Pitt IRB Cedes Oversight to External Institution for a Multi-Site Study

Contents

Overview

This guidance is specific to research involving a Reliance/Single IRB (sIRB) mechanism for multi-site research. As one of the leading academic research centers in the nation, researchers at the University of Pittsburgh frequently collaborate with external investigators and institutions. In an effort to reduce duplicate submission and oversight by multiple IRBs for the same project, the University of Pittsburgh Human Research Protections (Pitt HRP) offers reliance opportunities. This guidance is intended to:

- Outline PI and study team responsibilities when the Pitt IRB is ceding oversight to an external IRB for a Multi-Site Study
- Provide step-by-step instructions for Pitt/UPMC investigators

The Pitt HRP will <u>not</u> enter reliance for the following scenarios:

- Institutions located outside of the United States

- In most cases, the Pitt HRP will not enter into reliance agreements for (1) exempt research projects and/or (2) non-NIH funded research limited to chart review. If a request is submitted for this type of project, a determination will be made on a case-by-case basis, based on the justification provided.

The Pitt HRP reserves the right to decline entering reliance, for any project.

- Due to NIH and DHHS' mandates for use of a sIRB, if a decision is made to decline reliance on a federally funded project that requires sIRB, the project will be unable to be implemented at our site.
- If a decision is made to decline reliance on project that does not have federal funding, reliance will not be executed, and the Pitt investigator should submit directly to the Pitt IRB for oversight.

Pitt Investigators should never commit to using an sIRB mechanism without first communicating with the Pitt HRP. Contact the Pitt HRP Reliance Team (irb.reliance@pitt.edu) before (1) committing to the use of an sIRB with external parties and/or (2) completing "Site Activation" paperwork from an external party about Pitt/UPMC site(s).

Definitions

Engaged: The Pitt HRP utilizes the guidance document issued by the Office of Human Research Protections to determine engagement: Engagement of Institutions in Human Subjects Research (2008). Examples of when an institution/individual is engaged in human subjects research include:

1. Receiving direct federal funding for research (i.e., Primary Awardee of the grant)
2. Obtaining data about research subjects through intervention/interaction
3. Obtaining identifiable private information about research subjects
4. Obtaining informed consent
5. Implementing/administering research intervention

Single IRB Review (Reliance): A legal arrangement that allows one IRB to review the research on behalf of other engaged institutions.

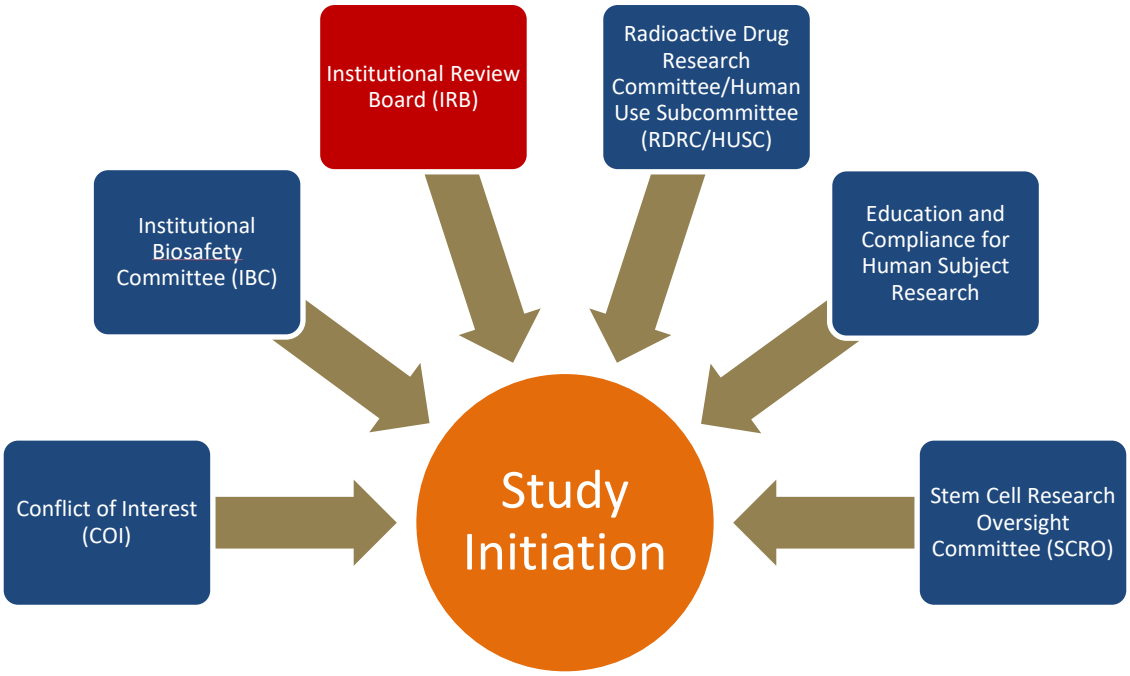
IRB of Record (Reviewing IRB): The IRB that reviews and makes required regulatory determinations.

Relying Site: Institution that cedes IRB responsibilities to the IRB of Record.

Reliance Agreement: A document (e.g., IRB Authorization Agreement, Master Service Agreement, etc.) signed by two or more institutions engaged in human subjects research that permits one or more individuals/institutions to cede review to another IRB. The signed Agreement permits a single IRB to review human subject research activities for more than one individual/site.

Note: Reliance Agreements for sIRB review are used to cede ONLY the IRB review of projects. All institutionally required ancillary reviews must still be obtained locally (e.g., Conflict of Interest, Human Stem Cell, Institutional Biosafety, IND/IDE Support, Radiation Safety, etc.) Oversight of these ancillary reviews still require local review and approval

regardless of ceding IRB review.



Federal Policy

Effective January 25, 2018, the National Institutes of Health (NIH) mandated the use of single IRBs as a contingency for funding of domestic multi-site studies submitted after that date. The NIH issued this policy to establish the expectation that a single IRB of Record will be used in the ethical review of non-exempt human subjects research projects funded by the NIH that are carried out at more than one site in the United States (Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research).

Effective January 20, 2020, the U.S. Department of Health & Human Services requires all domestic multi-site research projects supported by federal funding to utilize a sIRB mechanism, regardless of specific funding agency, under the Revised Common Rule.

Pitt/UPMC Study Team Responsibilities

- Obtaining a Letter of Support from the Pitt HRP (*if requested by the Lead study team)*
- Creation of an External IRB application in PittPRO
- Submission of Reliance Request to the Pitt HRP via online Reliance Request System
- Acting as the primary liaison between the Lead study team, IRB of Record and Pitt HRP
- Inserting local site language into the IRB-approved consent template (provided by the Lead study team) and emailing it to irb.reliance@pitt.edu for the Pitt IRB to insure all necessary local language has been included for our site
- Assist the Pitt HRP in completion of local context surveys (provided by the Lead study team)
- Submission of External IRB application in PittPRO
- Submission of applicable modifications/amendments (see page 5 for listing), continuing review materials and pertinent new reportable information in in PittPRO
- Dissemination of local site materials to the Lead study team and/or IRB of Record

- Ensuring that all engaged Pitt/UPMC affiliates are appropriately licensed and credentialed to complete the described research
- Ensuring all engaged Pitt/UPMC affiliates have completed required research training. Training requirements are available here: ORP Training Table List
- Ensuring all required local ancillary reviews are completed
- Ensuring all engaged Pitt/UPMC affiliates have declared any Conflicts of Interest and implementing any COI management plans required by the Pitt COI Office
- Ensuring all institutional requirements, beyond the Pitt HRP, have been met at Pitt/UPMC (e.g., execution of a Data Use Agreement (DUA) and/or Material Transfer Agreement (MTA) with the Pitt Office of Sponsored Programs).
- Maintaining compliance with the IRB of Record's policy and procedures

General Inquiries

All sIRB inquiries/issues should be directed to irb.reliance@pitt.edu, to ensure that the Reliance Team is promptly receiving all inquiries for response. Please do **not** email HRP staff's personal email boxes regarding sIRB issues, as it slows our ability to effectively respond.

Requesting a Grant Letter of Support

There is typically no requirement that Letters of Support be provided by Relying Sites for inclusion with a grant application. However, it is a requirement that the Lead PI of the grant obtain confirmation from each site indicating their willingness to rely on a specific sIRB. If you receive a request for written confirmation of willingness to cede, please submit a request for a Letter of support using the Reliance Request System.

Letters of support are NOT formal reliance agreements. If the project is funded, formal reliance agreements will then be put in place.

Note, if you receive any type of paperwork that needs to be completed related to the study after grant submission, but before the protocol is even written, contact irb.reliance@pitt.edu for completion assistance.

Timeline Overview When Pitt Cedes Oversight

1	***Pitt/UPMC study team*** creates an External IRB application in PittPRO to generate a STUDY# for the project. The application does **NOT** need to be completed at this time. This step is solely to generate a STUDY# for tracking purposes.
2	***Pitt/UPMC study team*** submits reliance request in online Reliance Request System. The reliance request system will prompt you to provide the STUDY# of the study you created in Step 1.
3	***Pitt HRP*** reviews reliance request at sIRB meeting to determine if reliance is appropriate.
4	***Pitt HRP*** communicates decision as to whether they will permit reliance and begins communication with IRB of Record to determine type of agreement to be used, whether one of the online reliance software platforms (i.e., IRB Reliance Exchange (IREx) will be utilized & facilitates agreement execution.

5	**Note, this step will NOT apply to *all* studies.** If the study includes procedures that require ancillary reviews such as: ○ Exposure to radiation (Radiation Safety) ○ Use of recombinant DNA (Institutional Biosafety) ○ *Pitt* held IND or IDE (Investigator-Sponsored IND and IDE Support) You must complete your External IRB application with as much information as you have available at this time and *Submit*. This will trigger local ancillary reviews that are required and provide any pertinent consent language that will need to be inserted into the study consent template. If any Pitt/UPMC study members have a Conflict of Interest, email the COI office at coi@pitt.edu and alert them COI Review is needed and inquire as to what materials the COI Office needs to conduct their review. For more information, including ancillary review timelines, contact the office responsible for the ancillary review (www.orp.pitt.edu).
6	If requested by the IRB of Record, ***Pitt/UPMC Study Team*** receives Local Context Survey for completion. If *consent* will be obtained at Pitt/UPMC, the ***Pitt/UPMC Study Team*** should receive IRB of Record approved consent template(s) for insertion of local language. The Pitt/UPMC Study Team will insert local language (including any required ancillary review language from step #6, if applicable) using tracked changes. **BEFORE INSERTING LOCAL LANGUAGE, CONFIRM THE TEMPLATES PROVIDED TO YOU BY THE LEAD SITE HAVE BEEN APPROVED BY THE IRB OF RECORD.** For Pitt/UPMC-specific language, see our website: www.hrpo.pitt.edu > Guidance & Forms > "C" for "Consent Guidance" > "Building Your Consent Document.
7	***Pitt/UPMC Study Team*** emails the tracked change consent with local language inserted AND Local Context Survey to irb.reliance@pitt.edu for review and completion.
8	The ***Pitt HRP*** completes the Local Context Survey and signs-off on the local consent form. At this time, the ***Pitt/UPMC Study Team*** submits these documents to IRB of Record for IRB approval.
9	IRB of Record reviews and approves Modification/Amendment/Site Application **adding Pitt/UPMC as a relying site**.
10	***Pitt/UPMC Study Team*** fully completes the external IRB application and submits in PittPRO.
11	***Pitt HRP*** reviews and activates the external IRB application.
12	***Pitt/UPMC Study Team*** submits external IRB application Activation Letter to Pitt Office of Sponsored Programs for grant/contract execution.
13	***Pitt/UPMC Study Team*** may begin the project.

Requesting Pitt IRB to Cede Review to External Institution

The *first step* in requesting that the Pitt IRB cede its oversight to an external IRB for a project is completing and submitting a request using the Reliance Request System.

Note, you cannot save work in the Reliance Request System and return to it later. A request must be made in one sitting. Therefore, the Pitt HRP created the *Overview of Reliance Request System Content* guidance document, which can be found at www.hrpo.pitt.edu > Guidance & Forms > "R" for Reliance Guidance. This document outlines all information and materials you will need to have available to submit a reliance request.

Upon receipt of this paperwork, the Pitt HRP reviews all reliance requests to determine if reliance is appropriate based on the details of the project.

When ceding IRB oversight to an external IRB, the Pitt study team is responsible for complying with the policies and procedures of the institution serving as the IRB of Record for the project.

Creating an External IRB application in PittPRO

When Pitt is ceding oversight to an external IRB, an external IRB application is submitted to the Pitt IRB for registration. The purpose of the External IRB application is two-fold:

- To ensure local ancillary reviews are completed at Pitt (e.g., RDRC/HUSC, Biosafety, O3iS)
- To track and report projects that the Pitt IRB has ceded oversight

Note, the Pitt IRB does not "approve" this application, but will acknowledge receipt and formally ACTIVATE the study to be conducted at the Pitt/UPMC site.

The following information must be completed *prior* to submitting an external IRB application in PittPRO for activation:

- Fully executed Reliance Agreement indicating that Pitt will cede IRB review
- The initial approval letter (i.e., first approval letter for the study) from the IRB of Record including all regulatory determinations for the study
- Modification/amendment/site approval letter officially approving Pitt/UPMC as a Relying Site
- IRB of Record approved protocol
- IRB of Record and approved Pitt/UPMC consent(s) (*if consent will be obtained at Pitt/UPMC*)

Login to PittPRO (www.pittpro.pitt.edu) and select the "Create New Study" button and address the following:

PITTPRO SECTION	
BASIC INFORMATION	**INSTRUCTION**
1. *Title of study:*	Put "sIRB" in front of the study title.
2. Short title:	Put "sIRB" in front of the short title.
4. *What kind of study is this?*	Select "Multi-site or Collaborative study".
5. *Will an external IRB act as IRB of record?*	Select "YES".
6. *Lead principal investigator:*	Leave this item blank.
7. *Local principal investigator:*	List the Pitt/UPMC PI.

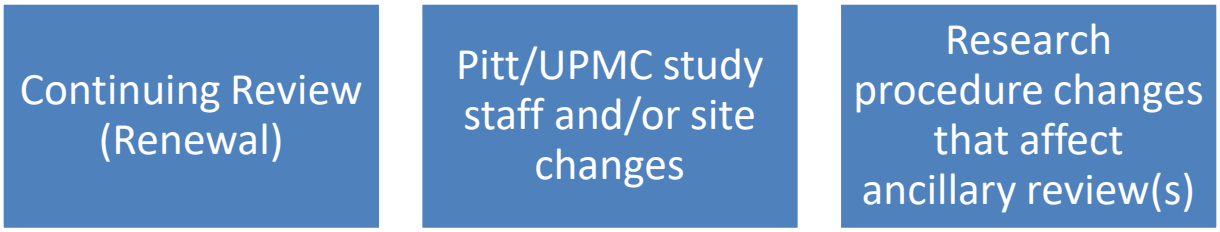
9. *Attach the protocol*	Leave this item blank; do <u>not</u> upload the protocol here.
BASIC LOCAL SITE INFORMATION	**INSTRUCTION**
1. *Brief description of activities this site will perform:* (enter "**<u>ALL</u>**" if this site will perform all procedures in the protocol)	Only list the activities that will occur at Pitt/UPMC. For example: • Write "ALL" if all research activities will be conducted at Pitt/UPMC. • If only some activities will be conducted, <u>only list those</u> activities (e.g., "*Recruitment, data collection only*", or "*Consent, data collection, identifiable data processing only*", etc.)
EXTERNAL IRB	**INSTRUCTION**
1. *External IRB:*	Select the IRB of Record in this section.
2. *External study ID:*	Leave this item blank.
3. *Specify the reason the study should be reviewed by an external IRB:*	Specify the reason WHY the study is being reviewed by an external IRB (e.g., Required as a contingency of funding, required by consortium, etc.).
ADDITIONAL LOCAL FUNDING SOURCES	**INSTRUCTION**
1. *Identify each organization supplying funding for the local site:*	Leave this item blank; all funding should be listed under the *Funding Sources* section.
MAIN STUDY-RELATED DOCUMENTS	**INSTRUCTION**
1. *Consent form templates:*	Leave this item blank; templates are not required for external IRB applications.
2. *Recruitment material templates:*	Leave this item blank; recruitment materials are not required for external IRB applications.
3. *Other attachments:*	Upload the following in this section: • IRB of Record approved protocol • Initial IRB approval letter from the IRB of Record (Note, this document includes all regulatory determinations for the study) • Modification/Amendment approval letter from the IRB of Record officially on-boarding Pitt/UPMC as a relying site • If the initial IRB approval letter has expired, upload *the most current* continuing review approval letter
LOCAL SITE DOCUMENTS	**INSTRUCTION**
1. *Consent Forms:*	If consent will be obtained at Pitt/UPMC, upload the IRB of Record approved Pitt/UPMC consent(s)
2. *Recruitment materials:*	Leave this item blank; recruitment materials are not required for external IRB applications.
3. *Other attachments:*	Upload the following in this section:

	• If applicable, upload forms required for any local ancillary reviews (e.g., the UPMC Fiscal Review form, HUSC form, etc.) • Fully executed Reliance Agreement

NOTE: The *Recruitment Methods* section is not exposed for external IRB applications in PittPRO. If **Pitt+Me** will be used as a recruitment method, please email askirb.@pitt.edu for the Pitt HRP to administratively add this ancillary review to the submission.

Modifying an Activated External IRB Application

Once the External IRB application has been activated in PittPRO, there are *limited circumstances in which changes need to be made* to the application. The *only* times that an external IRB application should be modified are as follows:



There are two ways to modify an external IRB application in PittPRO, dependent upon the section that needs to be modified. See the chart below to determine which type of modification must be submitted for the specific section that requires the change.

Note, for some instances, the "Create Site Modification" function and the "Update Study" functions will need to be utilized if the proposed changes fall into the respective PittPRO section. If this is needed, the "Update Study" function should be completed *prior* to the "Create Site Modification" function.

"Update Study" function	**"Create Site Modification" function**
Basic Study Information	
	Basic Site Information
External IRB	
Study Funding	
	Additional Local Funding Sources
	Local Study Team
Study Scope	
	Local Research Locations
Study Related Documents	
	Local Site Documents
Drugs	
Devices	
	Consent Process
	Electronic Data Management
	Conflict of Interest
	Ancillary Review
	Clinical Trials Info

To modify an activated External IRB application using the "UPDATE STUDY" function in PittPRO:

1. Login to PittPRO
2. Open the External IRB application in PittPRO
3. Select the "UPDATE STUDY"
4. Complete and save the edits
5. PI press "FINALIZE UPDATES" function on the main page of the Update

To modify an activated External IRB application using the "CREATE SITE MODIFICATION" function in PittPRO:

1. Login to PittPRO
2. Open the External IRB application in PittPRO
3. Select the "CREATE SITE MODIFICATION" button
4. Select "*Modification / Update*"
5. Select "*Study Team and research location information*" and "*Other parts of the study*" under the "Modification Scope" item
6. Complete and save the edits
7. PI press "Submit" button

NOTE:

- Changes to the Fiscal Review Form (after activation) should be emailed to Joe Bickus directly at bickusjh@upmc.edu; do **not** Create a Site Modification for changes to the Fiscal Review Form.
- If **Pitt+Me** is being added as a recruitment method, email askirb@pitt.edu for the Pitt HRP to administratively add this ancillary review to your submission.

Submitting Continuing Review (CR) for an External IRB application

After the IRB of Record reviews and approves the study CR, the Pitt study team must submit the following documents:

- CR IRB approval letter from the IRB of Record
- Updated protocol, *if changes were made during the last year*
- IRB of Record approved Pitt/UPMC consent(s) with updated approval dates, *if applicable*

Submitting CR documentation must occur in **TWO STEPS**, as the "Update Study" and "Create Site Modification" functions in PittPRO allow for revisions to separate sections in the external IRB submission. Please complete the following:

(**STEP 1**) Submitting CR documentation using the "UPDATE STUDY" function in PittPRO:

1. Login to PittPRO
2. Open the External IRB application in PittPRO
3. Select the "UPDATE STUDY"
4. Include the following in the "Summarize the Updates" section: *Submitting continuing review documentation.*
5. Upload the following under the "Main Study-Related Documents" section, item #3:
    - Upload the CR approval letter from the IRB of Record.

Note, if there is a previous CR approval letter in this section, stack the most current CR on top of the old CR using the "Update" button; otherwise, do not replace any other approval documents in this section.

- Using the "Update" button, upload the most current version of the protocol, *if changes were made during the last year*

  Note, this document should be stacked on top of the previous protocol using the "Update" button.

6. Save changes
7. PI press "Finalize Updates" function on the main page of the Update

(**STEP 2**) Submit CR documentation using the "CREATE SITE MODIFICATION" function in PittPRO:

1. Select the "CREATE SITE MODIFICATION" button
2. Select "Modification / Update"
3. Select "Study Team and research location information" and "Other parts of the study" under the "Modification Scope" item
4. Include the following in the "Modification Information" section: *Submitting continuing review documentation.*
5. Upload the most current IRB of Record approved version(s) of the consent document(s); these documents should reflect the updated approval/expiration dates.

   Note, this document should be stacked on top of the previous consent(s) using the "Update" button.

6. Save changes
7. PI press "Submit" button

NOTE: If the study does not have updated consent document(s) for upload, the Pitt/UPMC Study team **still needs to** Create Site Modification and submit, as this function allows the Pitt HRP to update the approval/expiration dates in the PittPRO system and corresponding activation letter.

Closing an Activated External IRB application

Closing an external IRB application in PittPRO is an administrative action taken by the *IRB Coordinator* assigned to the submission. To close an activated external IRB application, please complete the following:

1. Select the "Add Comment" function on the main page of the submission
2. Add a comment confirming the following:

   Requesting to close the study. We confirm that the following is true:
   - *Study is permanently closed to enrollment*
   - *All subjects have completed all study-related interventions*
   - *Collection of private identifiable information is complete*
   - *Analysis of private identifiable information is complete*
   - *Analysis of samples is complete*
   - *Remaining study activities are limited to de-identified data analysis OR all activities are complete including data analysis*

3. Attach any correspondence and/or reports related to the study closure

Upon receipt of the study team's confirmation above, the IRB coordinator will administratively close the study.

Reportable New Information (RNI)

Reportable new information should be submitted to the IRB of Record based on that IRB of Record's reporting guidelines. If the IRB of Record makes any of the following determinations **at the Pitt/UPMC site**, follow the instructions below and provide a copy of the RNI and the correspondence from the IRB of Record:

- Unanticipated problem involving risk to subject or others
- Serious non-compliance
- Continuing non-compliance
- Study termination and/or suspension

To create a RNI for an activated External IRB application:

1. Login to PittPRO
2. Select "Report New Information"
3. Complete and save the Reportable New Information
4. PI press "Submit RNI" button

SIRB Fees

The NIH issued a policy permitting the institution that is acting as the IRB of Record on a sIRB project to charge the Relying Sites for their services (Scenarios to Illustrate the Use of Direct and Indirect Costs for Single IRB Review under the NIH Policy on the Use of a Single IRB for Multi-site Research).

The Pitt HRP does **not** charge fees when ceding IRB oversight to an external IRB; however, the IRB of Record for the project reserves the right to charge Relying Sites for their oversight. Contact the IRB of Record to determine what fees may apply.

Other Research Agreements

If data and/or materials will be transmitted to/from Pitt and the IRB of Record, additional agreements may need to be obtained from the Pitt Office of Sponsored Programs (e.g., data use agreement, material transfer agreement, etc.). The IRB Reliance Agreement does **not** cover this transfer of data/materials. For more information, contact the Pitt Office of Sponsored Programs.

Dissolving Reliance Agreements

Once reliance has been established between two institutions, if one institution determines they no longer plan to implement the project at their site, reliance must be formally dissolved through a written memo between the Relying Site IRB and IRB of Record.