Early Feasibility Study
Regulatory Roundtable
CTTI Single IRB (sIRB) Resources

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Disclaimer

The views and opinions expressed in this presentation are those of the individual presenter and do not necessarily reflect the views of the Clinical Trials Transformation Initiative.

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Public-private partnership
Co-founded by Duke University & FDA
Involves all stakeholders
80+ members

MISSION: To develop and drive adoption of practices that will increase the quality and efficiency of clinical trials
Outline

- Overview of CTTI single IRB (sIRB) projects
- Results from recent in-depth interviews about sIRB
- CTTI sIRB Tools and Resources
  - Considerations document
  - Evaluation checklists
  - IRB authorization agreement (IAA) template
  - sIRB resource of resources (RoR)
  - Engagement documents

CTTI definition of “central IRB” - a single IRB of record for all sites involved in a multi-center protocol. A range of entities may serve as the sIRB (e.g. another institution’s IRB, a federal IRB, an independent IRB). Now use term single IRB (sIRB).
Overview CTTI sIRB Timeline

- FDA Guidance: Using a Centralized IRB Review Process in Multicenter Clinical Trials
- National Conference on Alternative IRB Models
- NEJM Menikoff Editorial: Start of CTTI Single (Central) IRB Work
- ANPRM: Common Rule Revision
- CTTI Single (Central) IRB Recommendations
- ANPRM: Common Rule Revision Document
- SMART IRB Online Reliance System Launched
- NIH Single IRB Policy Effective Date
- CTTI & NCATS Continue to Develop Resources to Assist with Implementation of Single IRB
- SMART IRB Agreement & Platform Launched
- NIH Draft Policy: Use of a Single IRB for Multi-Site Research
- NPRM: Common Rule Revision
- SMART IRB Agreement & Platform Launched
- Final NIH Single IRB Policy Published
- NCATS Trial Innovation Network: IRB Reliance Exchange Portal Launched
- CTTI Single (Central) IRB Advancement Recommendations, IAA Template, Evaluation Checklists

From: Resources to assist in the transition to a single IRB model for multisite clinical trials
https://doi.org/10.1016/j.conctc.2019.100423
Single IRB Projects Overview

Goal
Identify Barriers & Propose Solutions
- Considerations Document

Assist with Implementation
- Evaluation Checklists
- IAA Template (reliance agreement template)

Provide Additional Resources and Plan Evaluation
- sIRB RoR
- Engagement Documents
- Results of recent interviews
- Evaluation framework for NIH sIRB policy

Central IRB*
2010 - 2013

Central IRB* Advancement
2013 - 2015

Single IRB Adoption
2017 - 2019

Single IRB Evaluation
2018 - 2019

https://www.ctti-clinicaltrials.org/projects/single-irb
Qualitative interviews - sIRB mandate

- Part of Single IRB Adoption project
- Purpose: Gather evidence on the use of the sIRB process from FDA stakeholders
- Interviews from March-August 2018 (n=34)
  - U.S.-based industry representatives (pharmaceutical, device, and other similar companies)
  - U.S.-based representatives of IRBs (academic and independent)
  - Investigators who conduct multi-site, U.S.-based research that is regulated by the FDA
  - Regulatory and study coordinators of FDA-regulated multi-site clinical research
Single IRB Evaluation

- CTTI collaboration with NIH sIRB policy workgroup
- Purpose: Develop comprehensive plan to evaluate NIH sIRB policy
- In-depth interviews from November 2018 – April 2019
  - Research administration leadership representatives from several organizations (n=13)
  - 360 case study interviews at two research institutions (n=21)
- Final report submitted to NIH in September 2019
  - Engage stakeholders implementing the sIRB model
  - Define critical time points and factors to be measured
  - Routinely collect and share established metrics to promote best practices and develop a continuous learning environment
Findings of Interviews: sIRB Benefits

Three main benefits were identified:

- Speed & Efficiency
- Streamlining & Simplification
- Consistency & Standardization
Findings of Interviews: sIRB Challenges

Four main challenges were identified:

- Local Aspects
- Timeliness
- Variability
- Communication
Findings of Interviews: Suggested Solutions

- More training on/experience with the sIRB model
  - Increase familiarity
  - Enhance trust, build relationships
    - More comfortable ceding review
  - Establishing communication plans

- More standardized policies/procedures/forms
  - SMART IRB helpful

- Increased interoperability and/or access to electronic IRB systems

- Better systems for providing/tracking local context

- Clearer criteria for what constitutes local context
CTTI sIRB Resources
Considerations Document

Addresses blurred distinctions between responsibilities for ethics review and other institutional obligations

Designates the responsibilities of:
- the Institution
- the IRB
- Either sIRB or Institution
- Both sIRB and Institution

CONSIDERATIONS TO SUPPORT COMMUNICATION BETWEEN INSTITUTIONS AND OUTSIDE IRBS WHEN RESPONSIBILITIES ARE BEING ASSIGNED FOR MULTICENTER CLINICAL TRIAL PROTOCOLS

This document outlines categories of legal and ethical responsibilities of an institution and an institutional review board (IRB) in overseeing the conduct of clinical trials. It is meant to support communication between institutions and external IRBs when responsibilities are being assigned for multicenter clinical trial protocols that are using a single IRB (sIRB) model. This document is most relevant for institutions that have the option to use their own local IRB and should be used as a starting point for decoupling institutional and IRB responsibilities.

The sIRB for a multicenter protocol is the IRB of record for the protocol. It has regulatory responsibility for assuring the protection of the rights and welfare of research participants from initial review to termination of the research, including review and approval of informed consent.

The institution is the local entity setting standards to determine whether a research investigator can conduct research under its auspices (e.g., allowing admitting privileges to a hospital, authorizing an investigator to use facilities to conduct research, determining faculty status). Clinical sites participating in a multicenter protocol may, in some instances, not be associated with an institution. In these cases, the clinical investigator or the study sponsor would assume some of the institutional responsibilities.

RESPONSIBILITIES OF BOTH THE sIRB AND THE INSTITUTION:

A. Execute an IRB Authorization Agreement:

1. Identify and define roles and timeframes for reporting to sponsors and federal and applicable state agencies serious adverse events, serious and continuing non-compliance, unanticipated problems involving risks to subjects or others, or suspension or termination of sIRB approval.

2. Clearly communicate expectations, including regulatory requirements, sharing of information between the institution and the IRB, and a process for determining potential corrective/remedial actions in the event of non-compliance.

3. Develop a communication plan for sharing information about the site, the investigators, the sponsor, and the clinical trial between the institution and the IRB.
   i. Identify the plan to evaluate investigator qualifications.
   ii. Communicate any substantive changes to the institution, its human research program, or the local research context in connection with the clinical trial to the reviewing IRB and vice versa.

4. Identify a process for responding to participant concerns and grievances, including coordination of communication to subjects.

https://www.ctti-clinicaltrials.org/projects/single-irb
Three Evaluation Checklists

Are you CONSIDERING adopting a Central IRB model for multicenter clinical trial protocols?

- Institutional Self-Evaluation
  
  General considerations for institutions deciding whether to adopt the Central IRB model

- Institution / Sponsor Evaluation of a Central IRB
  
  General considerations for institutions and sponsors when selecting a particular Central IRB

- Central IRB Evaluation of an Institution
  
  General considerations for Central IRBs when deciding whether to work with a specific institution

Central IRB=single IRB of record
IAA Template

16 template IRB agreements/waivers were reviewed to determine the kinds of clauses included and the frequency which those clauses appeared.

Common template agreement created.

Starting from scratch is not recommended, other templates available:
- SMART IRB Agreement – [https://smartirb.org/agreement/](https://smartirb.org/agreement/)
Single IRB Resource of Resources (RoR)

- Excel document to allow users to save and add their own resources to their copy
- This list is not exhaustive, nor does CTTI officially endorse the resources created by other organizations

Columns:
- Topic
- Audience
- Questions answered by resource
- Link to resource
- Description of resource

Topics include:
- Site training on use of sIRB
- Selection of sIRB
- Reliance Platforms
- Reliance Agreements
- Relying institution responsibilities
- Informed consent modifications
- Serving as the sIRB
- Metrics for sIRB review
- Communications plans for
  - Unanticipated problems involving risk
  - Adverse events
  - Post approval monitoring
### Single IRB – RoR

**Clinical Trials Transformation Initiative (CTTI) - Single IRB (sIRB) Resource of Resources Document**

**Overview:** The following is a list of educational resources, textual and graphic, to facilitate the use of a single IRB for efficient, effective, and efficient research.

**Resources:** This document highlights the benefits of single IRB, the resources available, and the alignment with various IRB policies and standards.

### Questions and Answers

<table>
<thead>
<tr>
<th>Topic</th>
<th>Audience</th>
<th>Question</th>
<th>Existing Resources</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Site Training on Use of Single IRB</strong></td>
<td>Sites, investigators, coordinators, other study staff</td>
<td>1. How will the single IRB ensure informed consent is obtained?</td>
<td>Implementation of the single IRB for sites is recommended. [CTTI Circulars: Single IRB]</td>
<td>Reduces the burden of site IRB oversight and streamlines the review process.</td>
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<td></td>
<td></td>
<td>2. What new regulatory requirements are associated with single IRB?</td>
<td>[CTTI Circulars: Single IRB]</td>
<td>Provides guidance on new regulations and requirements for sites using a single IRB.</td>
</tr>
<tr>
<td></td>
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<td>4. What are the implications for institutional review boards (IRBs)?</td>
<td>[CTTI Circulars: Single IRB]</td>
<td>Highlights the adaptation and implementation of single IRB policies and procedures.</td>
</tr>
<tr>
<td></td>
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<td>7. How do I leverage existing resources?</td>
<td>[CTTI Circulars: Single IRB]</td>
<td>Identifies existing resources that can be leveraged to support single IRB implementation.</td>
</tr>
<tr>
<td><strong>Reliability Agreements</strong></td>
<td>IRBs, institutions</td>
<td>10. What are the key elements of a reliability agreement?</td>
<td>[CTTI Circulars: Single IRB]</td>
<td>Outlines the key elements and considerations for developing a reliability agreement.</td>
</tr>
</tbody>
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### Practical Resources


**More Information:**

- [https://www.ctti-clinicaltrials.org](https://www.ctti-clinicaltrials.org)

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**Notes:**

- The resources and information provided are subject to change and updates. Please refer to the latest version on the CTTI website for the most current information.

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**References:**

- [CTTI Circulars: Single IRB]
- [Single IRB - RoR]
Engagement & sIRB Background

In a multicenter study utilizing a sIRB of record, the sIRB will be required to review the protocol on behalf of each engaged institution.

The institution engaged in research is required to:

- Certify that the research has been reviewed and approved by an IRB on the institution’s behalf
- For federally funded research – hold assurance that it will comply Common Rule (45 CFR part 46)

As sIRB review has increased the need to make engagement determinations is more common

sIRB Adoption Team developed engagement documents
- Overview, flowchart, scenarios, definitions
Engagement Flowchart & Scenarios

PURPOSE: Assist in determining if activities an institution’s employees or agents perform constitute human subjects research and thus engage the institution in that research.

EXPERTISE NEEDED: Ability to assess
- Who is performing activities,
- Where the activities are being performed, and
- The relationship of those performing activities with the institution.

LIMITATIONS: Intended only as tools
- Contact IRB office and/or research administration for determination
- Consult OHRP resources for additional information

https://www.ctti-clinicaltrials.org/projects/single-irb
Engagement Flowchart

STEP 2: Determine if institution is engaged in the research

Will the role of the institution be limited EXCLUSIVELY to permitting the use of their facilities for intervention or interaction with subjects by investigators from another institution?

Will the institution's employees/agents interact for research purposes with any human subjects for the study?

Will the institution's employees/agents intervene for research purposes with any human subjects in the study by manipulating the environment?

Will the institution's employees/agents intervene for research purposes in any of the following ways:
- Provide services or procedures, that are dictated by the protocol, and are NOT typically performed by the institution for non-research clinical or commercial purposes?
- Request, and activities merit, professional recognition or publication privileges?
- Obtain informed consent from human subjects?
- Administer study intervention begin tested or evaluated in protocol?

Will the institution's employees/agents obtain identifiable private information and/or identifiable biological specimens for research purposes?

https://www.ctti-clinicaltrials.org/projects/single-irb
Engagement Scenarios – Example

Research is conducted at different sites (separate entities) throughout one health system – which institutions are engaged?

<table>
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<tr>
<th>Hospital</th>
<th>University</th>
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<tr>
<td>Not receiving direct funding</td>
<td>Prime awardee</td>
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<tr>
<td>Research activities at hospital</td>
<td>University employees are performing all research</td>
</tr>
<tr>
<td>Hospital employees are not involved in research, have no interaction with human subjects</td>
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</tbody>
</table>

**Analysis**

**Hospital**
- Not receiving direct funding
- Research activities at hospital
- Hospital employees are not involved in research, have no interaction with human subjects

**University**
- Prime awardee
- University employees are performing all research

**Determination**

**Not engaged** –
- Role limited to use of facilities by university employees

**Engaged** –
- Receiving direct funding
- Employees interacting with subjects

https://www.ctti-clinicaltrials.org/projects/single-irb
All CTTI sIRB resources available at:

https://www.ctti-clinicaltrials.org/projects/single-irb

QUICK LINKS TO TOP DELIVERABLES

<table>
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<th>Recommendations</th>
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<th>Engagement Overview</th>
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<tr>
<td>April 27, 2015</td>
<td>January 30, 2013</td>
<td>September 03, 2019</td>
</tr>
<tr>
<td>Advancing the Use of Central IRBs for Multi-center Clinical Trials</td>
<td>Use of Central IRBs for Multi-center Clinical Trials</td>
<td>Single IRB: Determination of Institutional Engagement Overview</td>
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<tr>
<td>Single IRB Resource of Resources Document</td>
<td>Considerations Document: To address blurred distinctions between responsibilities for ethics review and other institutional obligations, sites and IRBs can use this tool to support communication and contractual relationships between institutions and a central IRB.</td>
<td>Evaluation Checklist: To assist organizations with adoption of a central IRB model for multi-center clinical trials</td>
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</tbody>
</table>

Discover Additional Deliverables Generated From This Project
THANK YOU.

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www.ctti-clinicaltrials.org