



Understanding Single IRB (sIRB) Review Requirements

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Agenda

- Regulatory and Policy Requirements for sIRB Review
- National Initiatives to Support sIRB Review
- Understanding the sIRB Model
- Organizational Approach to sIRB Review
- Preparing for sIRB review
 - What to do at the time of Grant Application
 - Requesting for the JHM IRB to serve as the sIRB
 - Requesting to Rely on an External IRB

NIH Policy

Use of a Single IRB for Multi-site Research

June 21, 2016: New policy requires single IRB (sIRB) review for **multi-site NIH-funded research**

Effective Date: January 25, 2018

What types of studies does this policy apply to?

- NIH-funded **multi-site studies** that involve non-exempt research
 - **Multi-site 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 or competitive renewals submitted on or after the effective date

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

Exceptions:

- Does not apply to Exempt research
- International sites [Policy applies to Domestic Sites only]
- Does not apply to studies conducted under career development, research training or fellowship awards
- Exceptions to this policy will be made where sIRB review would be 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 extends the Single IRB review requirement to all “cooperative research” [Research involving more than one institution]
- ❖ Required compliance 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 [May include requirements for sIRB review in the future].

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

NATIONAL INITIATIVES TO SUPPORT SINGLE IRB REVIEW

Trial Innovation Network

- Initiative launched by the National Center for Advancing Translational Science (NCATS) to leverage the resources of the CTSA's and help accelerate clinical trials
- Three Trial Innovation Centers [TICs] each with their own central IRB [CIRB]:
 - University of Utah
 - Duke University/Vanderbilt University
 - Johns Hopkins University School of Medicine/Tufts University
- Recruitment Innovation Center [RIC]: Vanderbilt University
- Trial Assignment through the Network

CIRB Development

- ❖ Development of SOPs
- ❖ Develop systems to support the activities of the CIRB
- ❖ Develop plans to monitor the IRB approval process and develop metrics to evaluate CIRB success
- ❖ Work with other TICs to develop innovative strategies for operationalizing CIRB review.

Activity of the TIC CIRBs is supported by a platform hosted by Vanderbilt

TRIAL **INNOVATION NETWORK**



IRB Reliance Exchange

formerly SMART IRB EXCHANGE

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]
 - As of September 2016, this agreement is now available: <https://smartirb.org/>
 - FWA-holding Institutions sign on to use the agreement through a joinder process.
 - Once you are a signatory to SMART, you may use SMART as your reliance agreement for any specific study that also involves institutions that are SMART signatories

Key Facts:

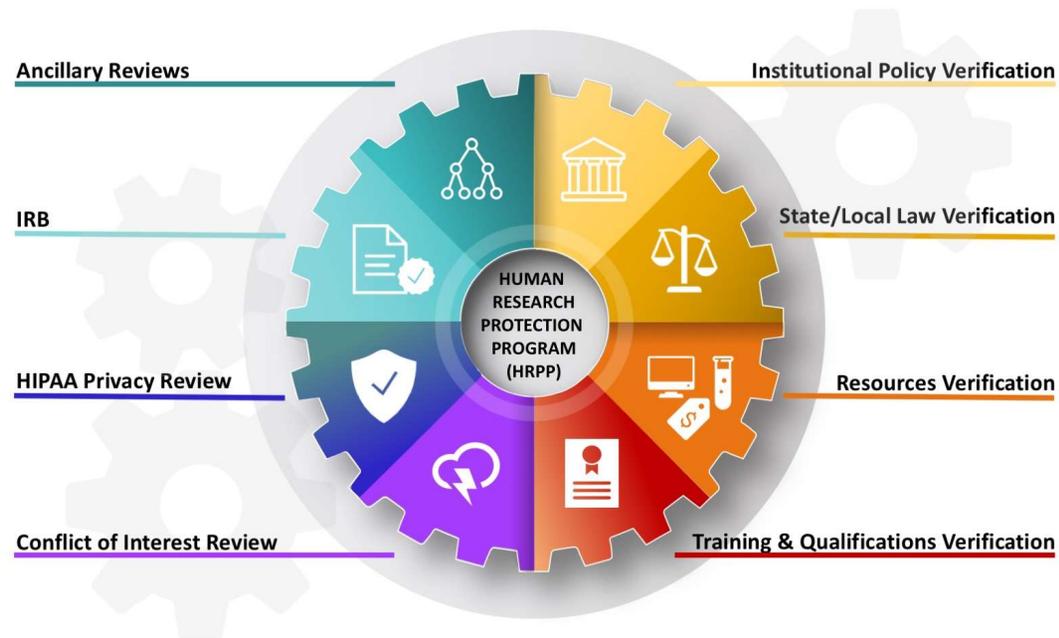
- Eliminates the need for study-specific reliance agreement negotiations
- Institutions may have “addendums” to cover items not specified in the agreement such as indemnification [*JHM IRB does require an indemnification addendum*]
- Institutions must have an FWA [FederalWide Assurance] to sign on

675+
signatories
64
CTSA Hubs

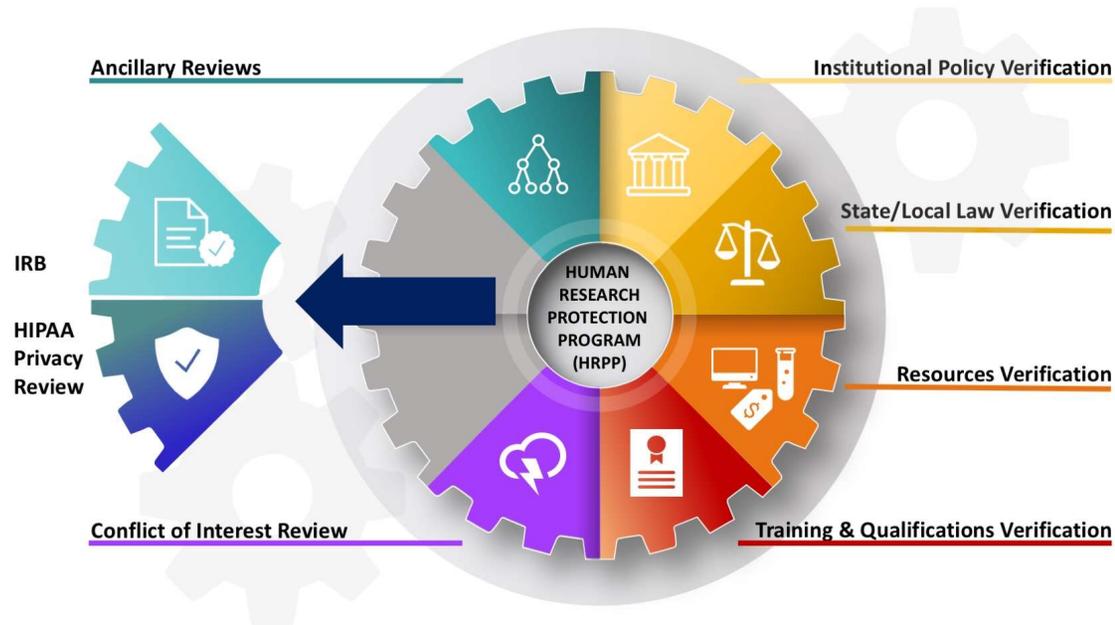
SMART IRB 

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.

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 NIH-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 Online Reliance Request Tool:**
 - Investigators may not indicate in a grant application that JHU is willing to rely on an external IRB without first securing a letter of support from the appropriate IRB office.
 - Online Reliance Request Tool enables easy communication with the JHM IRB at the time of grant proposal
- **Required letter of support**
 - Question added to electronic grant submission systems to require upload of a letter of support to verify the organization agreed to rely on an external IRB
 - Creates an electronic hard stop to ensure the organization agreed to rely on an external IRB
 - This decision must be made at the institutional rather than the investigator letter



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.

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

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



- **Is the IRB of Record 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 IRB of Record reputable?**
 - AAHRPP-accredited
 - Experienced with type of review that will be performed
 - Valid reason for the selection of the IRB of Record [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 currently required by NIH [as of 1/25] and for certain funding opportunities
- Not required and currently not granted 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

GRANT PREPARATION

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



- Study teams must include their plan for single IRB review at the time of grant application
 - Communication plans
 - Identification of the IRB of record
 - Confirmation from all sites that they will comply with the NIH policy on sIRB review [often in the form of a letter of support]
 - Budget for sIRB fees
- New PHS Human Subject and Clinical Trial Information Form “Forms E” is required for submissions on/after 1/25/18.

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

Additional Considerations for Grant Applications

- Funding agencies may have unique sIRB requirements – look at the details of the funding announcement for any requirements
- Where JHM is serving as the sIRB we will provide the following:
 - Grant text
 - A Letter of Support
 - A budget for sIRB fees
- Where JHM is relying on an external IRB we will provide a letter of support

Budgeting for IRB Fees



- sIRB fees will 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:

Step 1: Initial Submission

- Convened Review occurs per normal procedure
- Initial submission will include multisite protocol [eForm A is **not** acceptable]; master template consent, other study documents and a JH tailored site-specific consent information [SSCI] form [*if JH is an enrolling site*]
- **Board can ask for specific items for local context review**

Step 2: Participating Site [pSite] performs Local Context Review

- JH approved protocol and master template consent are distributed to pSites along with a local context questionnaire [LCQ] and template for site specific pages of the consent
- pSites can communicate any site-specific concerns, locally required language for the consent, etc. via the LCQ and SSCI

Step 3: Addition of sites via Psite Addition

- Most pSites will be processed expedited by our sIRB team [Operations & Compliance Staff]
- If warranted, pSite additions may be sent to the convened IRB for review [site-specific factors impact the criteria for approval]

How does this all work?



When JHM IRB is the sIRB

Step 1: Submit a request through the Reliance Request Tool

Teams will need:

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

Step 2: JHM IRB will assist with on-boarding sites to the appropriate reliance agreements

- Template emails are provided
- Many sites have already signed on

Step 3: Protocol and Template consent reviewed by the JHM IRB per normal process

- Pre-screen of new multi-site protocol and consent forms is offered as a courtesy to our investigators

How does this all work?



When JHM IRB is the sIRB

Step 4: Approved documents released to relying sites to perform local context review [Local investigator qualifications/training, local ancillary reviews, identification of any specific local issues]

Step 5: Sites are on-boarded/approved when ready

How will relying sites talk to the JHM IRB ?



Current State

- Site documents are communicated through the lead PI/Coordinating Center
- Sites are added as pSites
- Study-wide amendments controlled by overall PI
- Site-specific amendments/problem events/change in research can be submitted simultaneously
- pSites can opt to have direct access
 - *Federated authentication or account provisioning*

Future State

- pSites will submit site-specific continuing review enrollment data via eIRB

PROCESS WHEN JHM IS RELYING ON AN EXTERNAL IRB

External IRB Applications



- If JHM IRB agrees to rely after receiving the reliance request, the JHM investigator will receive an email at the time of approval of the reliance request, a cede letter to share with the External IRB [if applicable], and a summary of next steps, including 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/forms/

Local Context Review – Review Process & Workflow



(1) Pre-requisite: Reliance Request Survey has been completed; JHM has agreed to cede to the External IRB. PI submits external IRB application in eIRB

- Pre-reviews required by the institution still occur per normal procedure [e.g. ED review, etc.]

(2) sIRB Pre-Reviewer verifies compliance training is complete; confirms that JHM has agreed to rely; confirms application includes requested documentation [e.g., multi-site protocol; template consent and/or a tailored version of the JHM consent].

Local Context Review – Review Process & Workflow



(3) Compliance Reviewer performs regulatory and local/institutional policy checks; confirms required ancillary reviews are complete/in-process; confirms applicable regulatory determinations [e.g., pediatric risk, IND/IDE exemptions] were made by the External IRB and are documented in the application; returns to the study team, moves to CFS review **OR** refers to IRB reviewer/Convened meeting, as necessary. **[Ancillary reviews, not required pre-IRB submission, occur at this stage]**

Local Context Review – Review Process & Workflow



(4) *If the study is returned*, upon re-submission, the response is reviewed by the sIRB team and if adequate, referred to the sIRB Post- Reviewer for finalization.

- The sIRB post-reviewer completes any local context forms required by the External IRB and confirms that any pending ancillary reviews have been completed.

(4a) *If Hopkins will consent participants*, the Consent Form Specialist (CFS) reviews the consent and confirm that JH-required language is present (*if a tailored consent has been supplied*) or points out the JHM language needed (*if the external IRB will build the consent*) at this stage.

Local Context Review – Review Process & Workflow



(5) sIRB Reviewer records the local context review outcome, “Acknowledged pending external IRB approval”; Letter will include requested information required to activate JH as a participating site. The following must be submitted to the JHM IRB before the JHU site can be officially activated.

- Final approval letter from External IRB indicating JH is an approved site;
- Stamped version of JH consent from the External IRB

(6) JHM PI submits response with required information; sIRB Reviewer records the local context review outcome, “**Acknowledged**”, activating JH as a participating site. At this stage the expiration date is set in eIRB to match the expiration date of the external IRB for approval of the study.

- “Acknowledged” means the study is approved to be conducted at the indicated Hopkins sites. An “Approval” letter is not generated as Hopkins is NOT the IRB of Record.

ONGOING LOCAL CONTEXT REVIEW

Ongoing Local Context Review



- 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 would alter the PRA
 - 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 sIRB**
 - JHM IRB WILL set an expiration date in eIRB that WILL impact the study team’s ability to enroll subjects in CRMS.
 - 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 approval letter is submitted using the “**Upload External IRB Approval**” activity 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**

Training Requirements

- This training is required the first time a PI is listed on an external IRB application.
 - Required for all new external IRB applications submitted January 2019 or later
 - For PIs on existing external IRB applications the training will be required at the time of annual renewal of your external IRB application
 - Training must only be completed once
- Please upload a copy of your training certificate in Section 2.
- Training can be satisfied in-person or online
- All study team members are strongly encouraged to complete the training

Compliance Considerations: Monitoring



- Greater than minimal risk studies relying on external IRB will be subject to OHSR compliance monitoring
- Priority monitoring visit will occur within 1 year of study initiation

Resources



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

Questions/Discussion

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