SMART IRB

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

December: No SMART Talk → PRIM&R Annual Conference

January 2023: Everything You Wanted to Know About Single IRB but Were Afraid to Ask, Part Deux

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 Learning Center and Resources

- Learning Center for Investigators and Study Teams, including Start Up Packages: https://smartirb.org/study-teams/
- Learning Center for IRB and HRPP Administrators, including Start Up Packages: https://smartirb.org/irb-admin/
- List of Resources, which can be filtered by topic or Role: https://smartirb.org/resources/

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

In progress:
Local considerations recommendations

Single IRB and Noncompliance - A Case Study

Panelists:

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

Ann Meeker-O'Connell, Director, Office of Clinical Policy, Office of Clinical Policy and Programs, Office of the Commissioner, US Food and Drug Administration

Moderator: Nichelle Cobb, Senior Advisor for SMART IRB and Senior Advisor for Strategic Initiatives for the Association for the Accreditation of Human Research Protection Programs (AAHRPP)

A Conversation with the FDA and OHRP about Single IRB

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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, or FDA-regulated research, 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.

Outline

- Review OHRP's published draft guidance on the Common Rule's single IRB requirement.
- Summarize the Secretary's Advisory Committee on Human Research Protections (SACHRP) recommendations for OHRP's draft guidance.
- Highlight public comments on OHRP's draft guidance.
- Share additional resources and references.

OHRP's Draft Guidance on Use of a Single Institutional Review Board for Cooperative Research

Summary and discussion

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Draft Guidance and Next Steps

- OHRP published draft guidance in July for public comment.
- We are reviewing public comments along with SACHRP recommendations.
- See more online:
  - **Draft guidance:** https://www.hhs.gov/ohrp/regulations-and-policy/requests-for-comments/draft-guidance-use-single-institutional-review-board-for-cooperative-research/index.html
  - **SACHRP recommendations:** https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-a-july-25-2022-letter/index.html
  - **Public comments:** https://www.regulations.gov/search/comment?filter=HHS-OASH-2022-0011

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What is Cooperative Research?

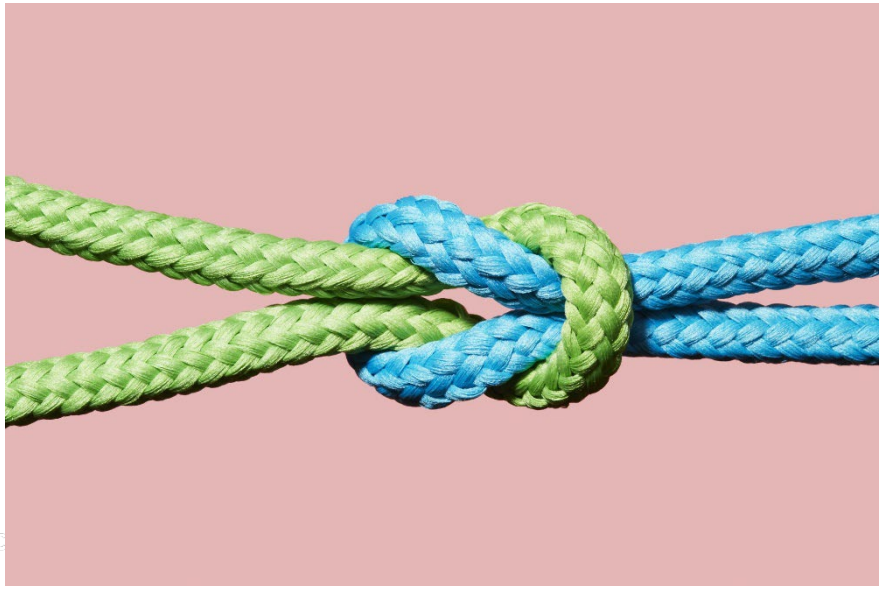
- HHS-supported or conducted
- Nonexempt human subjects research
- Involves more than one institution
  - The cooperating institutions *need not* be performing the same activities in the research to be subject to the single IRB (sIRB) requirement.
  - For example, one institution could be obtaining informed consent and another could be performing research interventions.
  - If an institution is *not* engaged (per OHRP's guidance), the institution's activities are *not* subject to 45 CFR 46.

When must an institution rely on a single IRB for approval of cooperative research?

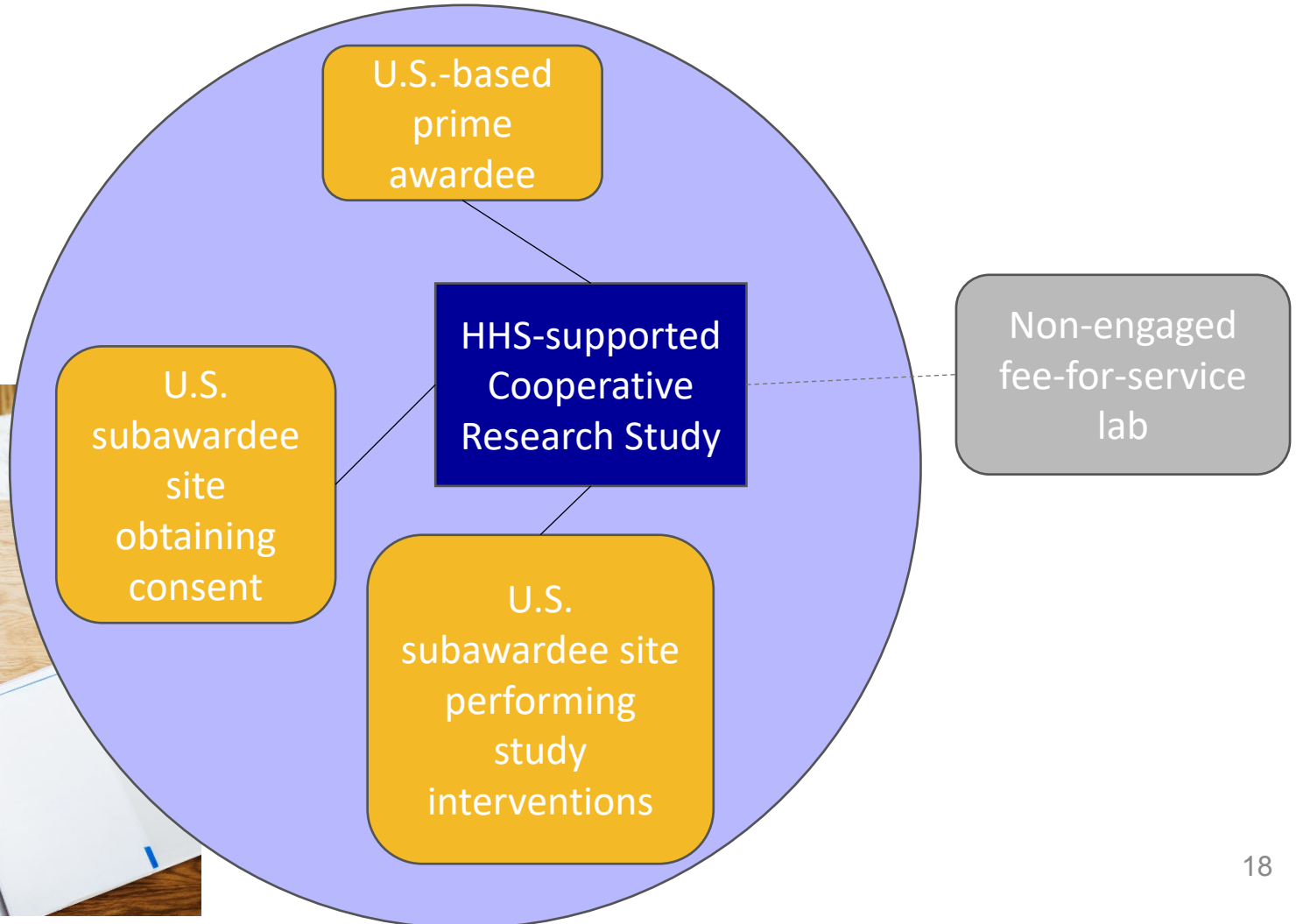
- The institution is engaged in HHS-supported or conducted nonexempt cooperative research subject to the 2018 Common Rule.
- The institution is located in the U.S.
- The sIRB approval is for the portion of the study taking place in the U.S.
- …Unless an exception under 45 CFR 46.114(b)(2) applies.

More about institutions that are not “engaged”

- If an institution is not engaged in the human subjects research (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.



More about institutions that are not "engaged"



More about exempt research

- Exempt research is not subject to the requirements at 45 CFR 46.114.
- To be exempt, research cannot involve any nonexempt activities.
- Research that involves both exempt and nonexempt activities **is not exempt**.
- The same is true for cooperative research.

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More about exempt research

- 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.

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More 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**

More about institutions that “check the box”

- This is because .114 refers to the role that the federal department or agency supporting or conducting the research plays in determining the reviewing IRB.

More about the exceptions in 45 CFR 46.114(b)(2)

- The law requires more than single IRB review:
  - This includes 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:
  - When multiple federal departments/agencies are supporting or conducting, any of them can make this determination for the study.
  - A department/agency's exception would apply to those institutions under the jurisdiction of the department/agency making the determination.

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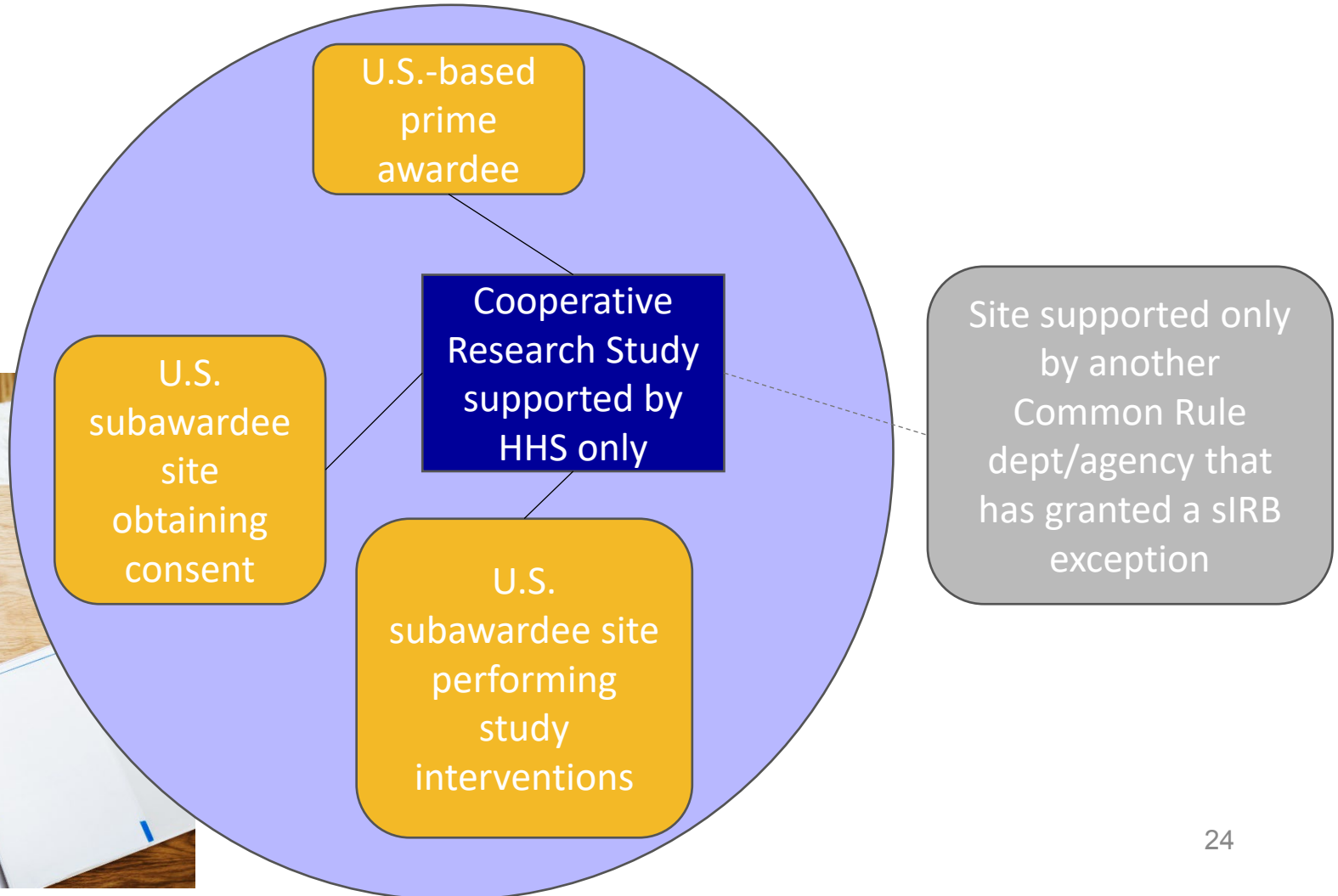
More about the exceptions when multiple Common Rule departments or agencies support the research



More about the exceptions in 45 CFR 46.114(b)(2)

- OHRP currently provides exception determinations for classes of research as opposed to single studies.
- Most recent exception: research impacted by the COVID-19 Public Health Emergency – requires that the *HHS funding agency concurs with the use of the exception.*
- All OHRP exceptions under .114(b)(2)(ii) can be found online:

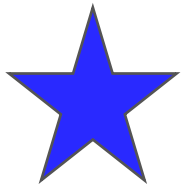
  https://www.hhs.gov/ohrp/regulations-and-policy/single-irb-exception-determinations/index.html

Who decides which IRB will be the sIRB for purposes of regulatory compliance?

- 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.



- In HHS, the particular funding agency plays this role. When multiple departments/agencies are involved, they should collaborate.

Can an institution that is not required to comply with .114 for a particular study still choose to rely on a sIRB?

- Yes - the Common Rule does not prohibit this.
- Institutions eligible for an exception made under .114(b)(2) are not required to use the exception.

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

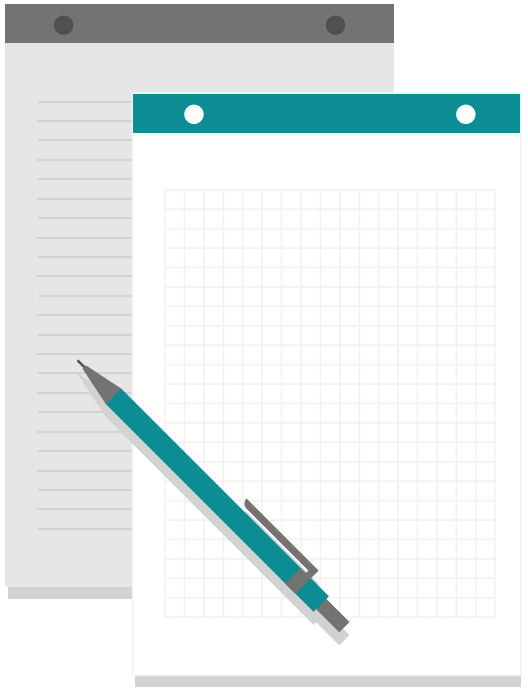
- Yes – although the local IRB review would *not have regulatory status* for compliance with the 2018 Common Rule.
- If the local IRB conducts an extra-regulatory review, OHRP recommends the results of the review be provided to the sIRB of record.
- Draft guidance largely echoes the preamble for the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

Are there documentation requirements for use of a sIRB?

- Yes – per 45 CFR 46.103(e), must document institution's reliance on the IRB and describe roles and responsibilities of each entity.
- 2018 Requirements allow flexibility in how this is achieved:
  - Reliance agreement
  - Institutional policy
  - Protocol

Are there documentation requirements for use of a sIRB?

- Documentation of reliance may cover one study, multiple studies, or all studies within specified parameters.
- Documentation might address, for example:
  - Responsibilities for event-reporting requirements
  - Monitoring and auditing
  - Reviewing/managing investigator qualifications and conflicts of interest
  - Maintaining and providing access to records



What operational capacities should the sIRB have?

- Track the status of research at multiple institutions
- Manage multiple consent forms and versions of consent forms from different institutions
- Communicate notifications of IRB actions to an individual institution or across all institutions as needed
- Store institution-specific information (e.g., approval documentation, informed consent documents approved by the IRB, and other study-specific materials)
- Access and apply relevant State and local law
- Maintain written IRB procedures that are available to relying institutions
- Monitor and/or audit research at the relying institutions
- *Not an exhaustive list*

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What are sIRB responsibilities re: sensitivity to community attitudes and the local context?

- "Local context" generally refers to local circumstances, preferences, and variability:
  - Culture and language
  - Geography
  - Socioeconomic factors
  - The professionals conducting the research
  - The institutions where the research will be conducted
  - Local standards of care
- Local context may be provided by the sIRB itself, e.g. via members with knowledge and expertise.
- 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.
- No requirement to have info not needed to support IRB's determinations.

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More about sIRB and local context

- The sIRB membership must meet requirements at 45 CFR 46.107(a) – emphasis added:
  - 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**
- The sIRB must have information required to make determinations in 45 CFR 46.111
  - 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"

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What are sIRB responsibilities re: state and local law?

- The sIRB membership must meet requirements at 45 CFR 46.107(a) – emphasis added:
  - 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
- This is not new in the 2018 Requirements – but communication and coordination might be.
- Flexibility in how sIRBs access the relevant information.
- If information on a particular state or local law is necessary to support determinations for approval under 45 CFR 46.111, the reviewing IRB must have access to such information.
- No requirement to have info not needed to support IRB's determinations.

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SACHRP Recommendations and Public Comments

A brief summary

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SACHRP Recommendations

- In July, the Secretary's Advisory Committee on Human Research Protections issued recommendations about OHRP's draft guidance.
- https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-a-july-25-2022-letter/index.html

SACHRP Recommendations

- The guidance needs more information on certain topics:
  - Local Context – how sIRBs should consider this information and what sIRBs should do when local context differs greatly among relying sites
  - State/local laws – responsibility for identifying relevant laws and need for a database of these laws
  - Responsibilities and authorities of reviewing and relying institutions re: compliance oversight
  - Applicability of the requirement to unfunded collaborators
- The guidance should discourage “shadow” reviews by local IRBs at relying institutions and should explicitly distinguish IRB from HRPP roles.
- The guidance should include criteria for additional exceptions from the sIRB requirement.

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Public Comments

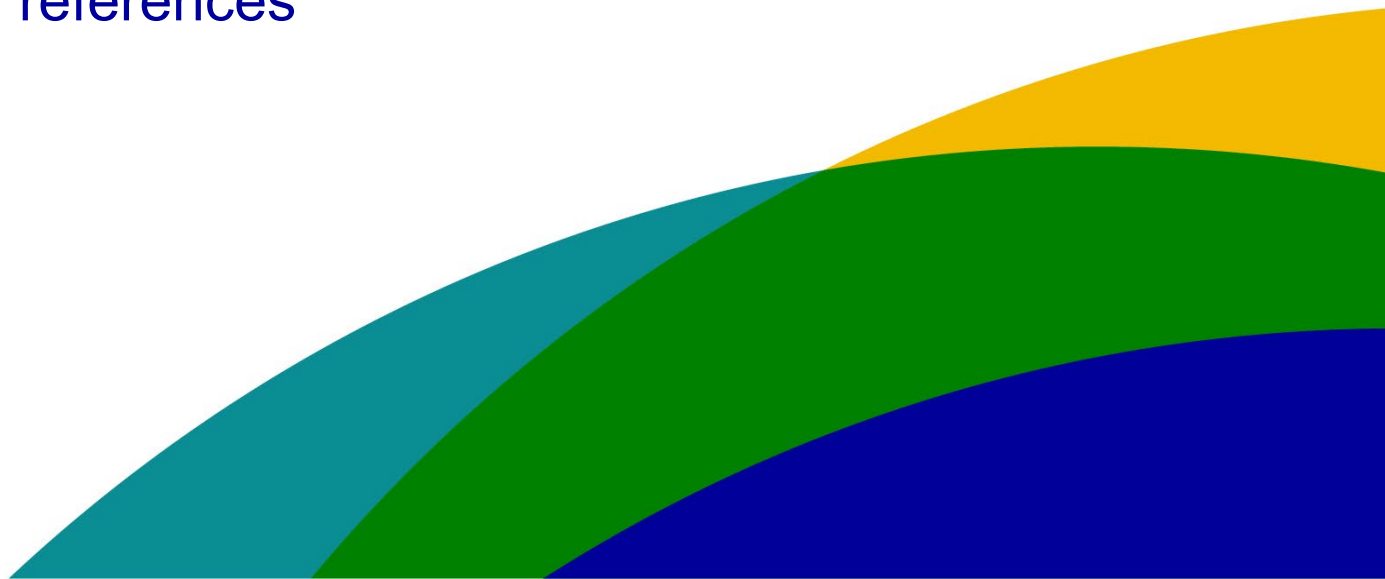
- OHRP solicited public comments during a 60-day window after publishing the draft guidance
- https://www.regulations.gov/search/comment?filter=HHS-OASH-2022-0011
- THANK YOU to individuals and institutions who responded!

Public Comments

- 16 public comments (1 was withdrawn)
- Some overlap with SACHRP in requesting:
  - Additional clarity on responsibilities for addressing local/state laws and a state law compilation
  - Additional guidance on local context
  - More prescriptive input on reliance procedures and responsibilities of involved parties
  - Caution regarding “shadow” reviews by the local IRB
- Reflected ongoing challenges at the operational level:
  - Communicating and coordinating
  - Resolving disputes
- Some comments raised questions about applicability of the requirement, and engagement and exempt determinations in the context of sIRB.
- Several comments described an ongoing need for discussion forums, tools, resources, and studies of effectiveness.
- Several comments reflected desire for harmonization.

Additional Materials

OHRP resources and recent scholarly references



Additional OHRP Resources

- Exploratory Workshop on sIRB: https://www.hhs.gov/ohrp/education-and-outreach/exploratory-workshop/2020-workshop/index.html
- OHRP's guidance and educational material on engagement/;
  - Mini-tutorial (video) on engagement: https://youtu.be/7gmRz0dNUmI
  - Engagement guidance: https://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-engagement-of-institutions/index.html
  - Additional non-engaged scenarios: https://www.hhs.gov/ohrp/regulations-and-policy/guidance/september-22-2011-non-engaged-scenarios/index.html
  - Correspondence on survey firms, FWAs, and engagement: https://www.hhs.gov/ohrp/regulations-and-policy/guidance/determining-when-institutions-are-engaged-in-research/index.html
- OHRP's human subject regulation decision charts: https://www.hhs.gov/ohrp/regulations-and-policy/decision-charts/index.html

Recent Scholarly References

- Burr, J. S., Johnson, A., Risenmay, A., Bisping, S., Serdoz, E. S., Coleman, W., Sward, K. A., Rothwell, E., & Dean, J. M. (2022). Demonstration Project: Transitioning a Research Network to New Single IRB Platforms. *Ethics & human research, 44(6)*, 32–38. https://doi.org/10.1002/eahr.500149
- Corneli, A., Dombeck, C. B., McKenna, K., & Calvert, S. B. (2021). Stakeholder Experiences with the Single IRB Review Process and Recommendations for Food and Drug Administration Guidance. *Ethics & human research, 43(3)*, 26–36. https://doi.org/10.1002/eahr.500092
- Johnson, A., Kasimatis Singleton, M., Ozier, J., Serdoz, E., Beadles, J., Maddox-Regis, J., . . . Bernard, G. (2022). Key lessons and strategies for implementing single IRB review in the Trial Innovation Network. *Journal of Clinical and Translational Science, 6(1)*, E53. doi:10.1017/cts.2022.391
- Johnson, A. R., Rigtrup, L. M., VanBuren, J., Rothwell, E., & Dean, J. M. (2021). An Approach to Reviewing Local Context for Exception from Informed Consent Trials Using a Single IRB. *Ethics & human research, 43(6)*, 42–48. https://doi.org/10.1002/eahr.500109
- Klitzman, R., Appelbaum, P. S., Murray, A., Pivovarova, E., Stiles, D. F., & Lidz, C. W. (2020). When IRBs Say No to Participating in Research about Single IRBs. *Ethics & human research, 42(1)*, 36–40. https://doi.org/10.1002/eahr.500041
- Murray, A., Pivovarova, E., Klitzman, R., Stiles, D. F., Appelbaum, P., & Lidz, C. W. (2020). Reducing the single IRB burden: streamlining electronic IRB systems. *AJOB empirical bioethics, 12(1)*, 33-40.
- Serdoz, E. S., Edwards, T., Pulley, J., Beadles, J., Ozier, J., Harris, P., ... & Rice, T. W. (2022). The IRB Reliance Exchange (IREx): A national web-based platform for operationalizing single IRB review. *Journal of Clinical and Translational Science, 6(1)*.

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Thank you!

For more information, please contact OHRP@hhs.gov

U.S. FOOD & DRUG ADMINISTRATION

Proposed Rules:
Institutional Review Boards; Cooperative Research
and
Protection of Human Subjects and Institutional Review Boards

16 November 2022

Ann Meeker-O'Connell

Director, Office of Clinical Policy

Disclaimer

The views and opinions presented here represent those of the speaker and should not be considered to represent advice or guidance on behalf of the U.S. Food and Drug Administration

21st Century Cures Act Section 3023

- Directs the Secretary of HHS to harmonize, to the extent practicable and consistent with other statutory provisions, the differences between HHS's human subject regulations and FDA's human subject regulations
- Specifically addresses single IRB review of cooperative research

FDA Rulemaking

- Series of three rules prioritizing revised Common Rule provisions
- 2018 proposed rule that, when finalized, would permit IRBs to waive or alter informed consent for certain minimal risk clinical investigations
- The other two proposed rules published September 28, 2022:
  - Institutional Review Boards; Cooperative Research
  - Protection of Human Subjects and Institutional Review Boards

PROTECTION OF HUMAN SUBJECTS AND INSTITUTIONAL REVIEW BOARDS

PROPOSED RULE

Summary Tables of Proposed Changes

Table 1: Proposed Revisions to Part 50 to Harmonize with the Revised Common Rule

Table 2: Proposed Revisions to Part 50 Unrelated to Harmonization with the Revised Common Rule

Table 3: Proposed Revisions to Part 56 to Harmonize with the Revised Common Rule

Key Proposed Revisions to 21 CFR Part 50

The proposed rule would, if finalized as proposed, revise the content, organization, and presentation of information included in the informed consent form and process to facilitate a prospective subject's decision about whether to participate in the research

Key Information

- Proposed 50.20 (d) and (e)

Additional Basic Element of Informed Consent

- Proposed 50.25(a)(9)

Additional Elements of Informed Consent

- Proposed 50.25(b)(7)-(9)

Key Proposed Revisions to 21 CFR Part 50

Proposes new and/or revised definitions, e.g.:

- legally authorized representative,
- written or in writing,
- private information,
- identifiable private information, and
- identifiable biospecimen

Key Proposed Revisions to 21 CFR Part 56

- Adds provision that would allow IRBs to eliminate continuing review of research in certain circumstances
- Revises IRB recordkeeping requirements for certain determinations related to the need for continuing review

Key Proposed Revisions to 21 CFR Part 812

- Part 812, Investigational Device Exemptions
  - Aligns submission of progress reports with revisions to continuing review requirements in Part 56

INSTITUTIONAL REVIEW BOARDS; COOPERATIVE RESEARCH

PROPOSED RULE

Overview of Proposed Rule

- If finalized as proposed, the proposed rule would generally require any institution in the U.S. participating in cooperative research to rely on a single IRB for that portion of the research that is conducted in the U.S.
- Includes four proposed exceptions relevant to FDA-regulated research

Key Anticipated Benefits:

- Streamline IRB review process by decreasing administrative burdens and inefficiencies without compromising human subject protections
- Facilitate an earlier start of cooperative research
- Provide clear, consistent requirements for stakeholders involved in FDA-regulated cooperative research

FDA's Proposed Exceptions to Single IRB Review Requirement

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

   Note: This is identical to the first exception in the revised Common Rule.

2. Cooperative research involving a highly specialized FDA-regulated medical product for which unique, localized expertise is required
3. Cooperative research on drugs that is exempt from submitting an investigational new drug application (IND) to FDA under 21 CFR 312.2(b)
4. Cooperative research on medical devices that is not required to submit an application (IDE) to FDA (that is, studies that are IDE-exempt and non-significant risk device studies).

Request for Public Comment

In the preamble, FDA is requesting public comment on:

- Whether an exception is appropriate for situations when a single IRB is unable to meet the needs of a specific population
- Whether an exception is appropriate for a multisite study with a small number of sites and what the appropriate threshold should be
- Any additional types of FDA-regulated clinical investigations that may benefit from an exception
- All the proposed exceptions and any other criteria that should be considered when assessing whether an exception might be warranted

Request for Public Comment (2)

Considering that some cooperative research may be subject to both FDA's regulations and the revised Common Rule, FDA is requesting comment on:

- Any impact that differences between FDA's proposed exceptions and an exception determination by a Common Rule Department or Agency may have on stakeholders
- Possible approaches to avoid or minimize any potential negative effects of differences between the exceptions from the single IRB review requirement
- Whether there are unique challenges to use of a single IRB review model for FDA-regulated cooperative research that could not be addressed by FDA's proposed exceptions
- Whether FDA should include an exception that provides for FDA to determine and document that single IRB review is not appropriate for the particular context

Extension of Comment Period

- Federal Register notice published on 14 November 2022 extended the comment period on both proposed rules to December 28, 2022
  - Protection of Human Subjects and Institutional Review Boards (Docket No. FDA-2021-N-0286)
  - Institutional Review Boards; Cooperative Research (Docket No. FDA-2019-N-2175).


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ADMINISTRATION

Save the date for the next
SMART Talk
January 18, 2023
2:00-3:30 pm ET

A Conversation with the FDA and OHRP about Single IRB

Questions?
Contact
help@smartirb.org

Register at
smartirb.org

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