Understanding Single IRB (sIRB) Review Requirements

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Agenda

- Regulatory and Policy Requirements for sIRB Review
- Understanding the sIRB Model
- Organizational Approach to sIRB Review
- Preparing for sIRB review
  - Grant Submission
  - Requesting for the JHM IRB to serve as the sIRB
  - sIRB Submission and Site Onboarding
  - Top Lessons Learned
- Considerations when JHM is relying on an External IRB
- Resources

NIH Policy
Use of a Single IRB for Multisite Research

June 21, 2016: New policy required single IRB (sIRB) review for **multisite NIH-funded research.**

Effective Date: January 25, 2018

What types of studies does this policy apply to?

- NIH-funded **multisite**, non-exempt research
  - **Multisite Studies** = The same protocol is being conducted at more than one site and the study is being funded wholly or in part by NIH
- New applications & competitive renewals submitted on or after the effective date

https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html

Exceptions:

- Exempt research
- International sites [Policy applies to domestic Sites only]
- Studies conducted under career development, research training or fellowship awards
- sIRB review is prohibited by a federal, tribal, or state law, regulation, or policy.

Requests for exceptions that are not based on a legal, regulatory, or policy requirement may be considered by NIH.

- **Compelling justification required**

sIRB is the selected IRB of record that conducts the ethical review for participating sites of the multi-site study.

Additional Regulatory Requirements for sIRB Review under the Revised Common Rule

- The Revised Common Rule extended the sIRB policy to all "cooperative research" [Research involving more than one institution]
- Effective date for this provision: **January 20, 2020**
- **Applies to studies that are approved on after January 20, 2020**

All research funded by any *federal agency that is a signatory to the Common Rule must comply

* Federal agencies that are signed onto the Common Rule: https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html

Under the 21st Century Cures Act, the FDA is required to harmonize its applicable regulations for human subjects protections to align with Common Rule [Requirements for sIRB review coming soon…].

Revised Common Rule – Cooperative Research

§ 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.

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

Revised Common Rule – Cooperative Research

- If your research project is supported or conducted by an agency that is a signatory to the revised common rule and involves more than one institution you must submit a **reliance request**.
  - The JHM IRB started to apply this requirement to all cooperative research as of **November 1, 2019**

What is a "Reliance Agreement"?

- A **Reliance Agreement** is a formal, written document that provides a mechanism for an institution engaged in research to delegate institutional review board (IRB) review to an independent IRB or an IRB of another institution.

- Institutions that are engaged in human subjects research, where one institution will rely on the other institution's IRB, must agree to the terms of the Reliance Agreement before research can begin.

SMART IRB Reliance Agreement

- In anticipation of the release of the NIH policy, the National Center for Advancing Translational Sciences [NCATS] funded a multi-institutional collaborative initiative to develop a national IRB reliance agreement [SMART IRB]
  - FWA-holding Institutions sign on to use the agreement through a joinder process: https://smartirb.org/join
  - Once a site is a signatory to SMART IRB, they may use the SMART IRB agreement has the basis of reliance for any specific study that also involves institutions that are SMART IRB signatories.

Key Facts:

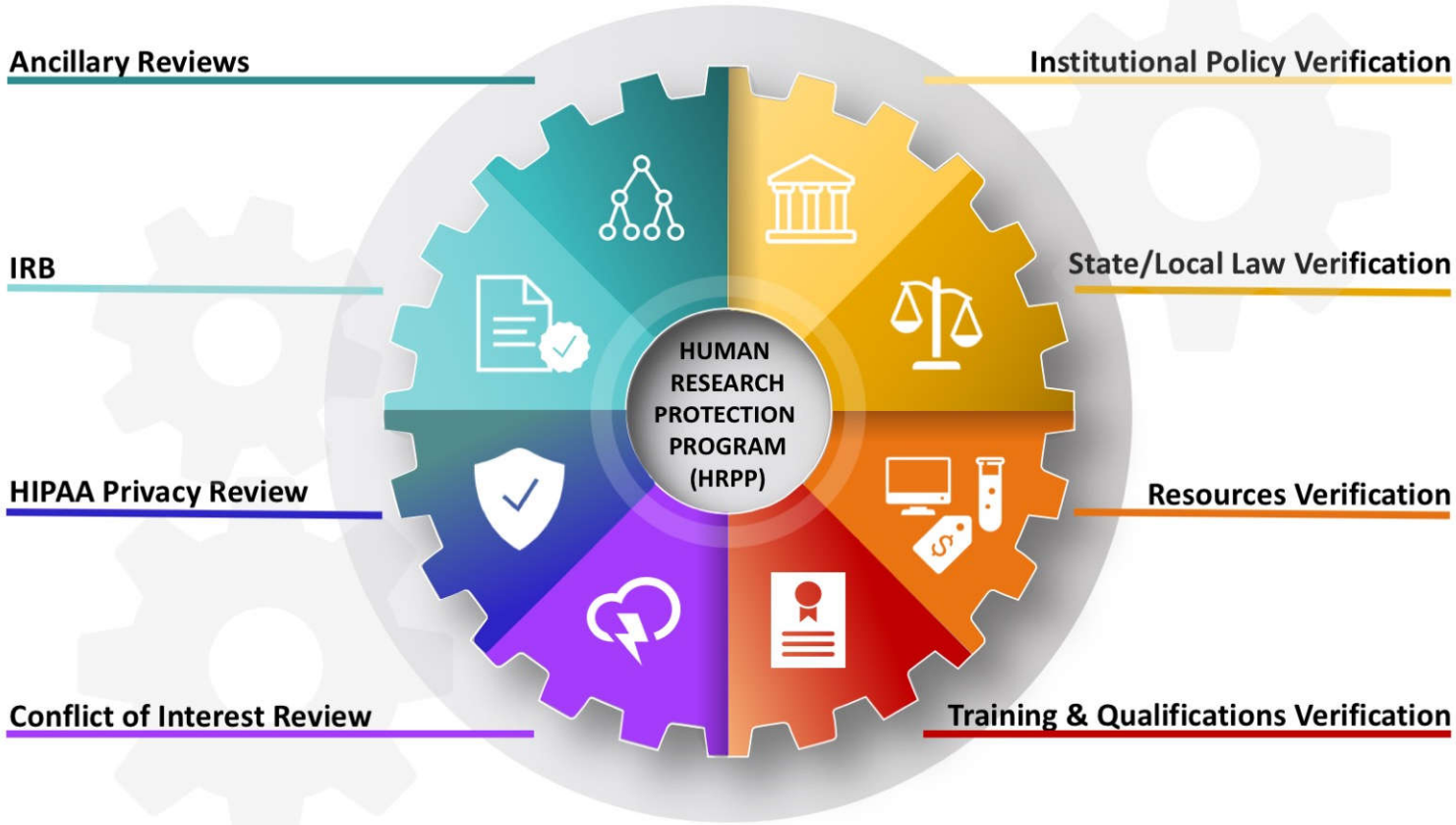
- Eliminates the need for study-specific reliance agreement negotiations
- Institutions may have "addendums" to cover items not specified in the agreement such as indemnification *[JHM IRB does require an indemnification addendum]*
- Institutions must have an FWA [FederalWide Assurance] to sign on

1300+ signatories
64 CTSA Hubs

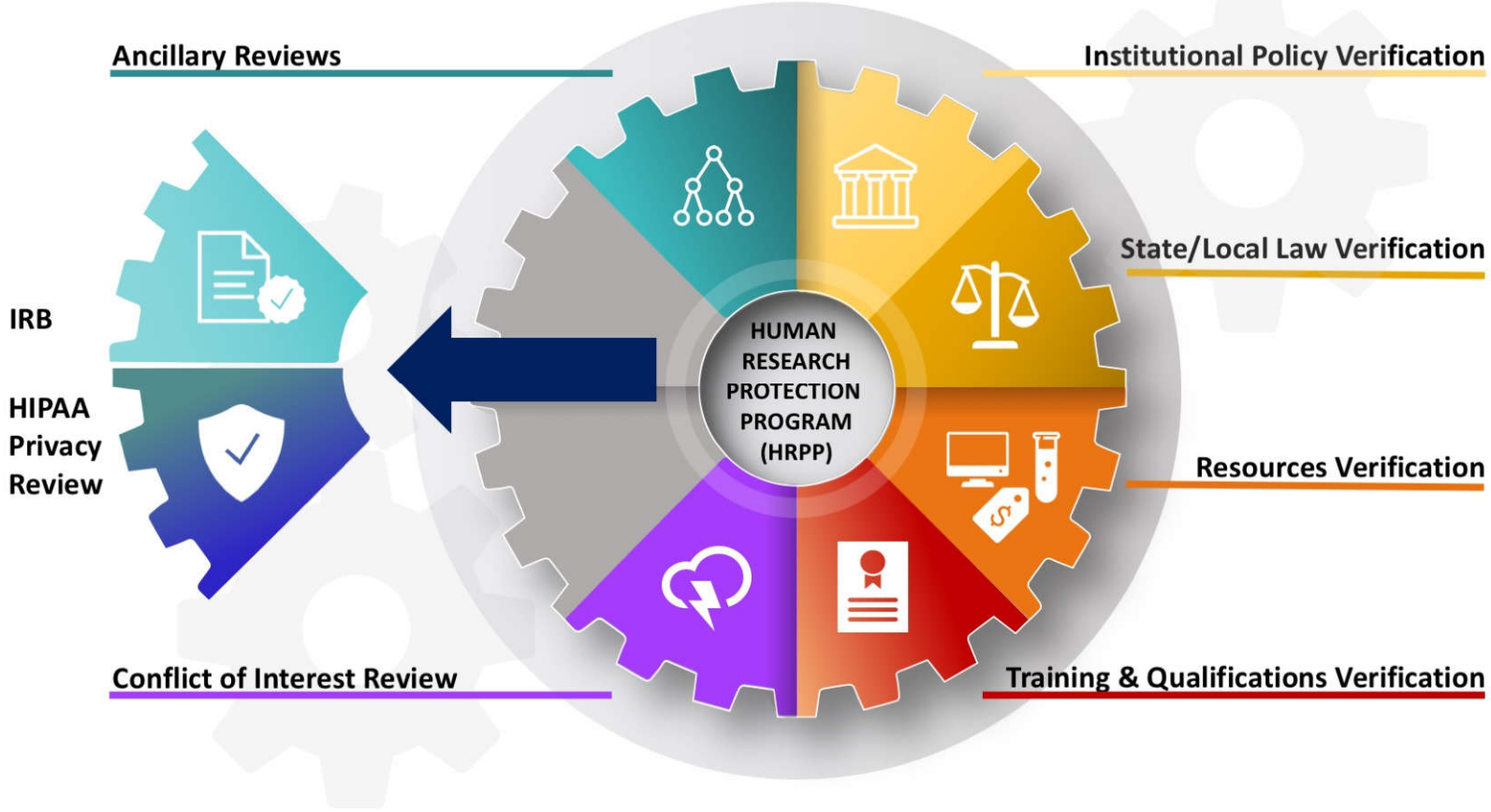
SMART IRB

UNDERSTANDING THE SIRB MODEL

Single IRB Review ≠ Single Institutional Review



Which Components is the Reviewing IRB responsible for?



What is a Relying Organization's Responsibility?

Each Relying Institution will… Communicate to the Reviewing IRB the requirements of any applicable state or local laws, regulations, institutional policies, standards, or other local factors, including local ancillary reviews, ***relevant to the Research*** *("Local Considerations") that would affect the conduct or approval of the Research at the Relying Institution. Such communication may be made through the Reviewing IRB's designee, as determined by the Participating Institutions* ***in connection with the specific Research***. [SMART IRB Agreement]

What types of things do relying sites remain responsible for?

- **Education/Training/Qualifications**. Ensuring that its Research Personnel have adequate education, training, and qualifications to perform the research and safeguard the rights and welfare of participants. This includes ensuring personnel are credentialed to perform the research procedures.

- **Compliance**: Ensuring research personnel comply with determinations of the reviewing IRB and all applicable laws/institutional requirements.

- **Institutional Reviews**: Ensuring all applicable institutional reviews required for the research to be conducted at that site are performed [e.g. radiation safety review, COI review, etc.]

- **Perform local context review**: Communicate to the reviewing IRB the requirements of any local laws, ancillary reviews, etc. and provide any required site-specific information for the consent form, where applicable.

ORGANIZATIONAL APPROACH TO SIRB REVIEW

Key Decisions for JHU

- Where single IRB services are needed, only JHM IRB will serve as the single IRB.
  - JHU has three separate IRBs [JHM, Public Health, Homewood Schools]
  - Only JHM IRB is accredited
- Mandatory Use of Online Reliance Request Tool:
  - Investigators may not indicate in a grant application that JHU is willing to rely on an external IRB or JHM IRB is willing to serve as the IRB of Record without first securing a letter of support from the appropriate IRB.
- For all federally-funded research and where possible for all other research, the SMART IRB agreement will be used as the basis for reliance

Reliance Request Process

Mandatory Use of Reliance Request Tool:

- Investigators may not indicate in a grant application that JHU is willing to serve as the sIRB or rely an external IRB without first securing a letter of support from the appropriate IRB office.
- The Qualtrics-based Reliance Request survey enables easy communication with the JHM IRB at the time of grant submission.

Required letter of support + sIRB budget

- The ORA/JHURA grant application includes questions to prompt investigators to engage the JHM IRB for multisite studies requiring use of a sIRB [JHM as the sIRB or an External IRB]
- Multisite = two or more sites participating in non-exempt research.

The JHM IRB is willing to review requests for reliance on an external IRB as well as requests for JHM to act as the IRB of record. Typically, requests for reliance are submitted to our IRB at two time points:

a) when studies are in their planning stage, or
b) when studies are ready to be submitted for IRB review

The first step in the reliance request process is completing this reliance request.

Questions about whether sIRB review is required for your study? Contact JHMIRBReliance@jhmi.edu.

https://www.hopkinsmedicine.org/institutional_review_board/about/agreements/index.html

PREPARING FOR SIRB REVIEW

Preparing the Grant Application: Key Considerations for federally-funded grants

- The NIH no longer requires a plan for use of a sIRB at the time of grant application, but JHM IRB does require investigators to submit a Reliance Request before grant submission. Investigators should include the following in the grant application:
  - JHM sIRB letter of support
  - Budget for sIRB fees

See: https://grants.nih.gov/policy/clinical-trials/new-human-subject-clinical-trial-info-form.htm

Additional Considerations for Grant Applications

- Funding awards and agencies may have unique sIRB requirements – look at the details of the funding announcement for any requirements.

Budgeting for IRB Fees

- sIRB fees should be included as direct costs in the budget
  - NIH policy permits the new “added” work for the sIRB to be charged as a direct cost
- In cases where JH is engaged as a prime or sub-awardee, the sIRB fees should be included in the award to Hopkins.
- JHM IRB needs to be engaged in budget planning when agreeing to serve as an sIRB for a project – **Contact us Early!**
- Total award amounts have not increased to accommodate sIRB fees

PROCESS WHEN JHM IRB IS THE SIRB

JHM sIRB Review Process

(A) Initial Submission - IRB review occurs per normal procedure.

Initial submission will include multisite protocol [eForm A is not acceptable],and a master consent and JH tailored site-specific consent information [SSCI] ***if JH is an enrolling site]***

Board can ask for specific items for local context review, which will be included in a protocol-specific local context questionnaire [LCQ].

(B) Participating Site [pSite] performs Local Context Review

IRB-approved protocol and master consent [**unstamped PDF**] are distributed to pSites along with a LCQ, SSCI template and any other broadly-approved study materials needed to facilitate site local context review.

pSites will communicate site-specific concerns, locally required language for the consent, etc. via the LCQ and SSCI.

(C) Addition of sites via Psite Addition

Most pSites will be processed expedited by our sIRB team.

If warranted, pSite additions may be sent to the convened IRB for review [site-specific factors impact the criteria for approval].

pSites are approved; approval documents are disseminated by the lead study team.

How does this all work?

Step 1: Submit a request via the Reliance Request Tool. Teams will need:

- Lead team members who can support the sIRB process
- Funds to cover the sIRB fees

Step 2: Reliance Team will assist with pre-screening the multisite protocol and consent form, and onboarding sites to the appropriate reliance agreements.

- Template emails are provided
- Many sites have already executed pre-requisite requirements to rely.

Step 3: Multisite protocol and consent form will be reviewed by the JHM IRB per normal process.

How does this all work?

Step 4: Approved documents are sent to pSites following IRB approval of the parent application.

- pSites will perform local context reviews [Local investigator qualifications/training, local ancillary reviews, identification of any specific local issues]

Step 5: Sites are onboarded/approved when ready

Top Lessons Learned

- **This takes a team.** The lead investigator takes on the work of educating local site teams about sIRB review and managing site correspondence. Teams often do not budget for sufficient personnel to manage these responsibilities.

- **Allow for "flex" in budgeting**. Teams often underestimate key costs that impact budget substantially (e.g. need to add additional sites, more modifications than planned). We encourage teams to not underestimate costs.

- **Communication plan.** sIRB review requires a well-coordinated communication plan between the lead investigator and pSites. There have been several cases where protocol events occurred and needed to be reported/reviewed that were the result of poor communication.

Top Lessons Learned

- **Site-specific policies**: pSites often have different policies/practices that limit the ability for the site to conduct the study as planned. It is highly encouraged that a pSite selection process is developed to ensure pSites can operationalize the protocol as planned.

- **Transition studies**. Studies initially reviewed “locally” that receive “renewal” funding do have to transition to sIRB review. Transitions are complex and require that participants be re-consented. We recommend coordinating with the IRB closely if you have a study that may require transition to a sIRB model.

PROCESS WHEN JHM IRB RELYING ON AN EXTERNAL IRB

Key Factors Considered when Reviewing Requests to Rely on an External IRB

- **Is the External IRB willing to utilize the SMART IRB agreement as the basis for reliance?**
  - Reviewing and executing study-specific agreements is time-consuming and burdensome
  - Requires review by JHU legal

- **Is the External IRB reputable?**
  - AAHRPP-accredited
  - Experienced with type of review that will be performed
  - Valid reason for the selection of the External IRB [e.g., it is the home IRB of the Overall PI for a multi-site study]
  - There is no list of approved External IRBs; all requests to rely are reviewed and cede determinations are made based on the above criteria and other study-specific factors.

Key factors Considered when Processing Requests to Rely on an External IRB

- **Is reliance required?**
  - If not required it may NOT be faster and reliance may not be recommended
  - Only required for federally-funded studies and for certain funding opportunities
  - Not required for most of the following:
    - Industry/commercially-funded studies
    - QI/NHSR activities – these determinations need to be made at the local IRB level
- **Are there any unique factors that would suggest local IRB review will be intensive [and thus reliance may not be appropriate]?**
  - E.g. unique state law issues, local review requirements

Local Context Review

If JHM IRB agrees to rely, the JHM investigator will receive:

- An official email confirmation of our willingness to rely
- A cede letter to share with the External IRB [or a request for their equivalent cede letter], and
- A summary of the next steps [instructions on how to complete an External IRB application]

Resources are available on the IRB website to assist with your submission: https://www.hopkinsmedicine.org/institutional-review-board/about/agreements/jhm-relying-on-an-external-irb

Ongoing Local Context Review

- Relying Organizations remain responsible for their "institutional responsibilities" throughout the life of the study.
- In order to fulfill these responsibilities, organizations must be kept up-to-date of changes that impact their local responsibilities/local context review.
- A signed copy of the **Statement of PI Responsibilities when Relying on an External IRB** must be uploaded with each external IRB application.
  - This document is meant to inform the PI what must be submitted to the JHM IRB during the life of the study.

Ongoing Local Context IRB: Submission Requirements

- **Study Team Changes**
  - Changes to study team members
  - Changes in PI
  - Newly identified conflicts of interest/changes in existing conflicts of interest [additional reporting to the sIRB may also be required]

Ongoing Local Context IRB: Submission Requirements

- **Changes that impact local/ancillary review**
- **Examples:**
  - Changes for which there is a specific institutional policy/state law requirement
  - Changes that impact procedures that have a billable code in EPIC (for which a change in the PRA would be required)
  - Changes to drug dispensation, dosing or the targeted population [e.g. changes to the inclusion/exclusion criteria for studies involving an investigational or approved drug used for research purposes]
  - Changes to plans for research radiation exposure [including a change to the number of subjects exposed or the inclusion of a new population, e.g. minors]
  - Changes that trigger additional JHM data access/storage review

Ongoing Local Context IRB: Submission Requirements

- **Annual Approval Letter from External IRB**
  - JHM IRB WILL set an expiration date in eIRB that WILL impact the study team's ability to enroll subjects in OnCore.
  - The annual re-approval letter must be supplied to the JHM IRB (***prior to expiration of the protocol in the JHM IRB database***) in order to maintain an active record (this record will align with the current approval as assigned by the IRB of record).
  - Any delay in submitting the annual approval letter from the external IRB may delay the study team's ability to continue enrollment locally.
  - The letter is submitted via an activity called "**Upload External IRB Approval**" rather than via continuing review. No continuing review submission is required for external IRB applications.

Ongoing Local Context IRB: Submission Requirements

- **Reportable Events:**
  - Study teams must submit any protocol event reports that meet JHU's reporting criteria in accordance with JHU's local reporting requirements
  - This is a parallel report to the report to the external IRB
  - Study teams must consult JHM IRB if they are uncertain whether an event requires dual reporting to the external IRB and JHM IRB. JHM reporting timelines should be followed locally for these event reports;
  - Study teams must promptly report to the JHM IRB any notifications of suspension or termination that they receive for the applicable study from the external IRB;
- **JHM IRB needs to be involved in the review and follow-up of these events**

Resources

- We are here to help!
- JHM IRB Reliance Program Website: https://www.hopkinsmedicine.org/institutional_review_board/about/agreements/index.html
  - Definitions
  - Polices and Requirements
  - Reliance Requests
  - Helpful Instructions and Forms

JHM IRB Request a Consult Service

Need help navigating the IRB review process?

Use the QR code or visit the IRB website: https://www.hopkinsmedicine.org/institutional-review-board/about/contact to request a consult and be matched with IRB staff who will address your needs.

Sample topics we can help with:

- Protocol planning
- Determining IRB review type & forms
- IRB regulations and policies
- Recruitment & consent
- Responding to IRB review
- Planning for Single IRB Review

Consult requests will receive a response within 24 hours – please reach out!

Questions/Discussion

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