18 IRB Reliance

When engaged in multi-site research, research involving external collaborators, or research that is otherwise under the jurisdiction of more than one IRB, CMU acknowledges that each organization is responsible for safeguarding the rights and welfare of human subjects and for complying with applicable federal regulations. CMU may choose to review the research in its entirety, only those components of the research CMU is engaged in, rely on the review of another qualified IRB, or make other arrangements for avoiding duplication of effort. When CMU is the prime awardee on an HHS grant, it will ensure that at least one IRB reviews the research in its entirety.

When relying upon another IRB or when serving as the reviewing IRB for an outside organization or external investigator, a formal relationship must be established between CMU and the outside organization or investigator through an IRB Authorization Agreement, Investigator Agreement, a Memorandum of Understanding, or other such written agreement. The written agreement must be executed before CMU will accept any human research proposals from the outside organization or investigator or rely on the review of an external IRB.

IRB reliance agreements establish the authorities, roles, and responsibilities of the reviewing IRB and the relying organization. The procedures for reliance, including for communication, information-sharing, and reports, may be outlined in the reliance agreement, in SOPs, or other written materials. IRB Staff utilize a checklist to ensure that reliance agreements and any accompanying materials address all requirements and are consistent with CMU's standards. To support compliance, CMU will make every effort to ensure as much consistency as possible across reliance agreements.

Requests for CMU to either rely upon an external IRB or to serve as the IRB of record for an external organization or investigator should be submitted as early as possible in the grant/contract process by contacting the IRB Coordinator.

18.1 Serving as Reviewing IRB

Generally, CMU's IRB does not serve as the IRB of record for an external organization unless CMU is also engaged in the research or has a master agreement in place with the external organization. CMU evaluates the following factors, and others as appropriate, when considering a request for the CMU IRB to serve as the IRB of record for a particular study or studies:

1. The terms of the external organization's FWA;
2. Prior experience with the organization and investigators;
3. The accreditation status of the external organization's HRPP;
4. The compliance history of the organization and investigators (e.g., outcomes of prior audits or inspections, corrective actions);
5. The research activities conducted by or at the external organization;
6. The willingness of the external organization to accept CMU's reliance terms and procedures;
7. The ability of the organizations to collaboratively provide meaningful oversight of the proposed research, taking into account factors such as:
    a. The risks and procedures of the research;

b. The resources available at each organization and ability to accommodate or collaborate with each other in observing the consent process, performing compliance reviews, investigations of potential noncompliance, and similar matters;
c. The expertise and experience of the CMU IRB with the proposed research, subject population, and applicable regulations;
d. The familiarity of the CMU IRB with the relevant local context considerations of the external organization; and/or
e. The willingness or ability of the external organization to provide information and respond to questions regarding investigator qualifications, conflicts of interest, organizational requirements, local context, and other matters that may inform the IRB review.

When the CMU IRB serves as the reviewing IRB for another organization, the requirements and procedures outlined throughout this manual apply unless an alternative procedure has been agreed to in the reliance agreement or outlined in a companion document.

For example, alternative procedures may be used for any of the following:

1. Management and documentation of scientific review, other ancillary reviews, and institutional permissions for research;
2. Training requirements and verification of qualifications and credentials for external investigators and staff;
3. For-cause and not-for-cause compliance reviews;
4. The disclosure and management of conflicts of interest. In all cases, any COIs and CMPs identified and developed by the relying organization will be communicated to the reviewing IRB. The reviewing IRB will determine the acceptability of the plan in accordance with their policies and procedures.
5. Review and management of matters such as site-specific consent language, HIPAA (e.g., authorizations, waivers, alterations), noncompliance, unanticipated problems, and federal reports;
6. Ensuring concordance between any applicable grant and the IRB application/protocol.
7. Procedures for and type of IRB review (e.g., expedited, convened) of additional sites after the research protocol is IRB-approved;
8. Procedures for submission and review of interim reports and continuing review materials; and/or
9. The communication of IRB determinations and other information to external investigators and organizations.

18.2 External IRB Review of CMU Research

All non-exempt human subject research (or exempt research for which limited IRB review takes place pursuant to § __.104(d)(2)(iii) or (d)(3)(i)(C) that CMU is engaged in must be reviewed and approved by the CMU IRB or an external IRB that CMU has agreed to rely upon prior to the initiation of the research.

CMU has standing agreements in place to engage the services of external IRBs for the review of specific categories of research including:

- WCGClinical for gene therapy studies (pending)

- NCI's Pediatric CIRB for NCI research involving children (pending)

Research that falls within the above parameters must be registered with CMU prior to submission to the external IRB following the procedures outlined in Section 18.2.1. Post-approval requirements are summarized in Section 18.2.2.

CMU may also choose to enter into an agreement to rely upon other external IRBs, most commonly when required as a condition of a grant or contract. Investigators should submit reliance requests as early in the grant/contract process as possible by contacting the IRB Coordinator.

The IRB Staff evaluates the following factors, and others as appropriate, when considering a request to rely upon an external IRB:

1. The accreditation status of the proposed IRB;
2. The compliance history of the IRB (e.g., outcomes of prior audits or inspections, corrective actions);
3. Prior experience with the IRB;
4. The federal IRB registration and organizational FWA, as applicable;
5. The expertise and experience of the proposed IRB (e.g., with reviewing the type of research, research procedures, and subject population(s));
6. The research activities that will be conducted at or by CMU;
7. The risks and complexities of the proposed research;
8. The proposed reliance terms and procedures including the procedures for collaborative management of matters such as conflicts of interest, noncompliance, unanticipated problems, and federal reports;
9. The plan for review and allowance of the incorporation of site-specific consent language; and
10. The plan for incorporation of other relevant local requirements or context information in the review process.

When reliance on a non-accredited IRB is proposed, the evaluation may also take into consideration one or more of the following based upon the risks of the research, the research activities that CMU will be involved in, and CMU's familiarity with the IRB:

1. When the research is minimal risk (or the activities that CMU is involved with are minimal risk), a statement of assurance from the proposed IRB that its review will be consistent with applicable ethical and regulatory standards, and that it will report any regulatory investigations, citations, or actions taken regarding the reviewing IRB, and, when applicable, to the organization's FWA;
2. An attestation about, or summary of, any quality assessment of the reviewing IRB such as evaluation by an external consultant or internal evaluation of compliance using the FDA's self-evaluation checklist or AAHRPP's self-evaluation instrument;
3. The willingness of the external IRB to accommodate requests for relevant minutes and other records of the proposed study and/or to copy CMU's HRPP office on correspondence such as determination letters and notices of suspensions or terminations of IRB approval;
4. The willingness of the external IRB to accommodate a request for someone from the relying organization to serve as a consultant to the IRB or to observe the review of the proposed study; and/or
5. An assessment of the external IRB's policies and procedures.

The external IRBs that serve as the IRB of record for CMU research have the same authority as the CMU IRB and all determinations and requirements of the external IRBs are equally binding. Investigators must be familiar with and comply with the external IRB's policies and procedures and any additional requirements or procedures outlined in the IRB reliance agreement or companion materials (e.g., reliance SOPs). CMU will support compliance with the terms of reliance agreements by providing investigators with information relevant to their responsibilities, such as a copy or summary of the agreement, an information sheet, or reliance SOPs.

Regardless of which IRB is designated to review a research project, CMU is responsible for the conduct of the research in which it engages. Research reviewed by external IRBs remains subject to review, approval, and oversight by CMU and must adhere to all applicable policies, procedures, and requirements, including those of the CMUHRPP.

18.2.1 Registration of Studies Reviewed by External IRBs

Investigators must register studies that will be reviewed by an external IRB by submitting basic information about the research to the HRPP/IRB office in an Application for Reliance on an External IRB. After opening the application form, when prompted, investigators should supply all requested information and upload all requested documents in the remaining sections of the application. The HRPP/IRB office staff will review the information and verify that CITI training, COI review, and any other applicable approvals or requirements have been completed, and determine the need for relaying local context information to the reviewing IRB in accordance with the reliance agreement. When applicable, and when the external IRB is not responsible for reviews of requests for waivers or alterations of HIPAA authorization (e.g., studies reviewed by the NCI CIRB), the HRPP/IRB staff will forward requests for waiver or alteration of HIPAA authorization and any relevant materials to the internal IRB Chair for review. The HRPP/IRB office staff will notify the investigators once the proposed research has been cleared for submission to the external IRB via an electronic system notification. Once approved by the external IRB, investigators must submit a copy of the approval notice and any approved consent document(s) to the HRPP/IRB office via the electronic system. If the protocol was modified during the external IRB review process, the approved version of the protocol should be provided as well.

18.2.2 Post Approval Requirements

Investigators approved through external IRB review must still report local unanticipated problems, complaints, and any noncompliance to the CMU HRPP/IRB office using an Adverse/Reportable Event Form in addition to reporting to the external IRB. Copies of the report submitted to the external IRB are generally acceptable, but additional information may be requested on an as-needed basis. Investigators must also submit copies of continuing review reports, updated protocols, updated consent forms, study closures, and the corresponding IRB approval or acknowledgment.

Changes in PI and the addition of other research team members must be submitted to the IRB office using a Protocol Change Form prior to the new PI or research team member assuming any study responsibilities. The HRPP/IRB office must verify CITI training, COI review, and any other applicable requirements.

Notices about and reports from external monitors, auditors, or inspectors must be provided to the HRPP/IRB Office using an Adverse/Reportable Event Form.

Any of the following issues must be reported immediately (asap once aware) to the CMU IRB office by phone or email:

- Any negative actions by a government oversight office, including, but not limited to, OHRP Determination Letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated (classification as "OAI" is typically made after the FDA has the opportunity to review any responses to a 483), FDA Restrictions Placed on IRBs or Investigators, and corresponding compliance actions taken under non-US authorities related to human research protections;
- Any litigation, arbitration, or settlements initiated related to human research protections; and/or
- Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding CMU's HRPP.

Investigators are reminded that other CMU reporting requirements, such as to Compliance, Privacy, and Risk Management, remain applicable in addition to HRPP reporting requirements.

18.3 NIH Single IRB (sIRB) for Multi-site Research

In June 2016, the National Institutes of Health (NIH) released a final policy requiring domestic awardees and domestic sites of NIH-funded multi-site research to use a single IRB (sIRB) for review of non-exempt human subject research unless there is justification for an exception. This policy is intended to streamline the IRB review process and reduce inefficiencies and redundancies while maintaining and enhancing subject protections. The policy **does not** apply to career development, research training, or fellowship awards, nor to sites that are not conducting the same protocol as the other sites (e.g., sites providing statistical support or laboratory analysis only) or to foreign sites.

Exceptions to the policy are automatic when local IRB review is required by federal, tribal, or state law/regulation/policy and when the proposed research is the "child" of a grant that predates the requirement for sIRB review. Such exceptions and the basis (and information regarding the "parent" study, when applicable) should be cited in the proposed sIRB plan and, when the exception is based on law/regulation/policy, apply only to the site(s) to which the law/regulation/policy applies. Other exceptions will be considered when there is compelling justification. The site(s) and justification for why the site(s) cannot rely on the single IRB of record should be included in the proposed sIRB plan. The NIH will consider the exception request and inform the applicant of the outcome.

18.3.1 Selection and Designation of a sIRB

Due to a lack of sufficient numbers of staff, CMU generally will not serve as a sIRB on multi-site studies.

CMU's investigators submitting applications for NIH-funded multi-site research must describe the sIRB plan in the funding proposal (grant application or contract proposal), and, if applicable, may

request direct cost funding to cover additional costs related to the requirements of the NIH policy. The sIRB can be the IRB at one of the participating sites or an independent, fee-based IRB. When the sIRB is named in the proposal, the IRB must have agreed to take on this responsibility in advance. Requests for the CMU's IRB to serve as the sIRB should be directed to the IRB office. The HRPP Director will consult with others within the organization as needed and make a recommendation to the IO for consideration. Requests for CMU to rely upon an external IRB as the sIRB should be submitted as early in the process as possible by an Application for Reliance on an External IRB.

When CMU will not be the prime awardee, investigators should, as early in the process as possible, submit a request for CMU to rely upon an external IRB as the sIRB by Application for Reliance on an External IRB.

18.3.2 Reliance Agreements for sIRB Studies

A Reliance Agreement (or "Authorization Agreement") between the sIRB and the participating sites is required. The Reliance Agreement documents the respective authorities, roles, responsibilities, and communication between an organization providing the ethical review and a participating organization relying on a reviewing IRB.

Reliance Agreements should describe the responsibilities of all parties and how communication between parties will occur, for example, notifications of the outcome of regulatory review and management of federally mandated reports such as reports of unanticipated problems, serious or continuing noncompliance, and suspensions or terminations of IRB approval. When IRB certification requirements apply (e.g., for NIH Genomic Data Sharing), the agreement or written procedures should indicate who is responsible for meeting the certification requirements.

The agreement or written procedures should also specify points of contact and contact information for the sIRB and relying institution(s).

The institution that is awarded the funding for the research is responsible for maintaining all agreements and for ensuring that adequate and appropriate communication channels between the sIRB and participating sites are in place. Participating sites are responsible for maintaining copies of the site agreement in accordance with the terms of their FWA.

18.3.3 Responsibilities

The sIRB will be responsible for compliance with the regulatory requirements for IRBs specified in the federal regulations (i.e., 45 CFR 46 and other applicable regulations) and for any other responsibilities outlined in the reliance agreement and/or procedures. Participating sites (Relying institutions) are responsible for providing relevant local context information to the sIRB, ensuring that the research is conducted in accordance with applicable regulations and the determinations and requirements of the sIRB, and for other responsibilities, as outlined in the reliance agreement and/or procedures.

When an external IRB serves as the sIRB for a study CMU is engaged in, investigators must register the study with CMU prior to submission to the external IRB following the procedures outlined in Section 18.2.1. Post-approval requirements are summarized in Section 18.2.2.

Research reviewed by external IRBs remains subject to review, approval, and oversight by CMU and must adhere to all applicable policies, procedures, and requirements, including those of the CMU HRPP.