ADVARRA

FDA sIRB Mandate: Déjà Vu All Over Again?

Learning Objectives

- Describe how FDA's proposed sIRB rule differs from other existing sIRB polices/mandates
- Learn how institutions can begin assessing policies now in advance of the final rule
- Understand how institutional responsibilities overlap (and don't) with FDA sIRB responsibilities

FDA Draft Proposed Rule: Why?

21st Century Cures Act mandates the HHS and FDA harmonize regulations on human subjects protections to the extent possible

The *Common Rule* (45 CFR 46) with 21 CFR 50/56

The Evolution of the sIRB Rules

1. NIH Single IRB Policy	2. Revised Common Rule
sIRB review is required when the research is: • **Multi-site** or **cooperative** • NIH **funded** or **supported** • Can request a policy exception – rarely granted (Tribal law) • Cannot be subject to the rCR	sIRB review is required when the research is: • **Multi-site** or **cooperative** • Federally **funded** or **supported** • Can request a policy exception • Requires federal agency approval (e.g., NIH) or subject to Tribal law

Definitions:

- ***Multi-site:*** One protocol being conducted at different sites/institutions/organizations
- ***Cooperative/Collaborative:*** Involves more than one institution, not necessarily conducting the same activities in a protocol
- ***Funded:*** Grants provided for the conduct of research
- ***Supported:*** Can include use of federally funded facilities, resources, etc.

The Evolution of the sIRB Rules

3. FDA NPRM (Proposed Rule)

sIRB review is required when the research is:

- **Multi-site** or **cooperative**
- A **clinical investigation** (as defined by the FDA)
- Policy exceptions but not by request:
  - Tribal law (or other law)
  - Highly-specialized FDA regulated product
  - IND exempt research
  - IDE exempt or abbreviated requirements

Definitions:

- ***Multi-site:*** One protocol being conducted at different sites/institutions/organizations
- ***Cooperative/Collaborative:*** Involves more than one institution, not necessarily conducting the same activities in a protocol
- ***Clinical Investigation:*** *§56.102(c) clinical investigation means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA…or need not meet [those] requirements, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit

Timeline

HHS/FDA **RIN:** 0910-AI08 **Publication ID:** Fall 2024

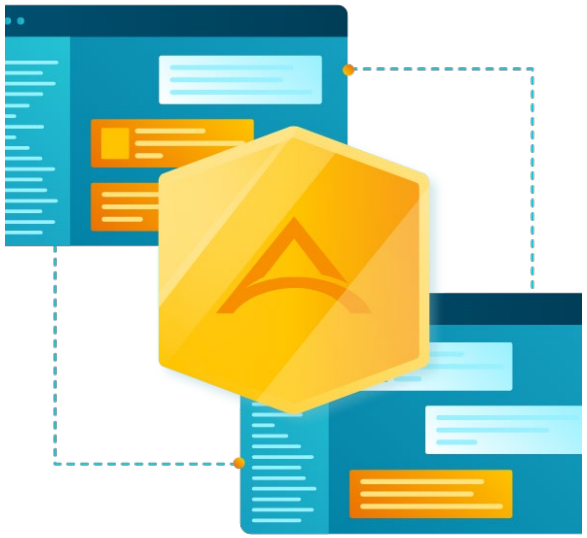
Title: Institutional Review Boards; Cooperative Research

Abstract:

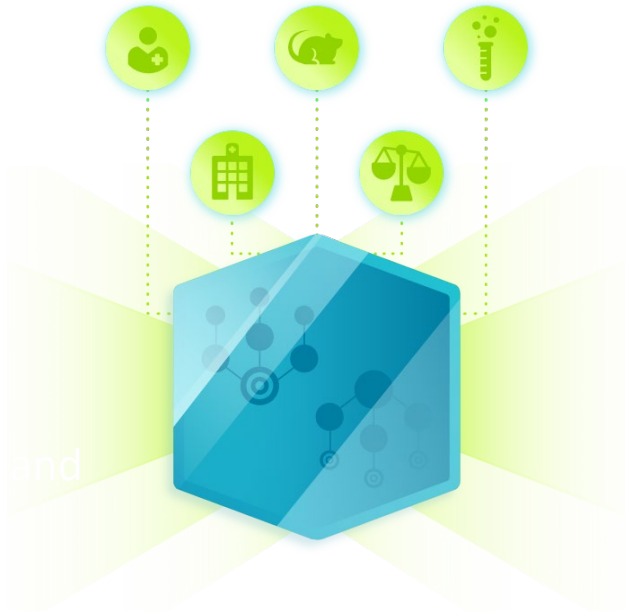
This rule will replace current FDA requirements for cooperative research such that any institution located in the United States (U.S.) participating in multisite cooperative research will need to rely on approval by a single Institutional Review Board (IRB) for that portion of the research that is conducted in the U.S., with some exceptions. This rule will also establish an IRB recordkeeping requirement for research that takes place at an institution in which IRB oversight is conducted by an IRB that is not operated by the institution.

Timetable:

Action	Date	FR Cite
NPRM	09/28/2022	87 FR 58752
NPRM Comment Period End	11/28/2022	
NPRM Comment Period Extended	11/14/2022	87 FR 68118
NPRM Comment Period Extended End	12/28/2022	
Final Rule	01/00/2026	



One protocol at more than one institution/site



Can involve different activities at each site

Is a clinical investigation

FDA: Clinical Investigation

- Experiment
- Test article *any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act…*
- One or more subjects
- Intent *to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit [excludes nonclinical lab studies]…*
- The terms *research, clinical research, clinical study, study,* and *clinical investigation* are deemed to be synonymous for purposes of this part

FDA Regulated That is NOT a Clinical Investigation

Studies involving (approved and/or investigational):

- Foods, drugs, biologics
- Medical devices
- Electronics: radiation emitting
- Cosmetics
- Veterinary products
- Tobacco products

Exceptions – studies involving:

- Products used as labeled, and
- No intent to change labeling, and
- No intent to change how it is given or used, and
- No intent to advertise about the product, and
- Products not part of a protocol

Possible Exceptions from FDA sIRB

- Research involving highly specialized FDA-regulated medical products requiring unique, localized expertise.
- Clinical investigations with drugs and biologics that do not require an Investigational New Drug (IND) application.
- Clinical investigations of medical devices that do not require an Investigational Device Exemption (IDE).

Concerns with FDA sIRB Mandate

- Selection of the IRB of Record under FDA
- Inadequate IRB Experience with Device Trials or Expanded Access
- Limited Resources for Oversight, Training, and Compliance
- Poor sIRB processes will be propagated across more studies
- Limited FDA involvement in mandate processes

Assessing Readiness for FDA Mandate

Aren’t we already prepared after working in sIRB for years?

Because FDA mandate is different, institutions should comprehensively look at their existing:

- Policies
- Procedures
- Tools and templates
- Education
- Staffing

Assessing Readiness: Policies

Example statements from institutional websites:

"NIH policy, the Common Rule, and certain sponsors require that multi-site and collaborative research use a sIRB model…"

"The [institution] IRB adheres to the NIH policy on the use of a single institutional review board for multi-site research. As such, the [institution] IRB may be a reviewing SIRB for domestic sites of NIH-funded multi-site studies …"

Assessing Readiness: Policies

Consider:

- Does your policy define when you will rely or serve as sIRB based upon sIRB mandates?
- Will your IRB need to consider any unique policy requirements for FDA mandate (e.g., Requiring IND Exempt determination from FDA rather than from Sponsor-Investigator)?
- Does your policy define what is FDA-regulated?

Assessing Readiness: Procedures

Example statements from institutional websites:

"The [institution] IRB does not routinely enter into reliance arrangements with independent/commercial IRBs. If you anticipate that your study will be reviewed by an independent IRB, contact …"

"[institution] is willing to rely on an external IRB when federally mandated, required by sponsors, or on a case-by-case basis."

Assessing Readiness: Procedures

Consider:

- How are you reviewing and approving reliance requests (whether to serve or defer IRB review) and does this work with an FDA mandate?
- What sorts of “child” submissions do you require for studies ceded to an external IRB?
- Is your office staffed appropriately/do you have reports to tell you when a change is necessary?

Assessing Readiness: Tools and Templates

Example tools and templates:

- Understanding local context when using sIRB
- Informed consent boilerplate language template
- Reliance agreement templates (IAAs, IIAs, MRAs, CRAs)
- Fee schedules

Assessing Readiness: Tools and Templates

Consider:

- Reliance is hard for everybody, not just the IRB/HRPP office
- Tools/templates help the IRB/HRPP office process sIRB studies but can also help lessen the burden the study teams feel
- Research teams can find it difficult talking with you (their internal IRB/HRPP); imagine what it's like if they have relationships with multiple IRBs across many studies?

Assessing Readiness: Education

Reasons for education:

- Why am I required to submit for two IRB reviews?
- What do I need to report and whom do I report it to?
- I thought this was supposed to lessen work?

Assessing Readiness: Education

Tips for education:

- FAQs are super helpful
- When reliance is and isn’t appropriate
- Talk about it often

Assessing Readiness: Staffing

Consider:

- What portion of your portfolio will be under a sIRB mandate?
- What if industry stops deferring sIRB decision to local PIs or institutions (in advance of a FDA mandate)?
- What is the required staffing levels for reliance studies?
- Theory of conservation of burden*

*Not a real theory

Assessing Readiness: Staffing

Consider:

- How can IRB staff be transitioned into broader HRPP roles to support changing research landscape?

Questions?

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