains with local IRB
  - Federally funded research goes to cIRB
Institutional Process for cIRB Submissions

**Centralized cIRB Submission Process**
- Institutional research oversight staff responsible for all submissions to cIRB

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<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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<tr>
<td>Institution has complete control over which studies are submitted to cIRB</td>
<td>More work for local research oversight staff</td>
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<tr>
<td>• Institution can confirm local requirements are addressed prior to cIRB submission</td>
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<tr>
<td>Institution is able to submit to cIRB more quickly</td>
<td>Limits communication between cIRB and specific study personnel</td>
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<td>• Only select group of institutional staff trained on cIRB submission process</td>
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**Decentralized cIRB Submission Process**
- Researchers submit their own studies directly to cIRB

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<tr>
<td>Less work for local research oversight staff</td>
<td>Not as much control over what is submitted to cIRB</td>
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<td>Offers more communication between cIRB and study-specific staff at institution</td>
<td>More training involved for increased number of coordinators/research staff who need to learn cIRB submission system</td>
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<td>• Can leads to quicker responses to IRB-related inquiries</td>
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Deferral of IRB Oversight

When another IRB (not the local IRB) will serve as IRB of record, the local IRB may need to provide documentation of deferral

- **21 CFR 56.114** permits deferral of IRB oversight

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<th>Possible Options for Documenting Deferral</th>
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<tr>
<td><strong>Cover Page</strong></td>
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<tr>
<td>• Customized document unique to institution</td>
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<tr>
<td>• May be required by local IRB or regulatory office</td>
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<tr>
<td>• Protocol specific</td>
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<tr>
<td>• Required if research is covered by institution’s Federal Wide Assurance (FWA)</td>
</tr>
<tr>
<td><strong>Research Oversight Jurisdiction Form</strong></td>
</tr>
<tr>
<td>• Signed by an authorized institutional official</td>
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<tr>
<td>• Can be used instead of IAA if FWA does not cover the research</td>
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<tr>
<td><strong>Master Services Agreement, Reliance Agreement or Global IAA</strong></td>
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<tr>
<td>• Covers all research reviewed by cIRB</td>
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<tr>
<td>• Can be established in advance of any new submissions</td>
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<tr>
<td>• No need for other deferral documents</td>
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<tr>
<td>• <strong>Exception</strong>: Institution may also require a signed cover page with each submission</td>
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Case Study: Industry-Sponsored Multisite Study

- Sponsor/CRO submits the protocol and all protocol level documents → Approved

- The institutional site submits site-specific documents → Approved
  - Submission form
  - Informed Consent
  - Investigator CV
  - Deferral information (if applicable)

- Sponsor/CRO has access to all protocol and site approval documents
- Sites have access to their own approval documents and any protocol-level documents the site may need
Conflict of Interest

- In most cases, cIRB will review investigator’s conflict of interest (COI) as part of standard review process and recommend management plan
  - But institution likely has its own COI policies and management approach
- Both the cIRB and the relying institution have a stake in ensuring COI is appropriately managed

- Talk to cIRB about COI management policies and possible collaboration on these issues to ensure each entity’s needs are met

For more information, see HHS Guidance Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection
HIPAA and Privacy Boards

- Under the HIPAA Privacy Rule, an IRB’s role is “limited to acting on requests for a waiver or an alteration of the Privacy Rule’s Authorization requirement”
  - IRB may serve as privacy board
  - IRB not required to review and approve Authorizations under the Privacy Rule
  - IRB not required to approve standalone Authorizations

- External IRB may serve as privacy board for covered entity

NIH Institutional Review Boards and the HIPAA Privacy Rule

HHS HIPAA FAQ 217-May a covered entity accept documentation of an IRB waiver of authorization
Ongoing Review
As with initial review, cIRBs typically conduct continuing or annual review once at the protocol level and individually for each participating investigator/site.

- Often study sponsor or coordinating site submits protocol level report on behalf of all sites
- Check with cIRB for specific instructions
Amendments

- Typically study sponsor submits amendments directly to cIRB
  - Sponsor distributes amended material to each site
  - cIRB updates each site’s informed consent as appropriate
Deviations and Noncompliance

- IRB is responsible for reporting these issues to the institution, study sponsor and appropriate regulatory authority 21 CFR 56.108(b)
  - Institution is responsible for reporting these issues to the IRB of record

- Talk to cIRB about reporting practices and how institution will be notified of these issues

Regulations do not define “noncompliance”
- Each IRB/institution has its own definitions and policies
- Check with cIRB to understand reporting requirements
Other Considerations
Transfer of IRB Oversight

Transfer of IRB Oversight: Research previously reviewed and approved by a local IRB is transferred to another IRB’s oversight.

The new IRB reviews and approves the research and takes over as the IRB of record.

Common Reasons for Transfers
- Dissolution of local IRB
- Change in scope of local IRB
- Sponsor request

For more information, see:
- FDA Guidance for IRBs, Clinical Investigators, and Sponsors – Considerations When Transferring Clinical Investigation Oversight to Another IRB
- OHRP Draft Transfer Document – Considerations in Transferring a Previously-Approved Research Project to a New IRB or Research Institution
Site Networks

- Therapeutically focused site networks designed to get studies started faster and more efficiently
  - These networks are becoming more prevalent
  - Networks assemble a roster of sites, and these preferred sites get first option to participate
  - Requiring sites to use a single IRB for network studies is becoming more common
Evaluating a cIRB Partner

- Regulatory audit history
- Accreditation
- Communication structure
- Submission deadlines and turnaround times
- Electronic tools
- References from other institutions
Conclusion

- Research and regulatory environment is changing
  - Whether we like it or are prepared for it
- Single/central IRB review is becoming the new standard
  - Need to work together to figure out how to work in this new paradigm
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