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

Policy and Procedure

TITLE: Initial Full Review

PURPOSE:

To describe the process for initial review of research by a full Institutional Review Board (IRB) at convened meetings.

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, including the IRB.

POLICY:

The IRB conducts initial review for non-exempt human subjects research at convened meetings at which a quorum is present unless the research is eligible for expedited initial review. (See Policies and Procedures: *Exemption Determination; Initial Expedited Review*). All studies that may involve more than minimal risk to subjects or that do not fit within the expedited review criteria, require review by a full IRB at convened meetings.

PROCEDURE:

1. The investigator or designee completes a *New Project Submission* package in IRBNet and submits it to IRB staff.

2. IRB staff is alerted to a *New Project* submission in IRBNet via email and by the appearance of the *New Project* submission flagged in the *Submissions Manager* page in IRBNet.

3. The submission is screened by IRB staff in accordance with federal regulations and institutional requirements. A new project submission must include the following:

a. a completed study initial application and applicable attachments;
b. study protocol;
c. principal investigator's (PI's) electronic signature;
d. grant manager's signature (for HPHC studies) or Atrius Director of Research signature (for Harvard Vanguard Medical Associates (HVMA) studies).

4. The new project submission may also be required to include the following, depending on the type of study:
a. IRB approvals from other institutions (and applications when appropriate);
b. proposed informed consent forms;
c. proposed data collection forms;
d. authorization to use and disclose protected health information (PHI) for research (HIPAA authorization form or waiver request);
e. co-investigators' letters of assurance or cooperation with research sites;
f. recruitment materials;
g. study materials (such as educational materials, surveys, questionnaires, assessments);
h. documentation of review if required by another institutional committee;
i. RSDC signature (for studies involving RSDC activity);
j. curriculum vitae (CV) of PI as requested;
k. Investigational New Drug (IND) or Investigational Device Exemption (IDE) number, if applicable;
l. Investigator's Brochure; and
m. other materials as requested.

5. If the submission is missing information or requires clarification, the submission package is "unlocked" in IRBNet and the required follow-up is listed in the message to the PI detailing the reasons. IRB staff may use the IRBNet Templates Language document to aid in drafting correspondence/communications documented in IRBNet. Once the required information is present and all updates are made, the PI (or PI's designee) shall 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, the submission package will be scheduled by the Senior Compliance Manager (SCM) or designee for full IRB review.

7. Submissions assigned to the full IRB agenda are assigned at least one week prior to the IRB meeting.

8. IRB staff will update the *Review Details* of the submission in IRBNet, adding the agenda date and review type.

9. IRB staff will record any comments regarding the review as applicable in the *Reviewer Comments* section.

10. IRB staff will *Share* the submission with the full IRB according to the *Policy and Procedure on Conduct of IRB Meetings*.

11. For U.S. Department of Health & Human Services (HHS) supported multicenter clinical trials, the IRB shall receive and review a copy of the HHS-approved sample informed consent document(s) and the complete HHS-approved protocol, if they exist. Even though a primary reviewer system is used via IRBNet, all members shall have access to a copy of the complete documentation. These materials should be received by members one week in advance of the meeting date to allow review of this material.

12. The primary and secondary reviewers shall perform an in-depth review of all materials for presentation at the IRB meeting using the *Reviewer Sheet – Initial Review.*

13. The primary and secondary IRB reviewers will upload the completed *Reviewer Sheet – Initial 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 (see previous paragraph). All other IRB members should at least review a protocol summary (of sufficient detail to make the determinations required under 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 shall be available in IRBNet to all members for review.

14. 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.

15. Consultant expertise shall be provided as necessary in accordance with the *Policy and Procedure on IRB Use of Consultants*.

16. Determinations

The IRB assigns a risk level based upon regulations as part of the review of each protocol. The IRB assesses the risk level and determines the appropriate review period. When risk is great in relation to the risk associated with alternative procedures, and for certain behavioral studies in which the degree of discomfort to the subject may be greater than normal, the IRB may require that continuing review be conducted in less than one year. The approval letter also informs the investigator that any changes in research activities require prior approval by the IRB and any unanticipated problems involving risks to subjects or others must be promptly reported.

a. Approved

The IRB may approve research when all of the criteria for IRB approval of research (45 CFR 46.111) are satisfied. These requirements:

(1) Risks to subjects are minimized by using procedures that are consistent with sound research design and do not unnecessarily expose subjects to risk and whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

(2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the

research (e.g., the possible effects of the research on public policy) as among research risks that fall within the purview of its responsibility.

(3) Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted. The IRB should be particularly cognizant of the special problems of research that involves a category of subjects who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative in accordance with 45 CFR 46.116.

(5) Informed consent will be appropriately documented or appropriately waived in accordance with 45 CFR 46.117.

(6) When appropriate, the research plans make adequate provision for monitoring the data collected to ensure the safety of subjects.

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(8) For purposes of conducting the limited IRB review required by 45 CFR 46.104(d)(7), (a) the IRB need not make the determinations at paragraphs (a)(1) through (a)(7) of this section, and shall make the following determinations: (i) broad consent shall not be used; and (ii) therefore, the requirement for broad consent documentation shall not apply; (iii) if there is a change made for research purposes in the way the identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data; and (b) when some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

b. <u>Approved with conditions</u>

Upon review of research, the IRB reviewers may require as a condition of approval that the investigator make specified changes to the research protocol or informed consent document(s); confirm specific assumptions or understandings on the part of the IRB regarding how the research will be conducted; or submit additional documents, such that, based on the assumption that the conditions are satisfied, the IRB is able to make all of the determinations required for approval under 45 CFR 46.111 and, if applicable, subparts B, C, or D of 45 CFR part 46, including:

(1) Substantive changes or requirements requests for more information for IRB consideration, and other issues related to the criteria for approval require review and approval by the convened IRB.

(2) Minor or prescriptive changes or requirements may be reviewed for approval by the IRB Chair (or designee) and further review by the IRB at a subsequent convened meeting is not necessary.

(3) The date of the approval is the date the conditions are determined to be met.

(4) When a protocol receives final approval, the start of the approval period is assigned as the date of the convened IRB meeting. If a protocol has received a Conditional Approval and the investigator completes the revisions, the date conditions are met will be the start of the approval date and the expiration date will be based on the approval period starting from the meeting date of the convened IRB on which the IRB initially reviewed the protocol.

(5) If the research expires before the conditions are reviewed and approved, all research activities must stop until approval is obtained.

c. Deferred
A study is deferred if it requires more than minor revisions or modifications to secure approval. Generally, this means that extensive and/or substantive changes are necessary before the study can be effectively reviewed.

d. Disapproved
Disapproved means the IRB has determined it will not approve the study as designed. The IRB shall provide the investigator with written notification in IRBNet of the reasons for its decision, any recommended modifications that might lead to approval in the future, the opportunity for the investigator to respond in person or in writing, and a review of the investigator's response.

17. After IRB review, IRB staff will update IRBNet with one of the following appropriate determinations within two weeks following the review:
    (1) The following fields will be updated: *Review Type, Action, Effective Date, Project Expiration Date, Initial Approval Date, Project Risk Level, Project Status.*
    (2) The expiration date is recorded as the first date that the protocol is no longer approved. The expiration date is based on the continuing review period as determined by the IRB effective from the approval date.
    (3) Minutes will be recorded as appropriate according to the *Policy and Procedure on IRB Meeting Minutes.*
    (4) Submissions subject to FDA regulations must also have the following determinations made as applicable and recorded in the minutes:
        i. The IRB must determine whether an IND/IDE is required according to 21 CFR 56.
        ii. If the study uses a device, determination must be made regarding non-significant risk or significant risk according to 21 CFR 812.
        iii. If the study involves children, the research must comply with 21 CFR 50, Subpart D.

18. 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. the matter reviewed;

c. the type of review by the convened IRB;
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:
   (1) a description of the required modifications;
   (2) the basis for requiring modifications.
f. If the IRB disapproves research:
   (1) a statement of the reason for disapproval; and
   (2) a description of how the investigator may respond.

19. IRB staff will apply submission tag(s), such as "federally funded (HPHC prime)", "genetic analysis", "FDA regulated", etc., as applicable to each study.

20. If applicable, the IRB staff will use the *Project Notes* section in IRBNet to document any special requirements or notes that apply to the entire study that are unavailable by tag (i.e., the category of expedited review that applies to the project; ceding or reviewing institution if a cede is involved). *Project Notes* can only be viewed and edited by users with administrative access.

21. If the submission is deferred, the determination letter will include suggestions to further develop the study design and/or materials. A deferred study with revised materials will be placed on the next available meeting agenda for review by the convened IRB, following the IRB submission deadlines.

REVISION HISTORY:

Department: OSP - Research Integrity & Compliance	**Title**: Initial Full Review
Effective Date: 01/21/19	**Owner:** Senior Compliance Manager
Replaces P/P Dated: IRB SOP (02/08/17); IRB Procedures: 001.03 (12/13), 004.01 (10/13), 011.01 (7/14); P/P (07/18/18)	
Related Documents: Policy and Procedure: *Conduct of IRB Meetings;* Forms: Initial Application; Initial Application – Data/Existing Health Information; Reviewer Sheet – Initial Review; IRBNet Approval Letter Template; IRBNet Template Language	
References: 45 CFR 46.103(b); 45 CFR 46.109; 45 CFR 46.116(b); OHRP Guidance on Written Institutional Review Board (IRB) Procedures; OHRP 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 Element II.2.D; AAHRPP Tip Sheets: 16 and 18	
Approved By: Research Integrity & Compliance Officer	