Document Title: IRB Application Instructions for Multi-site Research U-M IRB as the IRB of Record (Single IRB/sIRB)

A. Introduction

This document provides guidance to the University of Michigan (U-M) research community when completing an IRB application for a multi-site research project where an U-M IRB is the IRB of Record (sIRB). This guidance document has been prepared jointly by the IRB-HSBS and IRBMED to summarize harmonized procedures established between the two departments.

B. Preparing the initial IRB application

NOTE: When an U-M IRB is willing to serve as the sIRB, the study team will be notified of the determination in writing following completion of the single IRB request form. Do not submit an IRB application without receiving this confirmation from the supporting IRB office. For additional information regarding this step, visit this website.

NOTE: Read the "sIRB Overview" document to understand the terminology and processes.

NOTE: The participating site applications for external sites will not be available until after the initial IRB approval of the study.

NOTE: For studies reviewed by IRBMED, If U-M is also a performance (participating) site, a separate IRB application (Ceding application type) is required in order to route information through appropriate ancillary committees.

The IRB application, section-by-section, instructions:

1. Create New "Human Subjects Study Application" within eResearch Regulatory Management system.
2. **Section 01: General Study Information**
   a. In 1.1 Study Title, include a short study title and then right after the short study title, add "**U-Michigan is sIRB**" for quick-identification purposes.
   b. In 1.3, list U-M study team members only. Do not list the external site study team in this section of the IRB application unless specifically requested by the IRB office. Information will be added in Section 03-1 (see below).
   c. In 1.8 Project Summary, provide project specific key information and disclose whether external siets will share any of the coordinating center responsibilities.
   d. In section 01-1 Application Type, select the radio button for "Multi-Site Research" (referred to as MSR in the remainder of this document).

   i. By this point, the U-M IRB office should have already provided confirmation that the U-M IRB is willing to serve as the single IRB. IF this confirmation has not be received, reach out to the U-M IRB.

3. **Section 03: UM Functions**
   a. Select appropriate U-M functions.
   b. Answer "Yes" to the "Will U-M be the IRB of Record" question.
4. **Section 03-1: Performance Sites**
   a. *Participating sites Spreadsheet*: In the MSR application, participating sites are not individually listed within the application. To simplify the process, a Participating site Spreadsheet (see Resources below) was developed to capture the required information for each participating site. This spreadsheet will need to be completed by the U-M study team and then uploaded to Section 3-1.
   b. See Section 44 of this instruction for additional supporting documents pertaining to non-UM sites.
5. **Section 05 Research Design**
   a. Along with a protocol document, the MSR application may also require a Manual of Operations and Procedures (MOP) document to be uploaded (see Resources below for templates). The role of the MOP is to facilitate consistency in protocol implementation and data collection across participants and study sites. In addition, the MOP may also include a specific communication plan and specific information related to sample/data collection and shipping.
   b. The protocol should include generic statements regarding study practices and procedures (for example, the protocol cannot be too specific to the U-M standard of care procedures because standard of care procedures vary between sites).
   c. The protocol must include a comprehensive data safety monitoring plan that specifies the adverse event (AE) reporting requirements and the monitoring activities as appropriate. Although Section 32 of the IRB application is designed to capture this information, it is important to include this information within the protocol so all sites are consistently informed of the requirements. Note that U-M may or may not be the Sponsor/Coordinating Center in all situations. Thus, the protocol should also indicate what forms the site(s) should utilize when reporting AEs. If available, consider uploading a sample case report form in the protocol and/or MOP.
6. **Section 8 Recruitment**
   a. Upload any template or overall recruitment materials that will be used by some or all of the participating sites.
7. **Section 10 Informed Consent (Assent) Process**
   a. Describe the over-all informed consent process, any limitations, alterations, and exceptions.
8. **Section 10-1 Informed Consent Documents**
   a. For MSR sIRB projects, informed consent documents are considered templates and will be used across all the performance sites.
      i. IRB-HSBS: The consent template will need to have fillable sections in place that allow the performance sites to fill in site-specific information.

ii. IRBMED: There are two different models.
    1. If the study qualifies for use of a specialty consent template, that template can be used with fillable sections that allow for the performance sites to fill in site-specific information.
    2. For studies that do not qualify for the above templates, there is a Part 1/Part 2 Multi-Site Research Informed Consent template that is to be utilized. *Part 1 General Information* provides information applicable to all study sites and is not modifiable by participating sites. *Part 2 Site Information* will include information provided by and specific to the sites relying upon IRBMED for review. Both parts must be provided to the participants.
        a. The U-M study team will be completing and submitting *Part 1 General Information* ensuring consistency with the MSR application and the Protocol.
        b. *Part 2 Site Information* will be completed by the participating site study team or the participating site IRB, as appropriate. It is not expected that Part 2 consent documents will be ready at the time of initial IRB application as there are other steps (collecting local context information from the sites, completing reliance agreements, etc.) that will need to be completed. **Though, the U-M study team is expected to review the consent signature boxes at the end of this Part 2 consent template and leave only those that are apprioriate for the study design.**

9. **Section 32 Data Safety Monitoring Plan**
    a. The IRB offices strongly recommend the use of the **sIRB AE Reporting plan** for this purpose. If the study team would like to propose an alternative AE reporting plan, upload a study-specific AE reporting plan.
    b. Include a monitoring plan that will specify the frequency (weekly, monthly, etc.) and type of monitoring activities (in-person monitoring, remote monitoring, DSMB, etc.). If a DSMB charter or clinical trial monitoring plan is available, upload these separately in 32-2 of the IRB application.
10. **Section 44 Additional Supporting Documents**
    a. In Section 44.2 of IRB application, include the document name and version numbers or version dates of all the supporting documents that the performance sites will be using.
        i. Text entered here will AUTOMATICALLY appear word-for-word on the approval letter and provides documentation to the external performance sites of what the IRB has reviewed and approved.

C. IRBMED Review and Approval

Once the MSR application is submitted, it will be reviewed by IRB regulatory staff in the usual manner for completeness, consistency, and compliance. When the application is ready, it will be assigned for review by the Board via the appropriate route for review.

Upon approval of the study, an approval letter will be issued to the U-M study team in eResearch.

Note: A memo regarding the study-specific IRB determinations (Informed consent waivers or medical device determinations) or applicable regulations (whether the project is considered to be FDA regulated) can be drafted by the IRB office upon request.

D. Post IRB Approval – PARTICIPATING SITE ACTIVATION

Each site that is relying on a U-M IRB will be required to log into eResearch and fill out a participating site application to collect local context and gain access to the approved study materials (protocol, Part 1 consent, template recruitment documents, etc.). Creating Participating site applications and notifying the external collaborators of that application will be managed by both the U-M Study team and the U-M IRB staff.

When this information (local context, personnel list, Part 2 Consent, etc.) is ready for each site, the participating site application is submitted for IRB review. The IRB regulatory staff will review the Participating site application and assign for review.

E. Post IRB Approval – MULTI-SITE APPLICATION OTHER SUBMISSIONS

Once the IRB approval has been issued, the study team will be able to submit other related submissions (such as Amendment, AEs/ORIO, and Continuing Review) in the eResearch system according to the normal procedures. All other submissions that take place on the Multi-site application should affect the study as a whole (such as study-wide amendments, study-wide reportable events and study-wide continuing reviews)

F. Amendments:

a. Note that two Amendments cannot be created at the same time in eResearch.
b. Use the Amendment Forms (Title) to indicate the type of Amendment. Include the statement **"U-Michigan is sIRB"** in the amendment title. This will be extremely helpful in the IRB review process.
c. If changes to the list of performance sites are being made to add new sites, do this by making those changes on the spreadsheet from the IRB application, section 3-1.
    i. After an amendment that makes this type of change is approved, the new PSite application can be created.

G. AE/ORIOs: (Do not submit submissions that are not required to be submitted per the approved AE/ORIO reporting plan.)

a. Use the ADV submission title to indicate the type of AE/ORIO.
b. Submit AEs/ORIOs per the approved AE/ORIO reporting plan.

H. Continuing Reviews:

a. At the time of continuing review submission, participating sites that have already reported their continuing review data will be wrapped up into the study-wide continuing review report. For sites that have not submitted in time for the continuing review, this will not prevent the overall study from being reviewed, but will prevent those specific sites from getting the new approval period until they have provided their continuing review data.

b. Ensure that screening ineligibles and withdrawals that are specific to just the U-M performance site are reported in the free-text field of 2-2.1.1. (This is due to there being no field to collect this information in the U-M performance site application.)
c. Upload any additional supporting documents according to the approved AE/ORIO reporting plan that apply study-wide.

I. Post IRB Approval – PARTICIPATING SITE APPLICATION OTHER SUBMISSIONS

Once the IRB approval for the participating site has been issued, the study teams will be able to submit the child-submissions (such as Amendment, Reportable Events, and Continuing Review) in the eResearch system. All other submissions that take place on the Participating site application should affect the participating site only (such as site-specific amendments, site-specific reportable events and site-specific continuing reviews)

1. **Amendments:**
   a. Note that two Amendments cannot be created at the same time in eResearch.
   b. If this is an amendment to the U-M performance site application, use the first page of the amendment forms to indicate the type of Amendment. Include the statement **"U-M performance site"** in the amendment title. This will be extremely helpful in the IRB review process.
2. **Reportable Events:** (Do not submit submissions that are not required to be submitted per the approved MSR reporting plan.)
   a. Use the reportable event submission title to indicate the type of event.
   b. Submit the reportable event per the approved reporting plan.
3. **Continuing Reviews:**
   a. Report any site-specific study activity in a timely manner using the continuing review report type.

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