Document Title: Multi-site Research (MSR) and Single IRB (sIRB) - What, When, and How

A. Introduction

This document provides an overview of the sIRB workflow to the research community when an University of Michigan IRB (U-M IRB) has single IRB oversight of a multi-site research study where the same research protocol is being used at multiple engaged research sites. This guidance document has been prepared jointly by the IRB-HSBS and IRBMED to summarize harmonized procedures established between the two units.

B. WHAT

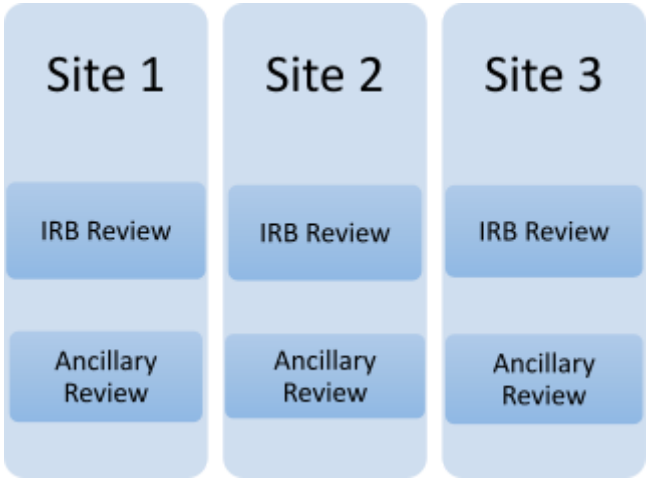
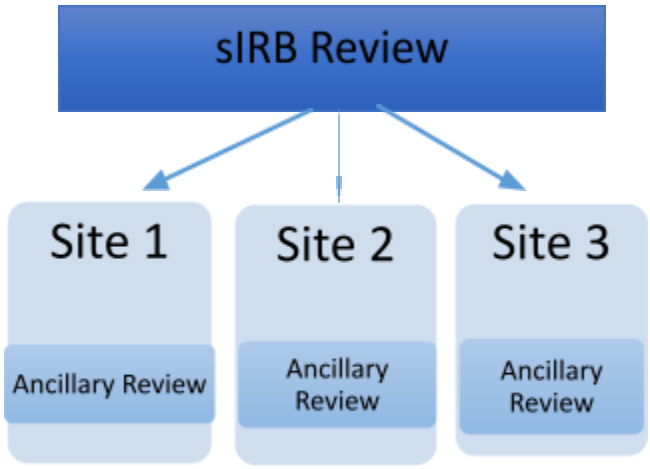
- Per NIH, "*For applications with due dates on or after January 25, 2018, and contract solicitations published on or after January 25, 2018, NIH expects that all sites participating in multi-site studies, which involve non-exempt human subjects research funded by the NIH, will use a single Institutional Review Board (sIRB) to conduct the ethical review required for the protection of human subjects*."
- Per the revised Common Rule (Final Rule), "45 CFR 46.*114 (b)(1) Cooperative research. 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*" (Effective January, 2020)

Definitions

- *Single IRB (sIRB), Reviewing IRB, or "IRB of record"* is an IRB that assumes IRB responsibilities for another institution and is designated to do so through an approved Federalwide Assurance (FWA) on file with the federal Office for Human Research Protections (OHRP).
- *Relying IRB or Relying Institution* is the entity that agrees to rely upon a sIRB or Reviewing IRB.
- *Multi-site research (MSR)* means that the same research protocol is being implemented at two or more independent investigational sites where participants are seen for an intervention and/or outcomes assessment or where that protocol is conducted. Protocols that address the same research questions, involve the same methodologies and evaluate the same outcomes are considered to be the "same research protocol." In a multi-site study, investigational sites are typically administratively or corporately distinct from each other.
- A *coordinating center* is an institution, department, or center that is responsible for some or all aspects of administration or coordination of study functions for more than one institution in a

multi-site research project (e.g., clinical coordinating center, data coordinating center, or statistical coordinating center).

- *A reliance agreement* (also called an IRB Authorization Agreement) is a document signed by institutions engaged in human subjects research that permits one or more institutions to cede IRB review to another IRB.
- *Local Context* includes information about local laws and institutional policies that may impact the research at a participating site and must be considered by the reviewing sIRB.

In the traditional model:	**In the sIRB model:**
	

C. WHEN

- The NIH sIRB policy is effective for grant applications received for due dates on or after January 25, 2018.
- Common Rule regulations for single IRB review for multi-site research became effective on January 20, 2020 for projects regulated under the Common Rule.
- If the single IRB model is selected for the oversight of a study (when federal policy or regulations is not otherwise applicable).

D. HOW

A federal organization grant application requires the use of a single IRB for all participating study sites. The grant application should define what organization will act as the single IRB as well as list the participating sites.

Determining which IRB will serve as the sIRB should occur as early as possible in the grant preparation process. Contact your IRB office to obtain information about sIRB process and potential budget development associated with single IRB service fees.

- See SECTION A for information about ACCEPTING OVERSIGHT.
- See SECTION B for information about CEDING OVERSIGHT.

I. Requesting a U-M IRB to serve as the sIRB (IRB of Record or Reviewing IRB)

a. **Study Team Responsibilities:** In the sIRB model, the U-M study team will have additional responsibilities in the protection of human subjects for all sites. Review the "Multi-Site Research: Overall Principal Investigator Responsibilities" document to understand the additional responsibilities in the sIRB environment and assure that there are adequate resources and infrastructure before assuming this responsibility.

b. **sIRB Request**: To request the U-M IRB to serve as the sIRB, complete the sIRB Request form. This form will provide the IRB with information about the project (overall summary, U-M study team, number of sites, study procedures, etc.). If an U-M IRB is willing to serve as the sIRB, the study team will be notified of the determination in writing.
NOTE: The sIRB Request should be submitted to theU-M IRB as early as possible in the grant preparation process.

c. **IRB application:** Once the U-M PI receives a notice of award, submit an eResearch application.
   - **If the external sites will require site-specific informed consent**, use the Multi-Site Research (MSR) application type within eResearch Regulatory Management. The MSR application must include the study protocol, spreadsheet of participating sites, template recruitment documents, template informed consent document(s), and any additional supporting documents. The MSR application does not route to ancillary committees.
   - **If the external sites will not require site-specific informed consent**, contact the applicable U-M IRB office for guidance on which application type best fits your scenario.
   - For studies reported to IRB-HSBS, due to the nature of the research, work in conjunction with the IRB-HSBS office to determine which of the above pathways is best

   NOTE: The IRB approval process for a sIRB application can be a lengthier process than a traditional IRB application because the IRB must consider additional requirements and responsibilities related to its role as the sIRB. If the funding agency requires a Just-in-Time IRB Review for award confirmation purposes, submit a separate IRB application, selecting the "Projects Lacking Immediate Plans…" application type, to permit an expedited review for this purpose.

d. **Participating Site Applications and Reliance Agreements**: Once the U-M IRB application is approved, if the external sites require site-specific document approval, IRB staff will work with the

U-M study team to create participating site applications for each site that will rely on U-M IRB and the U-M IRB staff will start working with the participating sites to establish reliance agreements.

e. **Local Context**: As the sIRB, the U-M IRB must receive local context information for participating sites. The U-M IRB will collect this information through the participating site application, in most scenarios. Each participating site that requires U-M IRB approval of site-specific study documents relying on a U-M IRB will complete this application type. The U-M IRB will review the completed applications along with any supporting documents attached within the application.

f. **U-M IRB Review:**
   - U-M IRB application: After the MSR application is submitted in eResearch, the IRB regulatory staff work with study teams to resolve any regulatory or application related issues and the IRB application is assigned for review.
     - The U-M IRB MSR approval letter, approved study wide documents and approved template documents (if applicable) must be provided to all participating sites.
     - Sites requiring U-M IRB approval of site-specific study documents will complete the participating site application and submit it to the U-M IRB.
     - The U-M IRB will review and approve local context information and site specific documents. A U-M IRB approval letter and finalized consent document(s) will be provided to each participating site.
     - NOTE: Human subjects research activities must not be initiated at the participating site until reliance agreements are completed and if applicable, site-specific documents are approved by the U-M IRB.
   - FOR IRBMED STUDIES: After the MSR application is approved, if U-M will also be a participating site, a separate IRB application is required for routing through appropriate ancillary committees for U-M site activities. Use the shortened 'Requesting Review by a non-UM IRB' (ceding) application type for this purpose (i.e., U-M is effectively ceding oversight to itself).

II. Requesting the U-M IRB to rely on an external IRB as sIRB (e.g., academic, commercial, hospital)

a. Submit the "Requesting Review by a non-UM IRB" application type, also called the 'ceding application,' within eResearch.
b. Once submitted, this application is reviewed by applicable ancillary committees, and reviewed and acknowledged by the U-M IRB.
c. IRB ceding arrangements are established through a reliance agreement (also called an IRB Authorization Agreement) that delineates responsibilities between the entities. Ceding only transfers IRB or other agreed upon regulatory assessments (e.g., HIPAA waivers of authorization); all other U-M required oversight (including ancillary committees) and workflows remain at the University of Michigan.

QUESTIONS

- IRB-HSBS: mardonne@umich.edu
- IRBMED: niduffy@med.umich.edu

ADDITIONAL RESOURCES:

- The following documents are uploaded and available in U-M Box Single IRB Documents
    - MOP Template
    - MSR Informed Consent Template
    - sIRB reportable event plan
    - Proformance Site Spreadsheet
    - MSR reporting plan
    - Participating Site Directions

SOURCES:

- NIH sIRB Policy
- Common Rule sIRB policy
- U-M HRPP single IRB website
- SMART IRB Investigator and Study Team Learning Center