21.0 Collaborative Research

21.1 Policy

In the conduct of collaborative or cooperative research projects, each institution (or entity) is responsible for safeguarding the rights and welfare of human subjects and for complying with any applicable regulations. Federal regulations allow for cooperative research projects which involve more than one institution. To avoid duplication of review efforts by IRBs, this institution may choose to conduct joint reviews, rely upon the review of another qualified IRB, provide review oversight for another IRB, or make other arrangements to establish an alternate oversight plan.

This institution may rely upon the review of another qualified IRB if the institution has a current, unexpired Federalwide Assurance (FWA) on file with the Department of Health and Human Services (DHHS) Office for Human Research Protections and one of the following criteria are met:

- The IRBs are part of an AAHRPP accredited institution.
- This institution's investigator is a collaborator on Human Research that is primarily conducted at another institution and the investigator's role does not include interaction or intervention with subjects.
- The institution is engaged in the Human Research solely because it is receiving federal funds, even where all activities involving human subjects are carried out by employees or agents of another institution. (Employees and agents of this institution do not interact or intervene with subjects, gather or possess private identifiable information about subjects, nor obtain the consent of subjects.)
- When this institution is engaged in the research and the greatest level of risk to study subjects occurs at another institution, this institution may agree to rely on that site's IRB. This policy assumes the IRB at the non-PBRC site will have the required reviewer expertise. If it does not, the IRB with the required reviewer expertise will be selected from among engaged Institutions.
- Mandated by NIH Single IRB Policy for Multi-site Research

The OHRP Guidance on Engagement of Institutions in Human Subjects Research will be used as the basis for determining engagement in human-subjects research. Such determinations will be made in collaboration and consultation with authorized representatives at this institution and the collaborating institution and/or the collaborating individual investigators, whichever is most appropriate.

Regulations & Guidance: HRPP Policy 302, FDA 21 CFR 56.114, DHHS 45 CFR 46.114, and NIH NOT-OD-16-094

21.2 Definitions

Agreement: may be referred to as a Cooperative Agreement, IRB Authorization Agreement (IAA) or IRB Reliance Agreement. When the agreement is designed to cover all future multi-site studies involving two or more sites, this is usually referred to as a Master Reliance Agreement..

Cede review: the act of transferring IRB review and oversight.

Collaborating institutional investigator: not otherwise an employee or agent of the assured institution; conducting collaborative research activities outside the facilities of the assured institution; and is acting as an employee or agent of an institution that does not hold an OHRP-approved FWA with respect to his or her involvement in the research being conducted by the assured institution; and employed by, or acting as an agent of, an institution that does not hold an OHRP-approved FWA and does not routinely conduct human subjects research.

Collaborative (also-known-as Cooperative or Multi-site) research: studies involving more than one institution.

Federalwide Assurance (FWA): a contract or agreement that establishes standards for human subjects research as approved by the Office for Human Research Protections (OHRP).

IRB of Record (also known as the Lead, Reviewing or Central IRB): means the IRB who is responsible for the review, approval, and regulatory oversight of a multi-site research study.

Individual Investigator Agreement (IIA): An IIA is an agreement between PBRC and an individual collaborator who is not affiliated with an FWA institution (e.g., former student working after graduation with their faculty mentor, professional in the community with specific expertise, community partners). This agreement type outlines the responsibilities of the individual investigator for the protection of human subjects. The IIA is signed by all of the following:

- Individual investigator
- PBRC Principal Investigator (PI)
- PBRC Institutional Official or designee

IRB Authorization Agreement (IAA): An IAA is an agreement between PBRC and another institution that holds a Federal Wide Assurance (FWA) with the Office of Human Research Protections (OHRP) of the U.S. Department of Health and Human Services (HHS). Any institution (e.g., university, medical centers, NGOs, community organization,

survey research organization) receiving funds from HHS must have an FWA. This agreement type is used to establish the IRB-of-Record (whether that's PBRC or the other institution). The IAA is signed by the Institutional Officials or designee at each institution.

Lead PI: The principal investigator with ultimate responsibility for the overall conduct, safety, regulatory oversight and data integrity for a multi-site research study.

Local Context Language: language specific to the conduct of human subjects research at each institution (e.g., subject injury language, HIPAA authorizations, data security, unique state or local laws, local practices or cultural issues, etc.).

Master Reliance Agreement (MRA): A MRA can be utilized when multiple studies are ceding review to a specific external IRB. Master Agreements may be reciprocal in that signatory institutions can act as the site providing IRB review and oversight or the site relying. Master Reliance Agreements may be for a single protocol or a number of protocols and are negotiated on a case by case basis. MRA eliminates the need for separate IAAs and individual negotiation and documentation. The PBRC IRB currently has master agreements in place with the following external reliance platforms:

- IRB Reliance Exchange (IREx)
- Smart IRB

Multi-site Review: Where one IRB accepts responsibility to serve as the IRB of record.

Multi-site study: a study where the same protocol is to conduct non-exempt human subject research at more than one site.

Participating Institution: a domestic entity that is a signatory party to the Reliance Agreement. The institution will rely on the lead IRB to carry out the site’s IRB review of human subjects research for the multi-site study.

Relying Institution or Site: A hospital, clinic, doctor's office where research will take place and which will rely on an external IRB (Central IRB) which will serve as the Reviewing IRB for a multi-site study. When academic institutions are involved, this term incorporates the Relying IRB and the Relying Participating Institution

Relying Site Investigator: A Principal Investigator at the Relying Institution for a study that may be overseen by a Lead or an external IRB

“Same research protocol”: a protocol that addresses the same research questions, involves the same methodologies, and evaluates the same outcomes are considered to be the “same research protocol.” Additionally, sites that are accruing research

participants for studies that are identical except for variations due to local context consideration would be considered to be conducting the “same research protocol.”

Site PI: A principal investigator who is responsible for the conduct of the research at their Participating Institution.

21.3 IRB Authority

This institution must approve research conducted by its employees or agents, regardless of the location of the study, before the research can begin. Thus, even in cases when a research project is performed at another institution, employees must contact the PBRC IRB to determine the level of engagement in human subjects research. This standard holds even if researcher’s participation is as co-investigator or the researcher has a limited role.

IRB approval at this institution does not extend to individuals on the project who are affiliated with other institutions. Those individuals must seek IRB review from their IRB of record, obtain an individual investigator agreement, or cede review through a reliance system.

The Executive Director of Pennington Biomedical Research Center is designated as the Institutional Official. The Institutional Official (IO) is vested with the authority to execute IRB reliance agreements on behalf of this institution. The IO may delegate this authority.

Legal Counsel facilitates arrangements of Single IRB review mechanisms as needed through an approved Reliance Agreement or Memorandum of Understanding (MOU). Initial review and subsequent reviews are conducted by the IRB of record for that study and in accordance with the arranged agreement between entities.

The IRB Chair and other individual(s) with sufficient expertise and authority may review investigator requests and determine the appropriateness of reliance on a case-by-case basis. However, all applicable parties (e.g. legal, conflict of interest review, clinical staff, pharmacy, radiation safety, biosafety review, license and technology, sponsored project services, etc.) are consulted regarding the reliance. If applicable, investigators must submit all additional required reviews to the IRB. Studies approved through reliance agreements are communicated to the IRB board in the meeting minutes.

The HRPP Director or designee will facilitate communication with the relying or reviewing institution about IRB actions on the human subjects research that is subject to the agreement, in accordance with its specific provisions.

21.4 NIH Single IRB Policy for Multi-Site Research

The National Institutes of Health (NIH) Policy on the Use of a Single Institutional Review Board for Multi-Site Research is effective for NIH grants submitted on or after January 25, 2018. The policy applies to NIH-funded multi-site studies where each site will conduct the same protocol involving non-exempt human subject research and requires that a single IRB (single IRB) provide IRB approval for all participating sites.

If all the conditions below are met, the NIH Single IRB Policy is applicable:

- The policy applies to domestic awardees and participating domestic sites only; foreign sites participating in NIH-funded, multi-site studies are not expected to follow this policy.
- The policy applies to Research Grants (R or U series) or a Program Project/Center Grant (P series).
- The human subject research is not exempt. The research requires IRB review and approval at the Expedited or Full Board level.
- Two or more U.S. sites/institutions conduct the research.
- The same protocol will be conducted at each U.S. site/institution:
    - Protocols that address the same research questions, involve the same methodologies, and evaluate the same outcomes and the only variations are in enrollment of subjects due to local context considerations; or
    - A separate site is used for study coordination or coordination of data and statistical analysis.
- Exceptions to the policy can be requested, based on law or regulation, or due to some other compelling reason.

The NIH Single IRB Policy does not apply to:

- Career development (K), research training (T) or fellowship awards (F) awards.
- Ongoing projects that are not being submitted for consideration of a competing grant (such as noncompeting continuing grant).
- Other Transaction Agreements (OTAs) under the authority of the Department of the Defense (DoD).
- Foreign research collaborating institutions/sites.
- Projects awarded before NIH sIRB effective date.

In some cases, NIH (or another funding sponsor) may specify the single IRB in the Funding Opportunity Announcement (FOA) or a request for proposal (RFP) funding announcement. However, for most grants, NIH expects the lead PI to identify a specific single IRB in the grant application.

Absent an NIH mandate to rely on a single IRB, the PBRC IRB will consider the risks to participants as well as the capacity and expertise for serving as the IRB of record for the study or ceding review to another institution. Exceptions for other federally funded research may be requested through the IRB Office and will be considered on a case by case basis.

21.5 Requirements for Single IRB Review under the Revised Common Rule

The Revised Common Rule extends the Single IRB review requirement to all "cooperative research."

- Required compliance effective date for this provision: January 20, 2020.

All research funded by any federal agency that is a signatory to the Common Rule must comply.

21.6 OHRP Exception to Single IRB Review

OHRP determined that for HHS cooperative research subject to the revised Common Rule (also referred to as the 2018 Requirements), and for purposes of 45 CFR 46.114(b)(2)(ii), an institution may continue to use multiple IRBs, in lieu of a single IRB, for the following research:

1. Cooperative research conducted or supported by HHS agencies other than the National Institutes of Health (NIH), if an IRB initially approved the research before January 20, 2020.
2. Cooperative research conducted or supported by NIH if either:
    a. the NIH single IRB policy does not apply, and the research was initially approved by an IRB before January 20, 2020.
    b. NIH exempted the research from its single IRB policy before January 20, 2020.

21.7 Reliance Agreements

Reliance agreements (or authorization agreement) between institutions is established through a legal agreement and may apply to the review of one study, to certain specific categories of studies or to all studies. This means that the PBRC IRB may become the IRB of Record (lead or reviewing IRB) or cede oversight of the research activity to another equally qualified IRB and become the relying IRB. Under the arrangement, IRBs may compare best practices, share SOPs and informed consent documents, and pool resources to facilitate a review.

A reliance agreement can be in many different forms, but some of the main agreements are Institutional Authorization Agreements (IAA), and Master Reliance Agreement (MRA). Such agreements are limited to IRB review, and do not include identification and management of researcher conflicts of interest and review by ancillary committees such as radiation safety and biosafety, and are unnecessary for research that qualifies as “exempt” under 45 CFR 46.101(b).

When following the NIH policy, the reliance agreement must document respective authorities, roles, responsibilities, and communication between an organization providing the ethical review and a participating organization relying on a reviewing IRB.

A reliance agreement is applicable and necessary only when both institutions are "engaged" in human subjects research. For example, if one site is only analyzing coded, de-identified data, and no one at that site can ever access the key linking codes to identifiers, then that site may not be "engaged" in human subjects research.

21.8 Selection of the IRB of Record

There is a minimum set of requirements to assist in the selection of the IRB of record. The evaluation criteria include the following:

- Evidence of a commitment to the highest ethical standards and ability to meet rigorous standards for quality and protection of research participants, e.g., through accreditation or assessment of policies, procedures, and practices;
- Ability to meet regulatory requirements;
- Well-established track record of compliance and performing high quality reviews, e.g., no regulatory errors or failures with Department of Health and Human Services (DHHS) or Food and Drug Administration (FDA);
- Appropriate expertise and experience to review the proposed research and the capacity to review the study protocol and participating site study documents;
- Recognition of the importance of building trust across all sites;
- Capacity to develop and maintain the respect and trust of the research participants and the communities in which the research is performed;
- Willingness and ability to serve as a Privacy Board to fulfill the requirements of the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule for use or disclosure of protected health information for research;
- Adherence to communication standards and a commitment to transparency through sharing information about the review process, e.g., meeting minutes, approval status;
- Adequate institutional infrastructure and support, and evidence of quality and robustness of the institution’s human research protection program;

- Sufficient staff to handle communications between all sites for initial review, continuing review, adverse events, amendments, etc.;
- Available interoperable information technology resources to facilitate communication and exchange of information between the participating institutions;
- Sufficient resources to negotiate and track authorization agreements;
- Ability to account for the IRB costs for review and management and how those costs will be met;
- Adequate processes in place and administrative support to handle additional review responsibilities; and
- Institutional impact the single IRB (sIRB) will have on the institution's HRPP policies, accreditation status, tracking and management processes.

21.9 Responsibilities when PBRC is the Lead Site or Reviewing IRB

21.9.1 Organization

1. Ensuring that the composition of the IRB is appropriate for the research to be reviewed and complies with applicable laws.
2. Ensuring that business functions are separated from IRB review.
3. Conducting IRB review of research according to all applicable regulations and laws, including initial review, continuing review, and review of modifications.
4. Conducting review of the addition of investigative sites to previously approved protocols. The IRB may decide to review these additions as separate protocols or as modifications to previously approved research, and they may decide to handle such modifications using the expedited procedure rather than the convened IRB for review. When the expedited procedure is used, the IRB must specify the criteria for when the addition of an investigative site is considered to be a minor modification.
5. Ensuring that the organization has final authority to determine whether researcher/staff conflict of interest and any proposed management allows the research to be approved.
6. Reviewing unanticipated problems involving risks to subjects or other;
7. Ensuring procedure for suspending or terminating approval.
8. Having procedures for notifying the researcher of IRB decisions and, if applicable, the relying organization.
9. Making available relevant IRB records, including but not limited to minutes, approved protocols, consent documents, and other records that document the IRB's determinations to the relying organization upon request.
10. Having the authority to perform or request an audit of research under its review.

11. Making relevant IRB policies readily available to the relying organization, and communicating updates to the relying organization as needed.
12. Specifying the contact person/contact information for the reviewing IRB so researchers/staff can ask questions, express concerns, and convey suggestions.

21.7.2 Principal Investigator

1. The PBRC investigator must complete the IRB Cede Review Request form to initiate the reliance review process.
2. Ensuring that any necessary internal organizational reviews and approvals are obtained.
3. Assisting the PBRC IRB in obtaining information about the external site's local requirements or context relevant to the research.
4. Submitting all relevant documents to the IRB (e.g. protocol, consent forms, modifications to previously approved research, continuing reviews, etc.).
5. Ensuring reporting of any proposed changes to the research to the PBRC IRB prior to implementation unless the change is necessary to eliminate apparent immediate hazards to the subject(s).
6. Ensuring reporting of any unanticipated problems involving risks or others in accordance with the reliance agreement.
7. Ensuring researchers provide data safety monitoring to the PBRC IRB.
8. Ensuring reporting of noncompliance, complaints, deviations, and other reports in accordance with the PBRC reporting requirements.
9. Ensuring adequate space and resources are available to conduct the study.

21.10 Responsibilities when PBRC is the Relying Organization (when PBRC is NOT the IRB of Record)

21.10.1 Organization

The organization must ensure that the lead organization's policies and procedures describe the roles of the organization and researchers when relying upon another organization's IRB, including:

1. Specifying the internal contact person so researchers and staff may ask questions, express concerns, and convey suggestions regarding the use of the reviewing IRB.
2. Ensuring through education or other support, that researchers understand which activities are eligible for review by another IRB.
3. Ensuring that researchers/staff have the appropriate education/training, qualifications, expertise, and knowledge to conduct the research and fulfill

their responsibilities and obligations under law, regulation, guidance, or policy.

4. Complying with the determinations and requirements of the reviewing IRB.
5. Providing the reviewing IRB with requested information about local requirements or local research context issues relevant to the IRB's determination, prior to IRB review.
6. Notifying the reviewing IRB when local policies that impact IRB review are updated.
7. Ensuring that researchers of the relying organization may not approve research subject to the reliance agreement if it has not been approved by the reviewing IRB.
8. Acknowledging that researchers must cooperate in the reviewing IRB's responsibility for initial and continuing review, record keeping, and reporting, and that all information requested by the reviewing IRB must be provided in a timely manner.
9. Requiring researchers and research staff disclose conflicts of interest according to the process agreed upon between the organization and reviewing IRB, and comply with any conflict of interest management plans that may result.
10. Reporting promptly to the reviewing IRB any proposed changes to the research. The investigator cannot implement changes to the research (including changes in the consent document) without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to the participants.
11. Ensuring researchers will not enroll participants in research prior to review and approval by the reviewing IRB, and meeting all other applicable requirements and approvals for the study.
12. Ensuring that researchers, when responsible for enrolling participants, will obtain, document, and maintain records of consent for each participant or each participant's legally authorized representative.
13. Reporting promptly to the reviewing IRB any unanticipated problems involving risks to participants or others according to the requirements specified in the reliance agreement.
14. Ensuring researchers provide to the reviewing IRB data safety monitoring reports they receive, according to the IRB's reporting policy.
15. Ensuring reporting of non-compliance, participant complaints, protocol deviations or other events according to the requirements specified in the reliance agreement.
16. Conducting monitoring in addition to, or in cooperation with, the reviewing IRB, when appropriate.

17. Specifying the contact person and providing contact information for researchers and research staff to obtain answers to questions, express concerns, and convey suggestions regarding the use of the reviewing IRB.
18. Ensuring researchers and research staff have appropriate qualifications and expertise to conduct the research, are knowledgeable about laws, regulations, codes and guidance governing their research, and are knowledgeable about the organization's policies and procedures.

21.10.2 Principal Investigator

1. PBRC Investigators submit the following to the IRB when another IRB is serving as the IRB of Record:
   a. All funding information (including a copy of the grant, if available);
   b. Key Study Personnel and their qualifications;
   c. Any basic information about the study type and reviewing IRB;
   d. A description of the study;
   e. All enrollment information for participants at PBRC;
   f. A description of all drug/devices that will be used in the course of the study, and safety information, if applicable;
   g. A description of any PHI to be used/disclosed, if applicable;
   h. Any conflicts of interest;
   i. The IRB approved consent including local context information and PBRC-specific language (e.g., HIPAA authorization and subject injury language);
   j. The IRB approved study protocol;
   k. The IRB approval letter from the reviewing IRB;
   l. Reports of non-compliance and adverse events/unanticipated problems that occur at PBRC; and
   m. Submitting all relevant IRB records, including but not limited to minutes and other records documenting IRB determinations to the relying organization upon request.

21.11 Responsibilities Delegated to Reviewing or Relying Organizations

1. Providing education to researchers and research staff.
2. Conducting scientific review.
3. Ensuring concordance between any applicable grant and the IRB application/protocol.
4. Reviewing requests for waivers of alterations of the requirement for HIPAA authorization, when applicable.

5. Reviewing potential noncompliance, including complaints, protocol deviations, and result audits, including
    - Identifying which organization is responsible for deciding whether an allegation of noncompliance has a basis in fact;
    - Identifying which organization's process is used to decide whether an incident of noncompliance is serious or continuing.
6. Obtaining management plans for researcher and research staff conflicts of interest. If the relying organization maintains responsibility for this issue, the management plan must be provided prior to the decision by the IRB.
7. Managing organizational confict of interest related to the research.
8. Ensuring that, should termination of a reliance agreement occur, one of the parties is clearly responsible for continued oversight of active research until closure or a mutually agreed upon transfer of the studies.

21.12 When following DHHS or FDA regulations or requirements, the agreement or procedures address:

1. Whether the relying organization applies its FWA to some or all research, and ensuring that the IRB review is consistent with the requirements of the relying organization's FWA.
2. Which organization is responsible for obtaining any additional approvals for DHHS when the research involves pregnant women, fetuses, neonates, or children (or any other applicable federal agency or department requirements).
3. Which organization is responsible for reporting serious or continuing non-compliance; unanticipated problems involving risks to participants or others; and suspensions or terminations of IRB or EC approval. Reporting may be done by the reviewing IRB, the relying organization, or jointly, but must be clearly defined in policies or a written agreement

21.13 When following the NIH Single IRB policy, the agreement or procedures documents or describes:

1. The requirement for single IRB review applies to awardees in the United States and participating research sites in the United States.
2. The requirement for single IRB review does not apply to organizations outside the United States.
3. Awardee organizations are responsible for ensuring authorization agreements are in place, and that documentation is maintained.
4. Who is responsible for meeting additional certification requirements, such as Certificates of Confidentiality or the NIH Genomic Data Sharing Policy.

5. Participating sites are expected to rely on the single IRB, though they may conduct their own review in accordance with NIH policy on exceptions from single IRB review.

21.14 When relying upon an IRB that is not AAHRPP accredited:

1. The HRPP must ensure that the research is being reviewed appropriately and complies with applicable law and regulations.
2. The HRPP will conduct an IRB evaluation review based upon OHRP evaluation tools to confirm compliance with the organization's ethical standards and with applicable law and regulations. The extent of the review of the non-accredited IRB can vary, depending upon the level of risk to participants in the research.

21.15 When additional reviews relevant to the HRPP are conducted by an external organization, the HRPP will:

1. Inform the external review that additional regulatory requirements, for example, those of DoD or DoJ, may apply.
2. Provide education to researchers regarding additional relevant reviews.