

Title:	Review of Human-Subjects Research at a Convened Meeting
Department:	Human Research Affairs
Policy Type:	<input checked="" type="checkbox"/> Partners System-wide <input type="checkbox"/> Partners System-wide Template <input type="checkbox"/> Partners HealthCare <input type="checkbox"/> Partners HealthCare Departmental <input type="checkbox"/> Institution
Applies to:	Employees, Professional Staff or Other Agents of Brigham and Women's Hospital (BWH), Brigham and Women's Faulkner Hospital (BWFH), Massachusetts General Hospital (MGH), McLean Hospital (McLean), North Shore Medical Center (NSMC), Spaulding Rehabilitation Hospital (SRH), and MGH Institute of Health Professions (MGH IHP)
Approved by:	Chief Academic Officer
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Contact Person:	Director, Human Research Review and Compliance

KEYWORDS:

IRB, Institutional Review Board

PURPOSE:

The purpose of this policy is to define the procedures the Partners Human Research Committees (PHRC) follow when conducting initial and continuing review of human-subjects research and clinical investigations and review of proposed changes in approved research at a convened meeting of the PHRC. Non-exempt human-subjects research and clinical investigations reviewed by the PHRC at a convened meeting are subject to this policy.

This policy is established to comply in part with the regulatory requirement in 45 CFR 46.103(b)(4)(i) and 21 CFR 56.108(a)(1) requiring IRBs to have "written procedures which the IRB will follow for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution."

DEFINITIONS:

See Definition of Human-Subjects Research

Minimal risk means that 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(i)][21 CFR 56102(i)]

POLICY STATEMENT:

The PHRC must review all non-exempt human-subjects research and clinical investigations at a convened meeting at which more than half the members, including at least one physician-scientist member and one nonscientist member, are present unless the research is eligible for review using the expedited review procedure. When reviewing non-exempt human-subjects research and clinical investigations, the PHRC Chairpersons and PHRC members are subject to the Partners policy on *IRB Member Conflicts of Interest*.

PROCEDURES:

Meeting Dates

The PHRC meeting dates and times are determined by the end of each year for the following year. Members are informed of the meeting schedule prior to the end of the year in order to reserve the dates and times on their calendar. The meeting dates are posted on the PHRC website.

Quorum

Human-subjects research and clinical investigations that cannot be reviewed using the expedited review procedure are reviewed at a convened meeting of a quorum of the membership of the PHRC, including at least one physician-scientist and one member whose primary concerns are in nonscientific areas. In addition, reasonable efforts will be made to ensure that at least one unaffiliated member and at least one member representing the general perspective of subjects are present at each meeting. The unaffiliated member, the member representing the general perspective of subjects, and the non-scientific member may be the same person, or may be represented by two or three different persons. A *quorum* is defined as more than one-half the voting membership.

Determining Agenda, Attendance and Assigning Reviewers

Prior to each convened meeting, members are asked if they will attend the meeting. This is necessary to determine whether the requirement for quorum will be met and that members with the appropriate scientific or scholarly expertise will be in attendance.

The presiding PHRC Chairperson or Administrative Chairperson reviews the agenda and list of members expected to attend and assigns reviewers to each protocol. Up to 12 protocols may be scheduled on the agenda; however the presiding PHRC Chairperson or Administrative Chairperson at his/her discretion may reduce the number of protocols based on the nature or complexity of the protocols scheduled for review in order to allow sufficient time for discussion of each protocol at the meeting, or based on the availability of members for review. Generally, protocols are scheduled for review by receipt date; however, the PHRC reserves the right to reschedule protocols for review based on other factors, such as the experience and expertise of the members planning to attend the PHRC meeting or the expiration date of PHRC approval.

The presiding PHRC Chairperson or Administrative Chairperson is responsible for ensuring that at least one member attending the meeting has the necessary knowledge and expertise to review each of the protocols listed on the agenda.

When the agenda includes protocols that involve vulnerable populations, the presiding PHRC Chairperson or Administrative Chairperson is responsible for ensuring that at least one member attending the meeting has knowledge of and/or experience in working with the study population.

When making reviewer assignments, the presiding PHRC Chairperson or Administrative Chairperson takes into consideration the scientific discipline, the study population, and study procedures described in the protocol and the experience and expertise of the members attending the meeting.

The qualifications, experience, and expertise, as well as representative capacity of each member, are documented in the PHRC roster. Member CVs are also maintained by the Human Research Office in a secure area on the Partners network. The presiding PHRC Chairperson or Administrative Chairperson has access to the PHRC roster and member CVs when making reviewer assignments.

The primary reviewer is typically a physician-scientist or other scientist with experience in working with the population being studied and/or expertise in the type of research under consideration, although this is not an absolute requirement, depending upon the type of study.

The secondary reviewer is typically an individual who can provide another perspective, for example, a layperson, genetic counselor, nurse or parent. The secondary reviewer, therefore, complements the scientific or scholarly expertise of the primary reviewer.

Both the primary and secondary reviewers are responsible for performing an in-depth review of all aspects of the protocol, consent form and associated materials, including when applicable, the investigational drug brochure or investigational device information, or NIH or other federal grant application or proposal for funding.

Reviewers are encouraged, although not required, to contact the principal investigator prior to the meeting if they have questions about the study, particularly if they have significant concerns about the study or believe additional information is needed for the PHRC to be able to assess the risks and anticipated benefits, if any, to subjects and the importance of the knowledge that may be expected to result from the research.

Use of Consultants

Although rarely needed because of the depth and breadth of the membership of the PHRC, consultants may be used to supplement or provide expertise not available on the PHRC. When the presiding PHRC Chairperson or Administrative Chairperson reviews the draft agenda to make primary and secondary reviewer assignments, s/he is responsible for determining whether the PHRC membership includes the necessary expertise to review the protocol.

When, in the opinion of the presiding PHRC Chairperson or Administrative Chairperson, the PHRC membership lacks the expertise needed to review the protocol, the presiding PHRC Chairperson or Administrative Chairperson, in consultation with the Director and Chair of the PHRC or designee, identifies potential expert consultants.

Additionally, the PHRC may vote to defer action on a protocol and may require an expert in the scientific area or discipline to review the research and provide consultation to the PHRC. Potential consultants will be identified and agreed upon by the PHRC, or as indicated above.

Consultants are subject to the Partners policy on *IRB Member Conflicts of Interest* and must confirm in writing that they have no conflict of interest. If the consultant agrees to review the research and the consultant has no conflict of interest, s/he is provided with all of the forms and documents submitted to the PHRC for review.

Consultants are asked to attend the meeting to present their findings relative to the scientific merits of the study, the risks and potential benefits to subjects, and alternative treatments or procedures, and to answer questions; however, if the consultant is unavailable to attend the meeting, s/he may provide written comments for distribution or communication to the PHRC members. Consultants are not voting members, and their attendance is recorded in the Minutes as guests (consultant).

Distribution of Materials and Review by Members

Investigators who rely upon the PHRC for IRB review of human-subjects research and clinical investigations are required to complete Insight/eIRB application forms and provide all required information and documents to the Partners Human Research Office for review by the PHRC as described in the *Protocol Submission Instructions*, the *Continuing Review Submission Instructions*, and applicable forms.

At least 5 days prior to the meeting, the meeting agenda and Insight/eIRB application forms and documents submitted for PHRC review for each item on the agenda are made available in Insight to all members planning to attend the meeting. All members are provided with links to guidance documents that include the regulatory criteria for approval and requirements for informed consent. For initial review and review of proposed changes in approved research, the agenda also includes references and links to relevant regulatory documents and PHRC policies and procedures.

Members and reviewers are provided with the Guide to Review of Non-Exempt Human Research, Review Worksheet, and Consent Form Worksheet for reference and, when assigned to review, to prepare assigned reviews. Assigned reviewers are responsible for an in-depth review of all of the materials provided to them relevant to the research including, when applicable, the funding application. Members who are not assigned to review the protocol are expected to review all of the materials provided to them relevant to the research in sufficient depth to vote on the research at the convened meeting.

Initial Review

For initial review, all members attending the meeting receive the required Insight/eIRB application forms and documents submitted by the investigator for PHRC review, which include, but are not limited to, the protocol summary, recruitment materials, detailed protocol, instruments and questionnaires, consent forms, drug/device brochure, the application for funding (e.g., NIH grant) (see *Protocol Submission Instructions*).

Continuing Review

For continuing review, all members attending the meeting receive the required Insight/eIRB application forms and documents submitted by the investigator for PHRC continuing review (see *Continuing Review Submission Instructions*). The entire protocol file and minutes of prior meetings at which the protocol was reviewed are available to all members upon request.

Proposed Changes

For review of proposed changes (amendment) to approved research during the period of IRB approval, all members attending the meeting receive the required Insight/eIRB application forms and documents submitted by the investigator for PHRC review of the proposed change. The entire protocol file and minutes of prior meetings at which the protocol was reviewed are available to all members upon request.

Conflicts of Interest

PHRC members are subject to the Partners policy on *IRB Member Conflicts of Interest*. The agenda for every meeting includes a reminder about the conflicts of interest policy. Any member with a conflict of

interest is asked to recuse him/herself and leave the room while the protocol is being reviewed, except to provide information to the PHRC, after which the member must leave the room for the discussion and vote on the protocol. The names of those voting members who were recused from voting due to a conflict of interest are recorded in the Minutes. Recused members are not counted towards the quorum requirement; therefore, if a quorum of the membership is not present for the review of any protocol, no vote is taken and the protocol is held over for review at the next meeting of the same PHRC panel.

Discussion and Vote

The PHRC administrator takes attendance at the meeting and records voting members present and absent for each review. Late arrivals, early departures, and individuals recused or out of the room for one reason or another during the discussion and vote on each protocol are recorded in the Minutes.

The presiding PHRC Chairperson and assigned reviewers lead the discussion of each new protocol, continuing review, or amendment listed on the meeting agenda.

The primary reviewer presents a brief synopsis of the research protocol, with the expectation that the other members have reviewed the protocol materials. The primary reviewer is responsible for covering the scientific background and rationale, study design, how the research differs from and compares to standard care, appropriateness of the study population and the inclusion/exclusion criteria, the risks and potential benefits to subjects, alternative treatments or procedures, as well as the criteria for IRB approval and, when applicable, additional protections for pregnant women, human fetuses, and neonates; children; and individuals with impaired decision-making capacity.

Primary reviewers may have particular insight into referral patterns, clinical standards within the community, or routine care for the conditions under study, and it is expected that these are also part of the presentation to the PHRC.

Secondary reviewers are asked to present any additional clarifications or commentary on the study plan, and any questions or concerns, or modifications s/he would require for approval.

Both the primary and secondary reviewers are expected to provide an in-depth review of the consent form and identify missing required elements and when, applicable, additional elements for informed consent. Additionally, reviewers may comment on the reading level and style of the consent form and provide detailed suggestions for improvement. Consent form comments may be handwritten on the form, or provided in written commentary as part of the review.

Reviewers are encouraged to provide written comments to ensure that the PHRC Chairpersons convey the modifications required and/or questions and concerns raised by the PHRC completely, accurately and precisely.

After the primary and secondary reviewers have presented the study and their review comments, the presiding PHRC Chairperson opens the protocol up for discussion by the membership. The PHRC Chairperson and members may direct specific questions to the assigned reviewers or to other members with specific expertise or viewpoints (e.g., a layperson, nurse or other member who may bring a different perspective to the discussion).

At the end of the discussion, one of the reviewers or another member makes a motion to approve, require modifications in the research (to secure approval), defer action on (pending receipt of additional information), or disapprove the protocol. A vote on the motion is taken (for, against, or abstain) by show of hands or voice vote and recorded in the Minutes. All motions are decided by majority vote of the members present for the review. A quorum of the members of the PHRC (more than one-half the members) must be present in order for the PHRC to take a vote.

Determining Frequency of Continuing Review

When the motion is to approve or require modifications in the research (to secure approval), the motion includes the duration of PHRC approval (one year or less). When determining the duration of approval, the PHRC considers the degree of risk to subjects.

When the risks to subjects related to participation in the research are greater than the risk associated with alternative treatments or procedures, if any, the PHRC will consider requiring that continuing review be conducted in less than one year, or one year with case-by-case reporting. Examples of research that may be considered for review more frequently than annually include:

- phase I studies of a challenging or novel new drug or biologic;
- research involving Category A significant risk devices;
- research in which healthy volunteers may undergo anesthesia or medical procedures involving sedation with no direct health benefits;
- research for which there is little external oversight or data safety monitoring;
- research involving gene transfer or xenotransplantation; or
- research involving infectious agents.

For initial review, the approval period begins the date the PHRC voted to fully approve the protocol at the convened meeting or, if voted to require modifications to secure approval, the date the protocol is fully approved by the Administrative Chairperson when s/he reviews the principal investigator's response and determines that all of the required modifications have been made. The expiration date is based on the duration of approval voted on by the PHRC (one year or less) and is set from the date the protocol is fully approved. The expiration date is the first date the protocol is no longer approved by the PHRC.

For continuing review, the approval period begins the date of the convened meeting at which the PHRC voted to approve or require modifications in the research to secure approval. The expiration date is based on the duration of approval voted on by the PHRC (one year or less) and is set from the date of the convened meeting or the anniversary date of the initial or last continuing review approval if approved within 30 days prior to the current expiration date. The expiration date is the first date the protocol is no longer approved by the PHRC.

Continuing Review

Continuing review of the research is required until the research has been completed or has been closed prior to completion. The investigator must submit the continuing review form to document that the study has been completed or is being closed prior to completion. For multi-site research, the research may be considered completed or may be closed prior to completion when the investigator at this site is no longer collecting, receiving, or analyzing identifiable data.

Continuing review of research previously approved by the convened PHRC may be conducted using the expedited review procedure as follows:

- 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.

Additionally, continuing review of research previously approved by the convened PHRC may be conducted using the expedited review procedure where the research is not conducted under an investigational new drug application (IND) or investigational device exemption (IDE) where categories

two (2) through eight (8) do not apply but the PHRC determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified since the last review.

Determining Which Studies Need Verification from Sources Other Than the Investigators

Investigators are required to provide the PHRC with all relevant information regarding the conduct of the research and fulfill all requirements for prompt reporting to the PHRC of unanticipated problems involving risks to subjects or others.

In order to ensure that the research is conducted in compliance with all applicable regulations for the protection of human subjects, the PHRC may require verification of information from sources other than the investigator. Such independent verification may be considered in the following situations:

- complex projects involving unusual levels or types of risk to subjects;
- research being conducted by persons who have previously failed to comply with all regulations or requirements of the PHRC;
- research conduct that comes into question as a result of information provided at continuing review; or
- research in which substantial segments of the project are conducted off site by Partners investigators or non-Partners collaborators.

Independent verification may include, but is not limited to:

- audits by the Human Research Quality Improvement Program;
- communications between the FDA and the sponsor (IND/IDE holder);
- communications with the sponsor, collaborating institutions, coordinating centers, or regulatory agencies;
- communications from any monitoring group, e.g., DSMB or DMC
- General Clinical Research Center (GCRC) evaluations and reviews;
- NIH communications and reviews; and/or
- communications with IRBs at collaborating sites.

Requiring Modifications, Deferring Action, or Disapproving Research and Responses to Review Notification Letters

Require modifications in research to secure approval

When the PHRC votes to require modifications in the research (to secure approval), the Principal Investigator (PI) is notified in writing of the action voted on by the PHRC and the required modifications to the research. The PI is asked to submit a point-by-point response and revised documents to the PHRC.

When received, the presiding PHRC Chairperson or Administrative Chairperson reviews the PI's response, including revised documents, and documents on the review form and checklist whether the modifications required by the PHRC have been made and whether the protocol can now be fully approved. If the modifications have not been made as required, the response is scheduled for review at the next convened meeting of the reviewing PHRC.

Proposed changes submitted with the response are reviewed in accordance with the policies and procedures for review of proposed changes, i.e., either at a convened meeting or, if minor, using the expedited review procedure.

Defer research for more information

When the PHRC votes to defer action pending receipt of additional information, the PI is notified in writing of the action voted on by the PHRC and any questions and concerns that need to be addressed as well as modifications required to the research. The PI is asked to submit a point-by-point response and revised documents to the IRB.

When received, the PI's response, including revised documents, is scheduled for review at the next convened meeting of the reviewing PHRC.

Disapprove

When the PHRC disapproves the research, the PI is notified in writing of the action voted on by the PHRC and the basis for the disapproval. Disapproval means that, as designed, the study cannot be approved and the PHRC can think of no modifications or additional information that will likely result in an approval.

The decision of the PHRC to disapprove the research cannot be overruled by any other institutional body or individual(s); however, an investigator may appeal the decision of the PHRC in writing directly to the Director and Chair of the PHRC. The Director and Chair of the PHRC is responsible for reviewing the appeal with the presiding PHRC Chairperson. The appeal is then scheduled for review at a convened meeting of the PHRC that disapproved the research. The investigator may appeal the decision of the PHRC in person at the convened meeting.

Notification of Principal Investigator and the Institution

The Human Research Office is responsible for notifying the Principal Investigators in writing of PHRC approval of initial or continuing review, or proposed changes in research activities during the period of approval. The approval letter includes the date of expiration of PHRC approval. The expiration date is the first date the research is no longer approved by the PHRC.

Minutes of PHRC meetings are made available to the Institutional Officials in a secure area on the Partners network. In addition, the Human Research Office provides individuals and/or departments within Partners with responsibility for some aspect of the human research protection program access to PHRC review information and protocols via the Insight Research Portal.

OTHER APPLICABLE PARTNERS HEALTHCARE POLICIES:

IRB Member Conflicts of Interest

Review of Human-Subjects Research Using Expedited Review

Proposed Changes in PHRC-Approved Research and Exceptions

Continuing Review and Expiration of PHRC Approval

REFERENCE:

45 CFR 46

21 CFR 56

DEVELOPMENT AND CONSULTATION

Human Research Office