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

Policy and Procedure

TITLE: Continuing Review

PURPOSE:

To describe the process for conducting continuing review of research by the Institutional Review Board (IRB).

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:

An IRB shall conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk, not less than once per year, except as follows: Unless an IRB determines otherwise, continuing review of research is not required in the following circumstances:
(i) Research eligible for expedited review in accordance with 45 CFR 46.110;
(ii) Research reviewed by the IRB in accordance with the limited IRB review (described in 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) or (8);
(iii) Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:

(A) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or

(B) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

PROCEDURE:

1. The investigator or designee completes a *Continuing Review/Progress Report Submission* package, including the *Continuing Review Form*, in IRBNet and submits it to IRB staff.

2. IRB staff is alerted to a continuing review submission in IRBNet via email and by the appearance of the *Continuing Review/Progress Report* submission flagged in the *Submissions Manager* page in IRBNet.

3. The continuing review submission is screened by IRB staff against the *IRB Submission Checklist - Continuing Review*. The IRBNet record includes the following materials in the *Designer* tab:
   a. the full protocol;
   b. application, or a protocol summary containing the relevant information necessary to determine whether the proposed research continues to fulfill the criteria for approval;
   c. the current consent document;
   d. any newly proposed consent document; and
   e. a status report on the progress of the research.

4. The *Continuing Review Submission* also includes a status report on the progress of the research:
   a. the number of subjects enrolled;
   b. a summary since the last IRB review of:
      (1) adverse events and adverse outcomes experienced by subjects;
      (2) unanticipated problems involving risks to subjects or others;
      (3) subject withdrawals;
      (4) the reasons for withdrawals;
      (5) complaints about the research;
      (6) amendments or modifications;
      (7) any relevant recent literature; and
      (8) any interim findings.
   c. any relevant multi-center trial reports;
   d. the investigator's current risk-potential benefit assessment based on study results;
   e. a completed *Continuing Review Form* and applicable attachments; and
   f. electronic signature of the principal investigator (PI).

5. If the submission is missing information or requires clarification, the submission package is unlocked in IRBNet by IRB staff and the required follow-up is listed in the message to the PI detailing the reasons for being unlocked. Once the PI or designee provides the required information, the PI (or PI's designee) will mark the revisions complete in IRBNet which queues the submission back to IRB staff.

6. When the submission is complete and ready for IRB assignment, IRB staff will assign the submission package for expedited review or full IRB review according to the assignment process set forth in the Policy and Procedures: *Initial Full Review;* and *Initial Expedited Review*.

7. Continuing review through an expedited review procedure is permitted in the following situations (see Policy and Procedure: *Initial Expedited Review* for definitions of categories):

a. research that previously received initial expedited or continuing review and met the criteria for expedited review; or
b. continuing review of research previously approved by the convened IRB where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects (Category 8); or
c. no subjects have been enrolled and no additional risks have been identified; or where the remaining research activities are limited to data analysis (Category 8); or
d. continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified (Category 9).

8. For continuing review of research by a convened IRB, all IRB members (including alternate members) are provided and review:

a. the full protocol, application, or a protocol summary containing the relevant information necessary to determine whether the proposed research continues to fulfill the criteria for approval;
b. the current consent document;
c. any newly proposed consent document;
d. a status report on the progress of the research.

At least one IRB member is provided and reviews the complete protocol including any protocol modifications previously approved by the IRB.

9. The primary and secondary IRB reviewer will upload the completed Reviewer Sheet: Continuing Review in IRBNet. When the IRB uses a primary reviewer system, the primary reviewer(s) should do an in-depth review of all pertinent documentation. All other IRB members should at minimum receive and review a protocol summary (of sufficient detail to make the determinations required under the U.S. Department of Health and Human Services (HHS) regulations 45 CFR 46.111), the proposed informed consent document, and any recruitment materials, including advertisements intended to be seen or heard by potential subjects. In addition, the complete documentation should be available to all members for review.

10. As part of the continuing review for studies initially reviewed prior to 01/21/2019 (the effective date of the 2018 Rule), the IRB will make a recommendation as to whether the study will be transitioned to the 2018 Rule or if it should remain on the pre-2018 Rule. The

recommendation and the reason for the recommendation will be documented in the Reviewer Sheet uploaded in IRBNet.

11. Any study remaining on the pre-2018 Rule will have an IRBNet global tag, 'Pre-2018 Rule' on the project record in IRBNet.

12. IRB members may record any comments in the *Reviewer Comments* section in IRBNet to serve as reminders of issues they wish to discuss at the IRB meeting.

13. For continuing review of research, the IRB members shall determine:
- whether the protocol needs verification from sources other than the researchers that no material changes had occurred since previous IRB review;
- the current consent document is still accurate and complete; and
- any significant new findings that arise from the review process and that might relate to participants' willingness to continue participation will be provided to participants.

Consultant expertise shall be provided as necessary in accordance with the Policy & Procedure: *IRB Use of Consultants*.

14. 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, project expiration date* (as applicable);
   b. *project status* (if changed since last review);
   c. *next report due* (for research when continuing review is not required);
   d. minutes, recorded as appropriate.

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

16. An IRB determination letter will be generated by IRB staff in IRBNet and edited to reflect the determination. The letter will be published in IRBNet and the notification of the published letter will automatically be sent to the PI and is accessible to anyone with shared access on the project. The letter will include at least the following information:
   a. the date of the review;
   b. what was reviewed;
   c. the type of review;
   d. the decision of the IRB;
   e. whether the IRB requires modifications to the protocol or research plan in order to secure approval, such as:
      i. a description of the required modifications;
      ii. the basis for requiring modifications.
   f. If the IRB disapproves research:
      i. a statement of the reason for disapproval; and
      ii. a description of how the investigator may respond.

17. The study expiration is cited in the initial approval letter as applicable. The study team receives three expiration warnings automatically from IRBNet regarding upcoming expiration. IRB staff sends a fourth and final warning approximately two weeks prior to expiration.

18. For studies where a continuing review is not required. An annual automated email message will be sent to the PI via IRBNet (according to the *Next Report Due* field). This message will serve as a reminder for an annual check-in. The PI will respond to the annual check-in by submitting a brief form (Annual Check-in Form), to the IRB Office for administrative review via IRBNet. The form will ask the PI to confirm the following; the status of the study, that reportable events have been submitted to the IRB for review and acknowledgment, that changes to the study have been submitted for IRB review and approval prior to initiation, and whether or not there have been any complaints from subjects or others. It will also remind the PI if the study has since been completed, a closing report should be submitted. After administrative review of the Annual Check-in Form, 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, and effective date;
b. project status (if changed since last review);
c. next report due (for research when continuing review is not required);
d. minutes, recorded as appropriate.
e. A Board Action notification will automatically be sent to the PI in IRBNet.

19. If a PI fails to provide continuing review information to the IRB by the submission deadline or the IRB has not reviewed and approved a research study by the expiration date, all research activities, including enrollment, accrual, data collection and analysis must stop until reviewed and approved for renewal. Enrollment of new subjects or accessing subject data is not permitted after the expiration of IRB approval.

20. Lapses in studies requiring review by the convened IRB will be placed on the first available agenda following submission of renewal materials. Lapses in continuing review of an expedited study may be reviewed and approved via expedited procedures. The IRB reviewer has the discretion to request the lapsed study be reviewed at a convened IRB meeting.

The IRB and the investigator must plan ahead to meet required continuing review dates, which are binding. Approval of a study is effective only until the last day of the approval period. There are no "grace periods" permitted under federal regulations. IRB staff will notify the PI and OSP Grants Manager in IRBNet regarding approval expiration to ensure the research and funding has been stopped.

In certain circumstances, the IRB may allow current subjects to continue in some or all of the research procedures if it finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions. Enrollment of new subjects cannot occur after the expiration of IRB approval in such cases. Such expiration of IRB approval does not need to be reported to the U.S. Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP) as a suspension of approval under DHHS regulations.

21. Research activity shall resume only after IRB approval of continuing review. Investigators who submit late continuing review applications must include the following in their report:
    a. an explanation for why the review was not submitted timely;

b. a description of any study activities which took place during the lapse of approval; and
c. the number of subjects who engaged in research activities (or data/specimens analyzed) during the lapse of approval.

22. If a *Continuing Review Form* is not submitted within two (2) months after approval expiration, the study will be administratively closed at the discretion of the IRB with electronic notification through IRBNet to the PI and Grants Manager. Studies that are administratively closed require submission of a new research application for review by the IRB.

23. A single lapse in continuing approval does not require reporting to OHRP. However, continuous lapses in approval or serious issues of non-compliance with IRB and HHS requirements require notification to OHRP. The serious and continuing nature of non-compliance is determined by the IRB.

REVISION HISTORY:

Department: OSP - Research Integrity & Compliance	**Title**: Continuing Review
Effective Date: 03/16/21	**Owner:** Senior Compliance Manager, IRB
Replaces P/P Dated: IRB SOP (02/08/17); P/P (07/19/18, 01/21/19)	
Related Documents: Policy and Procedures: *Initial Full Review*; *Initial Expedited Review*; *IRB Use of Consultants*; Reviewer Sheet: Continuing Review; Submission Checklist - Continuing Review; Form: Continuing Review; Form: Annual Check-In	
References: 45 CFR 46.109; 21 CFR 56.110; AAHRPP Tip Sheets 16; AAHRPP Element II.2.F.2	