SMART TALK

A Community Forum to Explore Issues Surrounding Single IRB Review

Funded by the NIH National Center for Advancing Translational Sciences through its Clinical and Translational Science Awards Program, grant number 3UL1TR002541-04S2.

What Is SMART Talk?

An approximately monthly forum with:

- Presentations on topics relevant for single IRB review
- Q&A on topic presented as well as questions submitted when participants register

Open and free to anyone with interest

Upcoming sessions

February 8 & 10, 2022: *Single IRB Boot Camp: A How-To-Guide with SMART IRB*

March: TBD (likely about researchers' experience with SIRB)

FYIs

Please provide feedback by completing the survey – a link will be posted in chat and emailed.

A recording of this talk will be posted on the SMART IRB website

A link to the talk will be sent to those who registered for the talk when it is posted

If you have any questions for the panelists, please use the chat function or Q&A function to submit them

SMART IRB Updates

Harmonization Steering Committee Recommendations
https://smartirb.org/harmonization/

- Ancillary Review
- Conflict of Interest
- Post-Approval Auditing for Studies Subject to Single IRB Review
- Single IRB Continuing Review Process
- Single IRB Review: Responsibilities Associated with the Review of Study Personnel
- Reportable Events
- Institutional Profile
- Protocol-specific Document
- Fees and Costing Models under NIH sIRB Policy
- Institution v. IRB Responsibilities Guidance

A Conversation with NIH and OHRP about Single IRB

Adam Berger, Director, Division of Clinical and Healthcare Research Policy, Office of Science Policy, Office of the Director, National Institutes of Health

Natalie Klein, Director, Division of Policy and Assurances, DHHS Office for Human Research Protections

Moderator: Nichelle Cobb

SMARTIRB.org

National Institutes of Health
Office of Science Policy

NIH Single IRB Policy Overview

Adam C. Berger, PhD
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Office of Science Policy
National Institutes of Health

SMART Talk

01/19/2022

Overview

- Background
- Overview of NIH SIRB Policy Requirements
- SIRB Policy Guidance
- Additional Resources

Background

Origin of Single IRB Review

- Reliance on single Institutional Review Boards (IRBs) in multisite (or “cooperative”) research is not new
- FDA encouraged the reduction in duplicative review as early as 1979[1], codified in guidance in 2006[3]
- Following a 1997 recommendation for greater streamlining, NCI established the NCI Central IRB in 2001; pediatric CIRB in 2004[2]
- OHRP issued guidance in 2010[4]
- By 2015, nearly half of NIH-funded studies were multi-site

1. https://www.govinfo.gov/content/pkg/FR-1979-08-14/pdf/FR-1979-08-14.pdf (pages 47700, 47704)
2. https://www.ncicirb.org/about-cirb/history
3. https://www.fda.gov/regulatoryinformation/guidances/ucm127004.htm
4. https://www.hhs.gov/ohrp/regulations-and-policy/guidance/use-of-a-centralized-irb/index.html

Development of the NIH Single IRB Policy

- Draft NIH Single IRB Policy published in December 2014
  - 167 public comments received from a range of stakeholders including researchers, institutions, IRBs, patient advocates, scientific societies, Tribal Nation representatives, and others
- Final NIH Single IRB Policy published June 2016; effective date delayed until January 25, 2018
  - Applies to all competing grant applications for due dates on or after January 25, 2018
  - Applies to all R&D contract solicitations issued on or after January 25, 2018
  - Applies to intramural research studies submitted for initial review after January 25, 2018

Overview of NIH Single IRB Policy Requirements

Scope and Applicability (1/2)

- Applies to domestic sites of NIH-funded multi-site studies where each site conducts the same protocol involving non-exempt human subjects research

Scope and Applicability (2/2)

- **Multi-site research**: two or more sites
- **Same protocol**: protocols that address the same research questions, involve the same methodologies, and evaluate the same outcomes. Includes:
  - Sites accruing research participants for studies that are identical except for variations due to local context consideration
  - Sites that are conducting only part of the “same protocol”
- If NIH funds even one site in an applicable multi-site study, NIH expects all other sites using the same protocol will rely on a single IRB

NIH Single IRB Exceptions (1/3)

- Certain activities are explicitly excluded:
  - Sites in multi-site studies performing different functions and using different protocols
  - Foreign sites within multi-site studies
  - Career development (K awards), institutional training (T awards), fellowship awards (F)
  - When prohibited by federal, state, or tribal law, regulation, or policy

NIH Single IRB Exceptions (2/3)

- Ongoing, non-competing awards will not be expected to follow the policy until the grantee submits a competing renewal application after the effective date (January 2018)
- Ancillary studies to other ongoing studies will not be expected to comply until the parent study is expected to comply
- Ongoing large cooperative groups or networks with studies that will be determined at a later date are treated as any other ongoing award

NIH Single IRB Exceptions (3/3)

- Other exceptions will be considered by request
  - Must provide sufficient information which demonstrates a compelling justification for an exception to the NIH Single IRB policy
  - Temporarily and on a case-by-case basis, granting a concomitant exception to the NIH single IRB policy when NIH determines that a study has met the criteria established by OHRP for an exception to the Common Rule single IRB requirement during the COVID-19 public health emergency[5,6]

5. https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-006.html
6. https://www.hhs.gov/ohrp/regulations-and-policy/single-irb-exception-determinations/october-2020-exception-determination/index.html

Additional Consideration

- NIH will accept determinations by the VA or the DOD that the use of a single IRB is not appropriate for specified VA or DOD site(s) participating in NIH-funded multisite studies
  - A special exception request issued by NIH is not necessary. All remaining sites in NIH-funded multisite studies are expected to comply with the single IRB requirement unless they have received an exception issued by NIH or HHS.

Responsibilities (1/2)

- Applicants/offerors:
  - ~~Submit a plan describing use of an SIRB in application/proposal for research funding~~
- Awardees:
  - Ensure authorization agreements are in place and that a mechanism for communication between SIRB and relying sites is established

No More! Providing the name at just-in-time fulfills requirement if using FORMS-F or later[7]

7. https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-174.html

Responsibilities (2/2)

- SIRB:
  - Responsible for conducting ethical review of relying sites per 45 CFR 46
  - May also serve as a HIPAA privacy board if appropriate
- Participating sites:
  - Rely on the SIRB to carry out functions required for institutional compliance with IRB review per 45 CFR 46
  - Responsible for other requirements such as obtaining informed consent, implementing protocol, reporting unanticipated problems
  - Must communicate information necessary for the SIRB to consider local context issues and state/local regulatory requirements

SIRB Policy Guidance

Models for Single IRB Review

- Several models can satisfy the requirements of the Single IRB Policy, for example:
  1. An existing IRB at an awardee or participating site can agree to serve as the Single IRB of record
  2. An independent or unaffiliated IRB can serve as the Single IRB of record
  3. A Central IRB organized to review specific projects (e.g., the NCI CIRB) can serve as the Single IRB of record

Choosing a Single IRB

- FOA or solicitation may describe any specific requirements to meet the policy (such as intent to set up a Central IRB for the project)
- Participating sites should work together ahead of time to determine the best IRB for the study
- Reliance agreements should be in place and up to date
- May include working with local IRBs to determine the best IRB, gather relevant local context and policies
- The Single IRB must be registered with OHRP and must have membership to adequately review the proposed study

Additional Resources

Additional NIH Guidance

- Policy: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html
- FAQs: https://grants.nih.gov/faqs#/hs-single-IRB-policy-for-multi-site-research.htm
- Guidance on implementation: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-004.html
- Guidance on exceptions : https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-003.html
- Guidance and scenarios on charging SIRB costs as direct vs indirect: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-109.html
- Additional Guidance on NIH Policy (reminder re: Common Rule compliance): https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-058.html
- Exceptions to use of Single IRB during COVID public health emergency: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-006.html
- Guidance on Single IRB plan requirement: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-174.html
- For general Single IRB questions: SingleIRBpolicy@mail.nih.gov

Thank You!

SMART Talk

A Conversation with NIH and OHRP about Single IRB

Natalie M. Klein, PhD, CIP

OASH | Office for Human Research Protections

Disclaimer

- The opinions expressed are those of the presenter and do not necessarily reflect the policy of the U.S. Department of Health and Human Services.

Also…

- This focuses on HHS supported and conducted research under 45 CFR 46
- For research supported or conducted by other Common Rule departments and agencies, seek guidance from appropriate representatives

45 CFR 46.114 Cooperative research

(a) Cooperative research projects are those projects covered by this policy that involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy.

(b)

(1) Any institution located in the United States that is engaged in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States. The reviewing IRB will be identified by the Federal department or agency supporting or conducting the research or proposed by the lead institution subject to the acceptance of the Federal department or agency supporting the research.

(2) The following research is not subject to this provision:

(i) Cooperative research for which more than single IRB review is required by law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe); or

(ii) Research for which any Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular context.

(c) For research not subject to paragraph (b) of this section, an institution participating in a cooperative project may enter into a joint review arrangement, rely on the review of another IRB, or make similar arrangements for avoiding duplication of effort.

What is Cooperative Research in 45 CFR 46.114?

- Nonexempt human subjects research
- Involves more than one institution
  - The cooperating institutions need not be performing the same activities in the research to be subject to the single IRB (sIRB) requirement
  - For example, one institution could be obtaining informed consent and another could be performing research interventions

When must an institution rely on a single IRB?

- The institution is engaged in cooperative research subject to the 2018 Common Rule
- The institution is located in the U.S.
- The sIRB approval is for the portion of the study taking place in the U.S.
- *Except when 45 CFR 46.114(b)(2) applies*

What about institutions that “check the box”?

- If the research is not supported by a Common Rule department or agency, OHRP does not require institutions to comply with the sIRB requirement because they have “checked the box” on their Federalwide Assurance

(a) This Assurance applies whenever this Institution becomes engaged in human subjects research conducted or supported by any U.S. federal department or agency that has adopted the U.S. Federal Policy for the Protection of Human Subjects (also known as the Common Rule), unless the research is otherwise exempt from the requirements of the Common Rule or the department or agency conducting or supporting the research determines that the research shall be conducted under a separate assurance.

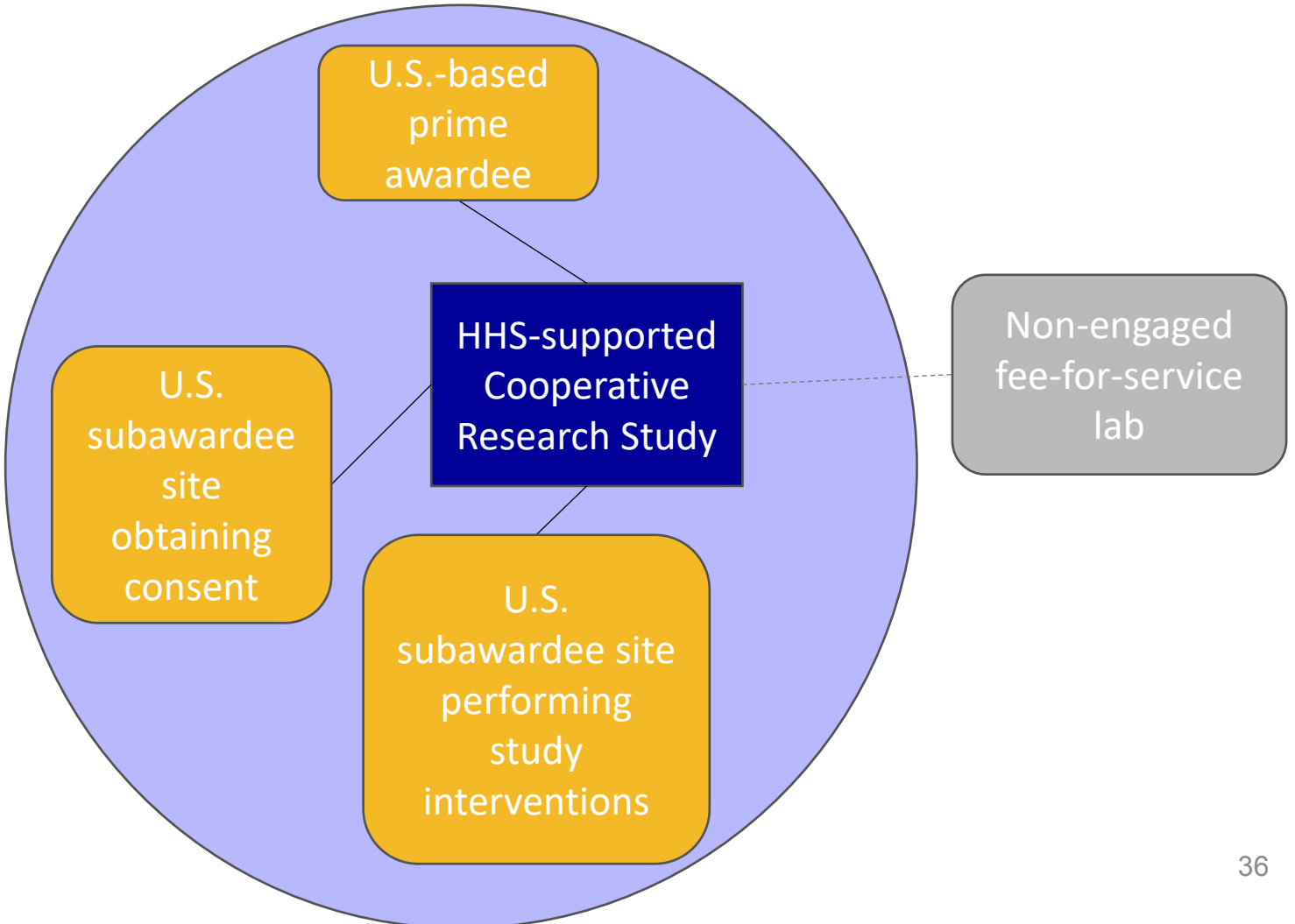
(b) *Optional for U.S. institutions:* This Institution voluntarily elects to apply the following to all of its non-exempt human subjects research regardless of the source of support, except for research that is covered by a separate assurance issued by another U.S. federal department or agency that has adopted the Common Rule:

- ☐ **The Common Rule** *(see section 3 of the Terms of the FWA for a list of U.S. federal departments and agencies that have adopted the Common Rule and the applicable citations to the Code of Federal Regulations)*
- ☐ **The Common Rule and subparts B, C, and D of the HHS regulations at 45 CFR part 46**

What about institutions that are not “engaged”?

- If an institution is not engaged (per OHRP’s guidance), the institution’s activities are not subject to the 45 CFR 46
- While the protocol may describe this institution’s role in the research, the institution need not obtain IRB approval or “rely” on the sIRB for oversight

Example


U.S.-based prime awardee
HHS-supported Cooperative Research Study
U.S. subawardee site obtaining consent
U.S. subawardee site performing study interventions
Non-engaged fee-for-service lab

What about limited IRB review of exempt research?

- Exempt research is not subject to the requirements at 45 CFR 46.114
- Institutions conducting cooperative, exempt research requiring limited IRB review do not need to rely on a sIRB
- Permitted but optional for limited IRB review
- When opting for sIRB for limited IRB review, the reliance documentation requirements in 45 CFR 46.103(e) apply

Can an institution relying on a sIRB also conduct local IRB review?

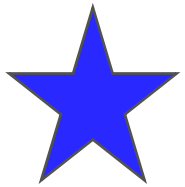
- Yes – although the local IRB review would not have regulatory status for compliance with the 2018 Common Rule
- If the local IRB conducts an extra-regulatory review, OHRP recommends the results of the review be provided to the sIRB of record

Who chooses the sIRB for a particular study?

- The federal department or agency supporting or conducting the research selects the IRB that will serve in this capacity

OR

- The lead institution proposes the sIRB, and this is subject to the acceptance of the Federal department or agency supporting the research



What capabilities might the sIRB need to have?

- Means to track the status of research at multiple sites
- Tools to manage multiple consent forms and versions of consent forms from different sites
- Method to communicate notifications of IRB actions to an individual site or across all sites as needed
- Ability to store site-specific information (e.g., approval documentation, informed consent documents and other study-specific materials)
- Knowledge to apply relevant State and local law
- Method to make written IRB procedures available to relying institutions
- Capability to monitor and/or audit research at the relying sites
- *Not an exhaustive list, and not all items may apply in all scenarios*

What about sIRB and local context? (1 of 2)

- In general, the relying institution should provide information on local context to the sIRB
- If local contextual information is necessary to support determinations for approval under 45 CFR 46.111, the reviewing IRB must have access to such information
- For example, .111(a)(3) – subject selection is equitable considering "the purposes of the research and the setting in which the research will be conducted"

What about sIRB and local context? (2 of 2)

- The sIRB membership must meet requirements at 45 CFR 46.107(a)
  - Sufficiently qualified through the experience and expertise of its members (professional competence), and the diversity of its members, including race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes
  - Able to ascertain the acceptability of proposed research in terms of institutional commitments (including policies and resources) and regulations, applicable law, and standards of professional conduct and practice
  - For IRBs that regularly review research involving vulnerable populations, should consider including one or members knowledgeable about and experienced in working with these categories of subjects

What are the exceptions in 45 CFR 46.114(b)(2)?

- The law requires more than single IRB review
  - This can include Tribal law
- Any federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular context
  - OHRP has the authority to do this for HHS
  - When multiple federal departments/agencies are supporting or conducting, any of them can make this determination for the study
  - The exception would generally apply to those institutions under the jurisdiction of the department/agency making the determination

Resources

- "Single IRB Review" link to OHRP's categorical exception determinations under 45 CFR 46.114(b)(2)(ii)
- OHRP's guidance and educational material on engagement
  - Mini-tutorial (video) on engagement
  - Engagement guidance
  - Additional non-engaged scenarios
  - Correspondence on survey firms, FWAs, and engagement

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Thank you!

For more information, please contact OHRP@hhs.gov

Discussion & questions

Save the date for the next
SMART Talk
March 16, 2022
2:00-3:30 pm ET

TBD

Questions?
Contact
help@smartirb.org

Register at
smartirb.org

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