**Harvard Pilgrim Health Care, Inc.**
**Harvard Pilgrim Health Care Institute, LLC**
***Office of Sponsored Programs***

**Policy and Procedure**

---

**TITLE:** Multi-Site Research

---

## PURPOSE:

To describe:

- the process for Institutional Review Board (IRB) review involving cooperative research conducted at different geographic locations and/or in collaboration with other institutions; and
- the steps the IRB follows to communicate among the sites involved in the multi-site study on issues other than IRB review, such as reporting of unanticipated problems, protocol modifications and interim results.

## PERSONS AFFECTED:

This policy & procedure (P/P) applies to all Harvard Pilgrim Health Care, Inc. (HPHC) and Harvard Pilgrim Health Care Institute, LLC (HPHCI) (collectively, HPHC/I) personnel engaged in research, teaching or research administration activities in support of the charitable and educational mission of HPHC.

## POLICY:

Protection of subjects in multi-site research projects remains the responsibility of all institutions involved in the research. Each institution is responsible for complying with applicable laws, its institutional policies and Federalwide Assurances (FWA), as well as its own IRB policies and procedures, including the reporting and investigation of unanticipated problems (UP) involving risks to subjects or others, interim results, and protocol modifications. The IRB at HPHC/I shall review all research involving human subjects conducted at or by HPHC/I employees, regardless of the research location, including research conducted in foreign countries. Other institutional HIPAA Privacy Rule contract responsibilities (e.g., data use agreements, business associate agreements, disclosure accounting) remain the responsibility of each institution.

When reviewing an international proposal, the IRB shall be aware of the local research context and shall take into account any ethics review conducted at the other research sites from the appropriate authorities as part of their review. Procedures normally followed in foreign countries to protect human subjects may differ from those set forth in HPHC/I policy and 45 CFR 46 (the "Common Rule"). The IRB may review translations of all relevant research documents (including informed consent, recruitment materials, and questionnaires) for accuracy. Protections afforded to subjects participating in research in a foreign county must reflect the protections provided to subjects in the United States. Requests to review and modify standard elements of domestic approvals may be considered by the IRB.

HPHC/I's responsibilities under its FWA apply whenever HPHC/I or its employees are engaged in human subjects research, regardless of the geographic location of the research.

When engaged in research projects involving more than one institution, HPHC/I may enter into joint reviewing arrangements or rely on the review of one of the institution's IRBs. Collaborative research requires IRB review by each site engaged in the research, unless an IRB Authorization Agreement (IAA) is in place. An IAA is the vehicle used to cede review to another IRB. At its discretion, the HPHC/I IRB may consider accepting review responsibilities for another institution or rely on another IRB for review.

Quality assurance reviews may be conducted to confirm that the study is in compliance with the protocol and the requirements of the IRB of record, regardless of whether HPHC/I reviews the research or relies on an external IRB. HPHC/I remains responsible for ensuring the safety of subjects and the appropriate performance of the research.

**DEFINITIONS:**

For the purposes of this policy:

*Cooperative (Multi-Site) Research*

Those research projects which involve more than one institution. In the conduct of multi-site research projects, each institution is responsible for safeguarding the rights and welfare of human subjects. An institution participating in a multi-site project may enter into a joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.

*Unanticipated problems*

Any incident, experience or outcome, including an adverse event that meets all of the following criteria:

a. unexpected (in terms of nature, severity, or frequency) given (1) the research procedures that are described in the protocol related documents, such as the IRB approved research protocol and informed consent documents; and (2) the characteristics of the subject population being studied;
b. related or possibly related to a subject's participation in the research; and

c. suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic or social harm) than was previously known or recognized.

**PROCEDURE:**

1. When the investigator is the lead investigator of a cooperative (multi-site) study, the IRB must evaluate whether the management of information that is relevant to the protection of subjects is adequate. The lead investigator is responsible for reporting:
   a. unanticipated problems involving risks to subjects or others;
   b. interim results; and
   c. protocol modifications.

2. Investigators must complete an application in IRBNet for the IRB to make a determination of the appropriateness of ceding or accepting review. The HPHC/I IRB must review a complete application package before agreeing to cede to another qualified IRB.

3. If HPHC will serve as the reviewing IRB for a multi-site study, a cede request form will be included with either the initial review application or an amendment application (if the site/cede request is added later).

4. IRB staff is alerted to a request to cede IRB review to another institution's IRB by the appearance of the *New Project* submission flagged in the *Submissions Manager* page in IRBNet. A New Project submission is made by the principal investigator (PI) or designee to document requests to cede review to another IRB.

5. The submission is screened by IRB staff in accordance with federal regulations and institutional requirements. A new project cede request submission must include the following:
   a. PI's electronic signature;
   b. Grants Manager's (GM) electronic signature;
   c. HPHC Cede Request Form;
   d. study protocol; and
   e. conflict of interest (COI) attestations, included in the Cede Request form.

6. The new project cede request submission may also include the following:
   a. the reviewing IRB's current approval;
   b. the reviewing IRB's completed application or amendment adding HPHC as a site;
   c. a copy of the SMART IRB Form (for sites that are part of SMART IRB); and
   d. other materials as requested by IRB staff.

7. The IRBNet submission package will be marked with the Tag "Cede Request Pending (HPHC ceding IRB)".

8. If IRB staff determine that the submission is missing information or requires clarification, the submission package is "unlocked" and the required follow-up is listed in the message to the PI detailing the reasons for being unlocked. Once the PI provides the required information and updates are made, the PI will mark the revisions complete in IRBNet which queues the submission back to IRB staff.

9. The submission will be reviewed by the Research Integrity & Compliance Officer (RICO) and/or IRB Chair to determine if the cede request is appropriate. In order to make this determination, the RICO and/or IRB Chair will consider:

a. if the HPHC/I PI is under any suspension or in a corrective action plan;
b. the FWA for the reviewing IRB is active;
c. the nature of the research study and rationale for the cede request.

10. If not appropriate, the PI will be notified of the decision in IRBNet and will be advised to submit a full application to the HPCH IRB for review. The submission would then be processed according to *Policy and Procedure on Initial Full Review*.

11. If the cede request is determined to be appropriate by the RICO and/or IRB Chair, and once the submission is complete, the submission package will be assigned for *Facilitated Review* by IRB staff. IRB staff will update the *Review Details* of the submission in IRBNet, adding the agenda date and review type.

12. IRB staff will communicate with the IRB contact at the external reviewing IRB to confirm the external reviewing IRB agrees with the request. IRB staff will record any notes in the comments section of the package in IRBNet regarding these communications.

13. Once the reviewing IRB confirms they agree to accept the cede request, IRB staff will facilitate execution of an IRB Authorization Agreement (IAA):

a. For SMART IRB cede requests: HPHC has signed a Master Reliance Agreement and therefore individually executed IAA's are not necessary. Confirmation of the cede review may also be documented in the SMART IRB system (https://smartirb.org). The lead site will have communicated to the relying IRB(s) the agreement to cede and will document the relationship in the SMART IRB system as applicable.
b. For all other cede requests: an IAA will be sent for review/execution by each institution's Signatory Official. A copy of the fully executed IAA will be attached to the comments section of the IRBNet package.

c. A package *tag* will be added documenting the type of IRB Authorization Agreement that is in place.

14. IRB staff will update IRBNet with the appropriate determination in the *Review Details* of the package. The following fields will be updated:
   a. review type, action, effective date;
   b. project expiration date if applicable (the reviewing IRB's current expiration date);
   c. next report due if project does not have an expiration date under the 2018 Rule; and
   d. Minutes.

15. A *Board Action* notification will automatically be sent to the PI in IRBNet.

16. A determination letter will be created by IRB Staff to reflect the cede review. The letter will be published in IRBNet and the notification of the published letter will automatically be sent to the PI.

17. IRB staff will apply or remove any additional submission tag(s) as appropriate to the study as necessary.

18. Throughout the life cycle of a study that has been ceded to another institution's IRB, approved amendments reflecting approved revisions or modifications and continuing review approvals may be submitted to IRB staff for inclusion in HPHC IRB files.

19. For Amendments to a study ceded to another IRB:
   a. IRB staff is alerted to an amendment approved by the reviewing IRB by the appearance of the *Amendment/Modification* submission flagged in the *Submissions Manager* page in IRBNet.
   b. The submission is screened by IRB staff in accordance with federal regulations and institutional requirements and to determine if the cede review continues to be appropriate. An amendment submission for a ceded project may include the following:
      (1) Ceded Study Submission Cover Sheet;
      (2) PI electronic signature;
      (3) GM electronic signature;
      (4) reviewing IRB's application;
      (5) reviewing IRB's approval; and
      (6) additional information as applicable to the modification or revision.
   c. Generally, the reviewing IRB does not review staff changes at local sites. When HPHCI has ceded to another institution, staff amendments only will be administratively reviewed and approved by the IRB office. A staff amendment submission may include the following:

(7) Amendment form detailing staff change;
(8) PI electronic signature;
(9) GM electronic signature;
(10) Conflict of interest (COI) attestations, included in the Amendment form; and
(11) Additional information as applicable to the staff change.

d. If the submission is missing information or requires clarification, IRB staff shall unlock the submission package and provide a message to the PI detailing the reasons for being unlocked. Once the PI provides the required information and updates are made, the PI will mark the revisions complete in IRBNet which queues the submission back to IRB staff.
e. Once the submission is complete, the submission package will be assigned for *Facilitated Review* by IRB staff to prepare for acknowledgment. Staff changes only will be assigned for *Administrative Review* by IRB staff to prepare for administrative approval. IRB staff will update the *Review Details* of the submission in IRBNet, adding the agenda date and review type.
f. IRB staff will then update IRBNet to acknowledge the submission. Staff changes only will be administratively approved. IRB staff will record any notes in the comments section of the package in IRBNet regarding this package. The following fields will be updated in the *Review Details* of the package:
(1) review type, action, effective Date.
(2) minutes will be recorded as appropriate.
g. An IRB action notification of acknowledgment, or administrative approval, will automatically be sent to the PI in IRBNet.

20. The PI is responsible for submitting copies of IRB approvals for continuing review in IRBNet at the time of renewal when applicable. Amendments and unanticipated problems previously reported to the reviewing IRB may be submitted with renewal documentation to the HPHC IRB. If it is determined by the RICO that it is no longer appropriate to cede review of the study, the RICO will notify the reviewing IRB and the HPHCI investigator of its decision and reasons. The RICO will make that determination based on review of the continuing review application that was submitted to the lead IRB. The application is reviewed for issues such as:
a. non-compliance relating to local investigator;
b. serious non-compliance issues at the lead site.

21. For continuing review of a study ceded to another IRB:
a. IRB staff is alerted to a continuing review approved by the reviewing IRB by the appearance of the *Continuing Review/Progress Report* submission flagged in the *Submissions Manager* page in IRBNet.

b. The submission is screened by IRB staff in accordance with federal regulations and institutional requirements and to determine the cede review continues to be appropriate. A continuing review submission for a ceded project may include the following:
   (1) Ceded Study Submission Cover Sheet;
   (2) PI electronic signature;
   (3) reviewing IRB's application;
   (4) reviewing IRB's approval;
   (5) additional materials as applicable.
c. If the submission is missing information or requires clarification, the submission package is "unlocked" and the IRB Staff will include the required follow-up in the message to the PI detailing the reasons for being unlocked. Once the required information is present and updates are made, the PI will mark the revisions complete in IRBNet which queues the submission back to IRB staff.
d. Once the submission is complete, the submission package will be assigned for *Facilitated Review* by IRB staff to prepare for acknowledgment. IRB staff will update the *Review Details* of the submission in IRBNet, adding the agenda date and review type.
e. IRB staff will then update IRBNet to acknowledge the submission. IRB staff will record any notes in the comments section of the package in IRBNet regarding this package. The following fields will be updated in the *Review Details* of the package:
   (1) review type, action, effective date
   (2) project expiration date (the reviewing IRB's current expiration date)
   (3) minutes, as appropriate
   (4) A *Board Action* notification of acknowledgment will automatically be sent to the PI in IRBNet.

22. The investigator must notify the HPHC IRB when the ceded study has been closed by the Institution providing review responsibilities and research activities are no longer taking place.

**REVISION HISTORY:**

| | |
|---|---|
| **Department:** OSP - Research Integrity & Compliance | **Title**: Multi-Site Research |
| **Effective Date**: 08/23/23 | **Owner:** Research Integrity & Compliance Officer |
| **Replaces P/P Dated**: IRB SOP (2/2017, 08/27/19, 08/13/20); IRB Procedure 001.3 (12/10/13); P/P (01/21/19, 07/19/18) | |
| **Related Documents:** Policy and Procedure: *Initial Full Review*; Cede Request Form; Ceded Study Submission Cover Sheet; Sample Cede Determination Letter; Submission Checklist HPHC Cede Review | |
| **References**: 45 CFR 46.114; AAHRPP Standard I-9; Element II.2.I; AAHRPP Tip Sheet 24 | |