**Harvard Pilgrim Health Care, Inc.**
**Harvard Pilgrim Health Care Institute, LLC**
***Office of Sponsored Programs & Office of Research Integrity and Compliance***

**Policy and Procedure**

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**TITLE:** Review of Modifications to Approved Research

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## PURPOSE:

To describe the amendment submission process for Institutional Review Board (IRB) review of proposed modifications or changes to previously approved research.

## AFFECTED PERSONS:

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, including the IRB.

## POLICY:

Investigators may not initiate any changes or modifications to approved research activities without prompt reporting to the IRB of the proposed changes in accordance with the amendment submission process for IRB review and approval prior to initiation of these changes or modifications. Examples of modifications or changes that require amendment submissions for IRB review include, but are not limited to changes in:

- study population;
- research personnel;
- recruitment procedures;
- consent/assent forms;
- inclusion/exclusion criteria;
- medications;
- advertising materials; and
- location where research will be conducted.

The IRB shall notify investigators and HPHC/I in writing of its decision to approve or disapprove the proposed modifications or the modifications required to secure IRB approval of

the proposed changes. If the IRB decides to disapprove proposed modifications or changes to a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.

If the investigator makes changes in approved research without IRB review and approval when necessary to eliminate apparent immediate harms or hazards to subjects, the investigator must immediately (within seven days) report the changes to the IRB for review in addition to submitting a determination as to whether the changes are consistent with the subject's continued welfare.

Investigators must promptly notify the IRB in writing of any change in a protocol's status, such as discontinuation or completion of a study.

**PROCEDURES:**

1. Prior to implementation of any change or modification to an approved study, the principal investigator (PI) or designee must initiate the amendment submission process by submitting an amendment to an approved study in IRBNet using either the *Amendment Short Form* or *Amendment Long Form*.

2. IRB staff is alerted to an amendment submission in IRBNet via email and by the appearance of the *Amendment/Modification* submission flagged in the *Submissions Manager* page in IRBNet.

3. The submission is screened by IRB staff to ensure it includes the following:
   a. a completed *Amendment Long Form* or *Amendment Short Form* and applicable attachments;
   b. PI's electronic signature;
   c. Grant Manager's signature (for HPHC studies).

4. The amendment submission may also include revised study materials to correspond with the change, such as:
   a. revised informed consent forms;
   b. revised protocol;
   c. revised authorization to use and disclose PHI for research (HIPAA authorization) forms or waiver requests;

   d. amendments that involve a change of PI (both the exiting and entering PI must sign the submission package); and
   e. other attachments as applicable to the modification or change.

5. All revised materials must be properly uploaded in IRBNet showing the "paper-stack" of the document history in the *Designer* section. All revised materials must contain tracked changes when appropriate to assist the IRB in their review.

6. If 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. Once the required information is present and updates are made, the PI (or PI's designee) will mark the revisions complete in IRBNet which queues the submission back to IRB staff.

7. When the submission is complete and ready for IRB assignment, the submission package will be assigned for expedited review or full committee review according to the Policies and Procedures*: Initial Full Review;* and *Initial Expedited Review*.

8. If the amendment submission is assigned for full IRB review, all members attending the meeting shall be given shared access to review the submission (including all modifications) when the item is assigned to an agenda one week prior to the convened meeting.

9. As part of the amendment review, the IRB will determine if any significant new findings that arise from the review process and that might relate to subjects' willingness to continue participation are provided to subjects (e.g., a revised consent form or a letter to subjects).

10. After IRB review, IRB staff will update IRBNet with the appropriate determination within two weeks following the review. The following fields will be updated:
    a. *review type, action, effective date*; and
    b. minutes, recorded as appropriate.

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

12. A determination letter will be generated and edited to accommodate the review. The letter will be published in IRBNet and the notification of the published letter will automatically be sent to the PI.

13. IRB staff will apply or remove any submission tag(s), such as "cede request pending", "genetic analysis", "waiver of auth approved", etc., as appropriate to the study if necessary according to the modification or change.

14. If applicable to the amendment, the *Project Notes* section in IRBNet will be used to document any special requirements or notes that apply to the entire study that are unavailable by tag (e.g., the category of expedited review that applies to the project; if a cede is involved,

list ceding or reviewing institution). *Project Notes* can only be viewed and edited by users with administrative access.

15. If the approved amendment included a change of local PI, an email notification shall be sent to the PI (or designee) requesting submission of a new empty package, *submission type* "Other". The local PI will change his/her name by clicking the edit field in the *Designer* tab to the newly approved PI and then submit the package to the IRB to document the approved name change in IRBNet.

Minor modifications or changes

When the IRB requires modifications to research to secure approval, verification of those modifications by the IRB Chair or experienced IRB reviewer without review by the convened IRB represents review by the expedited procedure. This process is sometimes referred to as "contingent approval" or "approval with conditions". When the IRB grants contingent approval, the IRB provides the researcher specific modifications required to secure approval; for example, "subjects must be 18 years or older" or "drop the placebo-controlled arm of this study".

The IRB does not grant approval contingent upon clarifications or modifications directly relevant to the determinations required of the IRB. Such requests include: "explain why subjects younger than 18 years of age will be allowed to participate", "provide additional justification for the use of placebo", or "clarify whether subjects will be offered counseling services at the end of the study". The convened IRB shall review responses to requests that require determinations not allowed under the expedited procedure. The IRB should exercise caution before using the expedited procedure to review clarifications, explanations, or additional information, or when a subcommittee of the IRB is needed to review requested modifications.

In addition, the IRB should exercise caution before delegating to an IRB member the authority to negotiate changes without review of those changes by a convened IRB.

Verification of IRB-requested modifications and other minor changes that would not materially affect an assessment of the risks and benefits of the study or do not substantively change the specific aims or design of the study may be reviewed by the IRB Chair (or designee – Director, Research Integrity and Compliance Officer), who is a voting member on the IRB) by expedited review. Examples of these kinds of minor changes include, but are not limited to: study staff changes; changes in a mailing address; grammatical or punctuation corrections; and changes in non-treatment equipment.

Expedited reviews of minor changes or modifications are reported to the IRB at the next available convened meeting.

Greater-than-minor changes or modifications

Any change or modification which materially affects an assessment of the risks and benefits of the study or substantially changes the specific aims or design of the study must be reviewed at a

convened meeting of the IRB. Amendments to the protocol require submission of an updated copy of the protocol and consent, if necessary.

Examples of greater-than-minor changes or modifications include, but are not limited to: omitted or changed items (e.g., funding) that may affect the level of risk; an increase in the number of study subjects; a change in procedure that requires a change in the consent; changes in the inclusion/exclusion criteria that result from changes in side effects.

Review of amendments for exempt studies

All proposed modifications or changes to studies that have previously met exempt criteria by the IRB must be submitted to the IRB for review. If the proposed modification or change alters the exempt status of the study, requiring either an expedited or convened IRB review, the investigator will be notified in writing to submit an application or amendment in IRBNet along with appropriate study materials for review.

**REVISION HISTORY:**

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| **Department:** Office of Research Integrity & Compliance | **Title**: Review of Modifications to Approved Research |
| **Effective Date**: 01/12/24 | **Owner:** Director, Research Integrity and Compliance Officer |
| **Replaces P/P Dated**: IRB SOP (02/17); IRB Procedures: 002.03 (07/17/14); 012.01 (07/17/14); P/P (01/21/19, 11/26/19, 11/19/20) | |
| **Related Documents:** Policies and Procedures: *Initial Full Review*; *Initial Expedited Review;* Forms**:** Amendment Short Form, Amendment Long Form; Reviewer Sheet: Amendment; Determination Letter templates | |
| **References**: 45 CFR 46.103(b)(4); 45 CFR 46.109; 45 CFR 46.116(b)(5); OHRP Guidance on Written Institutional Review Board (IRB) Procedures; Guidance on IRB Approval of Research with Conditions; 21 CFR 50.25(b)(5); 21 CFR 56.108(a); 21 CFR 56.109; ICH-GCP: 3.2.2, 3.2.3, 3.3.3, 3.3.4; AAHRPP Elements II.2.E.3 and II.2.F.3; AAHRPP Tip Sheets 16, 17 and 18 | |