I. PURPOSE

This standard operating procedure describes the IRB's procedures for review and oversight of research conducted under a cooperative agreement with an external (outside) IRB.

It is permissible under 45 CFR 46.114 and 21 CFR 56.114 for an institution to rely on an IRB of another institution for protocol review and oversight. Cooperative research projects include those where more than one institution is engaged in human subjects research activities. During the conduct of cooperative research projects, even when entering into reliance agreements, each institution is responsible for safeguarding the rights and welfare of human subjects.

II. POLICY STATEMENT

When participating in a cooperative project with another institution, the CHOP IRB may provide IRB oversight for another institution, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.

III. SCOPE

These policies and procedures apply to all research submitted to the IRB.

IV. DEFINITIONS

External IRB: The IRB at another institution or an independent IRB. An external IRB must be registered with OHRP (and FDA if the research if FDA regulated) in order to serve as the Reviewing IRB (IRB of record).

Local or Internal IRB: One of CHOP's IRB.

IRB Authorization Agreement (also referred to as a Reliance Agreement or Cooperative IRB Agreement): An agreement between the institution conducting the research and the Reviewing IRB. The CHOP Research Institute Signature Authority Matrix outlines the authorized signer of reliance documents.

Master Reliance Agreement: An agreement between two or more institutions or IRBs that can cover future research. Examples of Master Reliance Agreements include CHOP-Penn Master Reliance Agreement, SMART IRB Agreement, National Cancer Institute Central IRB Authorization Agreement. Typically, Master Reliance Agreements are used with determination letters or other mechanisms to document the implementation of the reliance agreement for specific studies (e.g., Determination Form, Cede Letter).

Relying Institution: The institution that has assigned another IRB to serve as the Reviewing IRB under an IRB Authorization Agreement.

sIRB (Single IRB): The designated Reviewing IRB for a multi-center research study where each US-based institution agrees to rely on the sIRB for specific non-exempt

human subjects research.

V. PROCEDURES

A. Documentation of IRB reliance

1. Reliance between the Reviewing IRB and Relying Institution will be governed by a signed IRB Authorization Agreement or Master Reliance Agreement.

    (a) The documentation will define the terms, scope and limits, and roles and responsibilities of the Reviewing IRB and relying institution.

    (b) IRB Authorization Agreements may apply to multiple studies between institutions or may be developed on a study-by-study basis for a single study. If the latter, the Director, Human Subjects Research, will work with an IRB administrator at the external IRB to execute an IRB Authorization Agreement.

    (c) Documentation of reliance may be executed as a separate form negotiated between two (or more) institutions or through an electronic reliance platform (e.g., SMART IRB), provided both the relying and reviewing institutions have signed onto that reliance agreement.

2. Fully executed reliance documentation and approval from the Reviewing IRB is required prior to initiation of human subjects research activities by the relying institution.

B. Serving as the Reviewing IRB for another institution

1. When appropriate, the CHOP IRB may serve as the Reviewing IRB for a relying institution. Examples of appropriate circumstances include, but are not limited to the following:

    (a) multi-center research studies where a CHOP principal investigator (PI) is the overall PI of the federal grant funding the study (e.g., NIH funding);

    (b) multi-center research studies where a CHOP PI is participating in the research and CHOP's IRB has agreed to be the sIRB;

    (c) research studies where greater than minimal risk study interventions or procedures occur at CHOP and where follow-up procedures are performed at external institutions;

    (d) the research funder mandates (e.g., NIH) the use of an sIRB;

    (e) other compelling circumstances where, due to the nature and location of the research activities, CHOP has unique experience to be better suited to provide oversight.

2. In addition to the submission requirements outlined in SOP 301, the following must be submitted when CHOP is the Reviewing IRB:

(a) Local context information, including local laws and institutional policies applicable to the research;

(b) Conflict of Interest management plans of all investigators at the outside institution (when applicable); and

(c) Site-specific consent form(s) and recruitment materials (when applicable).

3. The addition of a relying institution will be reviewed by the IRB as a minor change to previously approved research, as described in **IRB SOP 403**.

4. The IRB will issue IRB approval and the IRB-approved consent forms (when applicable) to the Principal Investigator at the Relying Institution, with a reminder to comply with CHOP IRB Policies and relying institutional requirements.

5. Continuing reviews, amendments and unanticipated problem involving risks to subjects or others submitted by the PI of the relying institution will be reviewed as described in accordance with the CHOP IRB SOPs.

C. Relying on an External IRB

1. When appropriate, CHOP may rely on an external IRB to serve as the Reviewing IRB. Examples of appropriate circumstances include, but are not limited to the following:

(a) multi-center research where a specialized central IRB has been established for the sole purpose of reviewing a category of investigative studies (e.g., the National Cancer Institute Central IRB);

(b) multi-center research where a cooperative study group has designated an IRB to serve as the sIRB for a study or group of studies.

(c) multi-center research where the funder (e.g., NIH) mandates the use of a sIRB.

2. The following must be submitted in CHOP's electronic system when CHOP relies on an external IRB:

(a) Unless otherwise agreed upon with the CHOP IRB, a list of all CHOP employees who will be engaged in human subjects activities for CHOP;

(b) A copy of the Reviewing IRB approval letter for the submitted protocol. Additional documentation such as review type (e.g., expedited or full board), the applicable IRB determinations (e.g., minimal risk,

Subpart D) and IRB meeting minutes may be requested, as applicable. Acceptable approval letters include, but are not limited to:

- Initial IRB approval of the protocol issued to the industry funder of the protocol or the overall study PI;
- Approval for a protocol amendment issued the overall study PI;
- Continuing review approval of another institution's submitted progress report.

(c) A copy of the multi-center protocol;

(d) A copy of the informed consent template(s) with CHOP site-specific information and any recruitment materials that will be used at CHOP;

(e) A copy of questionnaires/interview guides that will be used at CHOP;

(f) A copy of the Investigator's Brochure, if applicable;

(g) Device Manual, if applicable.

3. The reviewer will determine if the IRB review pathway indicated appears to be appropriate (e.g., full board review for a greater than minimal risk study) and local context issues are addressed, including the following:

(a) CHOP policies;

(b) State law;

(c) CHOP training requirements;

(d) COI disclosures; and

(e) Consent/HIPAA Authorization to be used at CHOP includes CHOP requirements (e.g., CHOP PI contact information, CHOP-specific injury compensation language, Authorization includes CHOP, as applicable).

4. CHOP acceptance of the Reviewing IRB's oversight will be issued once the ancillary approvals are issued (e.g., Conflict of Interest Committee, Device Committee, Pharmacy) and the local context review is finalized.

5. The following updates must be submitted in CHOP's electronic system as long as CHOP relies on an external IRB:

(a) Continuing Review approvals issued by the Reviewing IRB;

(b) Amendment/Modification Approval letters issued by the Reviewing

IRB and corresponding documents (e.g., revised protocol, modified consent documents, updated Investigator's Brochure);

(c) Unanticipated problem involving risks to subjects or others and the Reviewing IRB's determinations, as applicable;

(d) Allegations of non-compliance and the Reviewing IRB's determinations, as applicable; and

(e) Subject complaints and the Reviewing IRB's determinations, as applicable.

VI. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.114	Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html)

VII. REFERENCES TO OTHER APPLICABLE SOPS

CHOP Research Institute: Signature Authority Matrix	SOP 403: Amendments and Reports of New Findings SOP 404: Continuing Review of Approved Research

VIII. RESPONSIBILITIES

Title	Responsibility
Director, Human Subjects Research (HSR)	Director, HSR (or designee) is responsible for negotiating IRB Authorization Agreements, maintaining complete files on all research reviewed via an IRB Authorization Agreement negotiated with another IRB and for all applicable regulatory compliance requirements.
Institutional Official (IO)	IO (or designee) is responsible for approving and signing Cooperative Agreement Determination forms for studies conducted at CHOP and UPenn.

IX. ATTACHMENTS

The IRB website includes forms for IRB authorization agreements including:

1. Penn-CHOP Authorization Agreement and current Determination Form
2. NCI CIRB Authorization Agreement
3. CHOP Authorization Agreement (when CHOP will be the Primary IRB for an external institution)

X. REVISIONS:

02-14-2007	Revised to incorporate changes in IRB office staff responsibilities.
11-10-2008	Revision includes provision to permit CHOP to serve as the IRB of record for other institutions. Specific additional submission requirements when CHOP is the IRB of record and when CHOP is not the IRB of record were added (Sections V.D and V.E).
06-09-2010	Revised attachment section to reflect updates to the documents available on the IRB website. This revision also authorizes the Director, HSR to negotiate IRB and sign authorization agreements.
01-13-2013	Remove reference to facilitated review with the NCI Central IRB and clarified who may sign authorization agreements.
06-10-2022	Revised to reflect current processes and reference applicable policies.

XI. APPROVAL:

Approval Indicator: Approved by Amy Schwarzhoff and Barbara Engel on 06/10/22
Amy Schwarzhoff, Director, Human Subjects Research and Barbara Engel, Chair, CPHS

XII. APPENDIX A

Division of Responsibilities When CHOP is the IRB of Record

(terms contained in the CHOP Cooperative Agreement)

The responsibilities of the CHOP IRBs are to:

1) *Maintain an FWA with OHRP and the registration of its IRBs with both OHRP and the FDA;*

2) Maintain a Board membership that satisfies the requirements of 45 CFR 46, 21 CRF 56 and provide special expertise as needed from Board members or consultants to adequately assess all aspects of the study;

3) Make available to the local institution upon request, the CHOP IRB Standard Operating Procedures;

4) Perform initial reviews, continuing reviews, reviews of submitted Serious Adverse Events, reviews of protocol amendments, reviews of DSMB reports, and reviews of any other documents submitted by the Principal Investigator of the research study subject to this agreement;

5) Maintain and make accessible to the local IRB at the relying institution the CHOP IRB application, protocol reviews, letters to Principal Investigators, approvals and disapprovals, and minutes of the CHOP IRB meetings relevant to the protocol;

6) Notify the relying institution immediately in the event of a suspension or restriction of the CHOP IRB's authorization to review studies; and

7) Notify the local institution of any CHOP IRB policy decisions or regulatory matters that might affect the institution's reliance on CHOP IRB reviews or performance of the research at the local institution.

The responsibilities of the relying institution are to:

1) *Maintain a Federal Wide Assurance (FWA).*
2) Maintain a human subjects protection program, as required by the DHHS OHRP;
3) Provide the CHOP IRB with the current the names and addresses of a local contact person who has the authority to communicate for the IRB at the relying institution (e.g., the local IRB administrator);
4) Maintain a local IRB whose membership satisfies the requirements of 45 CFR 46 and 21 CRF 56;
5) Notify the CHOP IRB immediately if there is ever a suspension or restriction of the local IRB's authorization to review studies;
6) Ensure that the investigators and other staff at the relying institution who are conducting the research are appropriately qualified and meet the institution's standards for eligibility to conduct research;
7) Notify the CHOP IRB immediately if there is a suspension or restriction of the investigator at the relying institution;
8) Ensure the safe and appropriate performance of the research at the relying institution. This includes, but is not limited to: monitoring study compliance; reviewing major protocol violations, and any unanticipated problems involving risk to subjects and others that occur at the institution; ensuring a mechanism exists by which complaints about the research can be made by local study participants or others.

   Any actions taken as a result of problems that are identified in these areas should be shared with the CHOP IRB and the Principal Investigator at CHOP;
9) Require the PI at the relying institution to maintain appropriate copies of all approvals, and other correspondence documenting the review and approval of the research as required by the regulations;
10) Maintain compliance with any additional state, local, or institutional requirements related to the protection of human subjects.