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

Policy and Procedure

TITLE: Initial Expedited Review

PURPOSE:

To describe the process for conducting initial expedited review.

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 Institutional Review Board (IRB).

POLICY:

(1) An IRB may use the expedited review procedure to review the following:
   a. Some or all of the research appearing in the list of categories of research published in the Federal Register by the Secretary of HHS, unless the reviewer determines that the study involves more than minimal risk;
   b. Minor changes in previously approved research during the period for which approval is authorized; or
   c. Research for which limited IRB review is a condition of exemption (under 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), and (d)(7) and (8)).

(2) Under an expedited review procedure, the review may be carried out by the IRB Chair or by one or more experienced reviewers designated by the Chair from among members of the IRB. In reviewing the research, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non-expedited procedures of IRB review of proposed research at convened meetings at which a majority of the IRB members are present, including at least one member whose primary concerns are in nonscientific areas (45 CFR 46.108(b)).

(3) All research proposals approved using expedited review procedures are reported to the IRB at the next convened meeting.

DEFINITIONS

For the purposes of this policy:

Minimal Risk
The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. 45 CFR 46.102(j).

It is the reviewer's responsibility to determine whether the research meets the definition of minimal risk. The IRB reviewer must consider two questions:

- Is the probability of the harm or discomfort anticipated in the proposed research greater than that encountered ordinarily in daily life or during the performance of routine physical or psychological examinations or tests?
- Is the magnitude of the harm or discomfort greater than that encountered ordinarily in the daily life or during the performance of routine physical or psychological examinations or tests?

If the answer is "yes" to either of these questions, then the research does not meet the definition of minimal risk.

Federal Expedited Review Applicability and Categories

Research activities that present no more than minimal risk to human subjects and involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review process authorized by 45 CFR 46.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review process when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

The expedited review process may not be used where identification of the subjects and/or their responses would reasonable place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review – expedited or convened.

Categories one (1) through seven (7) pertain to both initial expedited and continuing IRB review.

Research Categories:

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met:
   a. Research on drugs for which an investigational new drug application (21 CFR 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review).
   b. Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture:
   a. from healthy, nonpregnant adults who weigh at least 110 pounds: the amounts drawn may not exceed 550 ml in an 8-week period and collection may not occur more frequently than two times per week; or
   b. from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected: the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than two times per week).

3. Prospective collection of biological specimens for research purposes by non-invasive means
   Examples:
   a. hair and nail clippings in a non-disfiguring manner;
   b. deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
   c. permanent teeth if routine patient care indicates a need for extraction;
   d. excreta and external secretions (including sweat);
   e. uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue;
   f. placenta removed at delivery;
   g. amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
   h. supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;
   i. mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; or
   j. sputum collected after saline mist nebulization.

4. Collection of data through non-invasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves:
Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications).

Examples:

a. physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy;
b. weighing or testing sensory acuity;
c. magnetic resonance imaging;
d. electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography; or
e. moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that:

a. have previously been collected for non-research purposes;
b. have previously been collected for research purposes, provided the materials were not collected for the currently proposed research; or
c. will be collected solely for non-research purposes.
(NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. This listing refers only to research that is not exempt).

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. This listing refers only to research that is not exempt).

8. Continuing review of research previously approved by the convened IRB:

a. 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; or
b. where no subjects have been enrolled and no additional risks have been identified; or
c. where the remaining research activities are limited to data analysis.

9. 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.

PROCEDURE:

1. Materials for IRB review shall be submitted by the principal investigator (PI) or designee to the IRB by established deadlines which are posted on the HPHC website

(https://www.hphcinstituteosp.org/institutional-review-board) and in the IRBNet FAQ document in the IRBNet Researchers Forms and Templates.

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

3. 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.

4. 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 application and applicable attachments;
b. study protocol;
c. PI's electronic signature;
d. Grant Manager's signature (for HPHC studies) or Atrius Director of Research signature (for Atrius/Harvard Vanguard Medical Associates (HVMA) studies).

5. 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 (Health Insurance Portability and Accountability Act of 1996 (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 investigator as requested;
k. Investigational New Drug (IND) or Investigational Device Exemption (IDE) number;
l. Investigators Brochure; and
m. other materials as requested.

6. 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) will mark the revisions complete in IRBNet which queues the submission back to IRB staff.

7. IRB staff make a preliminary determination that the study meets the criteria for expedited review, including minimal risk, and identifies the research categories. If the application does not

meet the criteria for expedited or exempt review, IRB staff schedule the study for full IRB review according to the *Policy and Procedure on Initial Full Review*.

8. After completing screening, IRB staff assign the study to the expedited reviewer(s), who conduct(s) the initial expedited review. The IRB Chair conducts all expedited reviews of new study submissions. Reviewer checklists are available in IRBNet and used to document areas requiring determinations.

9. IRB members may serve as an expedited reviewer for continuing reviews under the direction of the IRB Chair. The IRB Chair conducts all initial new study reviews but may also request an experienced member to serve as a secondary expedited reviewer, as needed. All expedited reviewers undergo initial training with IRB staff prior to conducting expedited continuing reviews. Members who have served on the IRB for at least three months may qualify as an experienced member.

10. The expedited reviewer notifies IRB staff if they are not available to conduct expedited continuing reviews during the assigned time period and re-assignment shall be done with the IRB Chair.

11. Submissions qualifying for expedited review can be assigned to the IRB Chair or designated IRB reviewer on a rolling basis.

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

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

a. IRB staff will *share* the submission in IRBNet with the appropriately assigned expedited reviewer. Staff will click on the "alarm bell" in IRBNet when assigning the reviewer to ensure automatic notification of a completed review.
b. IRB staff will notify the reviewer that the submission is ready by clicking to notify users that access to the submission has been granted and including a note regarding the submission.

14. The expedited reviewer shall:

a. Record any comments (if applicable) regarding their review in the *Reviewer Comments* section.
b. If the expedited reviewer requests additional information prior to completing the review, IRB staff will follow-up with the investigator and/or project manager, and will notify the expedited reviewer once a reply has been received.
c. Expedited reviewers review all information in the expedited review packet in enough depth to be familiar with the protocol, to determine whether the research is eligible for

expedited review, and to determine whether the research meets the regulatory criteria for approval.

d. Expedited reviewer(s) shall document federally mandated specific findings (e.g., Subpart B, C, D or waiver of informed consent or documentation), if applicable, by completing the Reviewer Sheet and uploading the completed Reviewer Sheet in IRBNet. Determinations are also recorded regarding expedited eligibility, applicable expedited category, and whether the research meets the federal criteria for approval.
e. Expedited reviewers shall record the determination of the review.
f. Expedited reviewers shall ensure that the investigators will conduct the informed consent process and obtain documentation of informed consent, as specified in 45 CFR 46.116 and 117 and 21 CFR 56.116 and 117 as applicable, unless the IRB waives the requirements in accordance with federal regulations.
g. The expedited reviewers shall raise those controverted issues or request changes that they have determined do not meet the criteria for approval.
h. The expedited reviewers shall mark the review as complete and an automatic notification will be sent to IRB staff to proceed with the determination letter.

15. The expedited reviewer may approve the submissions, approve with modifications, or request additional information. The expedited reviewer may also forward the submission to the IRB for review at a convened meeting.

16. 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, Initial Approval Date, Project Risk Level, Project Status*. 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.
b. If a continuing review is not required as documented in the Reviewer Sheet and as applicable under the 2018 Rule, the *Project Expiration Date* will be left blank, and the *Next Report Due Date* will be completed instead by setting the Report Due Date as 12 months from the initial approval.
c. Minutes will be recorded as appropriate.
d. Submissions subject to FDA regulations must also have the following determinations made as applicable and recorded in the minutes:
   (1) The IRB must determine whether an IND/IDE is required according to 21 CFR 56.
   (2) If the study uses a device, determination must be made regarding Non-Significant Risk or Significant Risk according to 21 CFR 812.
   (3) If the study involves children, the research must comply with 21 CFR 50, Subpart D.
e. If the submission is approved with conditions:
   (1) The date of approval is the date the conditions were determined to be met.
   (2) When a protocol receives final approval, the start of the approval period is assigned as the date the protocol was approved with conditions. 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 (if applicable) will be based on the approval period starting from the date on which the IRB initially approved the protocol with conditions.

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

17. A board action notification will automatically be sent to the PI in IRBNet.

18. 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 and is accessible to anyone with shared access on the project.

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 request is involved). *Project Notes* can only be viewed and edited by users with administrative access.

21. The expedited reviewer(s) can determine that the research is eligible for a less stringent mechanism of review (i.e., the project is exempt from requirements for review or the activities do not fall under the purview of the IRB). In these cases, the expedited reviewer, with assistance from IRB staff, if necessary, shall document the exempt categories or the rationale for determining that the activities do not meet the federal definitions of *research* or *human subject*.

22. If the PI has concerns regarding the IRB decision/recommendations for changes in the study, they may submit their concerns to the IRB reviewer via a written document that includes justification for changing the IRB decision. The PI will submit the request to the expedited reviewer and/or to the IRB Chair for final resolution via IRBNet as a response/follow-up submission. If the PI is still dissatisfied with the IRB decision, IRB staff will send the study to the convened IRB for review.

REVISION HISTORY:

Department: OSP - Research Integrity & Compliance	**Title**: Initial Expedited Review
Effective Date: 02/28/21	**Owner:** Senior Compliance Manager
Replaces P/P Dated: IRB SOP (02/08/17); P/P (07/19/18, 01/21/19, 02/25/20)	
Related Documents: Forms: Initial Application, Initial Application - Data/Existing Health Information; Reviewer Sheet- Initial Review	
References: 45 CFR 46.110; 21 CFR 56.110; OHRP Guidance on Written Institutional Review Board (IRB) Procedures; OHRP Guidance on the Use of Expedited Review Procedures; ICH-GCP: 3.3.5; AAHRPP Tip Sheets: 17 and 18; AAHRPP Element II.2.F.	