

**PARTNERS HEALTHCARE SYSTEM, INC.
PARTNERS HUMAN RESEARCH COMMITTEE**

GOVERNANCE AND OPERATING PROCEDURES

ARTICLE I – NAME, PURPOSE, AND RESPONSIBILITIES

1.0 Name, Purpose, and Responsibilities

The Institutional Review Boards (IRBs) of The Brigham and Women’s Hospital, Inc. (BWH), The General Hospital Corporation doing business as Massachusetts General Hospital (MGH), and The McLean Hospital Corporation (McLean) shall be known collectively throughout these institutions as the Partners HealthCare System Institutional Review Boards (the “Partners IRBs”) or the Partners Human Research Committees (PHRC).

The PHRC shall provide ethical and scientific review and continuing oversight of the human-subjects research of the BWH, Brigham and Women’s Faulkner Hospital, Inc. (FH), MGH, McLean and North Shore Medical Center, Inc. (NSMC) as further described herein in order that the rights and welfare of the participants in the research are protected. In so doing, the PHRC shall be committed to following the letter and spirit of the human-subject protection regulations and guidance to ensure the integrity of the PHRC decision-making process. The PHRC shall operate in full compliance with all applicable federal, state, and local laws and regulations, and with the Federalwide Assurances (FWAs) and incorporated “Terms of the Federalwide Assurance for Institutions within the United States” held by BWH, FH, MGH, McLean and NSMC. The responsibility for the protection of the rights and welfare of human subjects shall be shared both by the institutions and the investigators conducting the research.

ARTICLE II – ETHICAL PRINCIPLES

2.0 Ethical Principles

The PHRC shall be guided by the *Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, generally known as the “Belmont Report.”

ARTICLE III – AUTHORITY AND INDEPENDENCE

3.0 Authority

The PHRC are authorized to review and oversee human-subjects research that is conducted by employees or agents (e.g., professional staff) of the BWH, FH, MGH, McLean and NSMC in connection with their institutional responsibilities, regardless of the location of the research or source of funding, in accordance with federal, state, and local laws and regulations. Consistent with the federal regulations, the PHRC "shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities" constituting non-exempt human-subjects research under the regulations. [45 CFR 46.109(a)][21 CFR 56.109(a)] Further, the PHRC "shall conduct continuing review of [such] research" as appropriate to the degree of risk (in federally-funded research, no less than annually). [45 CFR 46.109(e)][21 CFR 56.109(f)] The PHRC shall also "suspend or terminate approval of [such] research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects." [45 CFR 46.113][21 CFR 56.113] These fundamental authorities of the PHRC have been explicitly recognized by the Institutional Officials (IOs) for BWH/FH and MGH and confirmed in written communications to the Director and Chair of the PHRC and the Director, Partners Human Research Affairs (HRA).

The PHRC also has the authority within the institutions for determining:

- whether a research activity involves human subjects within the meaning of the DHHS, FDA, or other applicable federal regulations
- whether the institution(s) is engaged in human subjects research within the meaning of DHHS regulations; and
- whether a research activity involving human subjects is exempt from 45 CFR 46 and 21 CFR 56.

Investigators or others within the organization may not independently make exemption determinations.

With respect to non-exempt human-subjects research conducted by employees or agents of BWH, FH, MGH, McLean and NSMC in connection with their institutional responsibilities, the PHRC has the specific authority to:

- approve, require modifications in (to secure approval of), or disapprove research activities involving human subjects;
- require progress reports from investigators;
- oversee the conduct of research;
- observe or have a third party observe the consent process and the research;
- suspend or terminate approval of research not being conducted in accordance with the PHRC's requirements or that has been associated with unexpected serious harm to subjects;
- place restrictions on a research activity;

- request a directed audit by the Partners Human Research Quality Improvement Program;
- otherwise investigate, address, remedy and, when required or appropriate, report on incidences of noncompliance with legal, regulatory, or PHRC requirements or determinations;
- conduct reviews and inquiries regarding human-subjects research as needed to obtain information necessary for the fulfillment of human research protection responsibilities and, for federally funded research, the institutional responsibilities outlined in the institutions' Office for Human Research Protections (OHRP)-approved Federal Wide Assurance (FWAs); and
- act as the HIPAA Privacy Board for research activities.

In exercising their authority, the PHRC shall communicate their decisions regarding human-subjects research to investigators and to the institution through the Partners Human Research Office.

3.1 Independence of the PHRC

The PHRC shall exercise independence as the entities authorized to review and oversee non-exempt human-subjects research for BWH, FH, MGH, McLean and NSMC. Consistent with federal regulations, no one within the institutions may approve such human-subjects research that has not been approved by the PHRC. [45 CFR 46.112][21 CFR 56.112] However, research approved by the PHRC may be subject to further institutional review and approval. Investigators may appeal the decision of the PHRC in writing directly to the Director and Chair of the PHRC as described in Article XI - Review of Research.

3.2 Undue Influence

In the event of undue influence (e.g., someone outside of the PHRC seeks to influence the outcome of PHRC review of a research activity), the PHRC Director and Chair shall work with the Director of HRA and the IOs, as necessary, to remedy any concern. Responses to such a concern shall preserve the PHRC's independence. Measures may include, for example, discussion between the Director of HRA and the person causing the undue influence and, when appropriate, discussion with such person's department chair or supervisor; reassignment of the protocol to another PHRC panel; and/or recusal of the PHRC member upon whom undue influence was exerted.

ARTICLE IV – SCOPE OF RESPONSIBILITY

4.0 Scope of Responsibility

The PHRC shall be responsible for the review and oversight of all non-exempt human-subjects research that is conducted by BWH, FH, MGH, McLean and NSMC employees or agents (e.g., professional staff) in connection with their institutional responsibilities, regardless of the location of the research or source of funding, except as follows:

- oncology research conducted under the auspices of the Dana Farber/Harvard Cancer Center, which is subject to review and approval of the Dana Farber Cancer IRBs;
- research involving prisoners, which is subject to review and approval of the Harvard School of Public Health IRB; and
- research reviewed by another institution or entity on behalf of BWH, FH, MGH, McLean and/or NSMC through an IRB authorization agreement executed by the relying and relied upon institution or entity.

At the request of the investigator or other institutional representatives, the PHRC may provide guidance on or review an innovative diagnostic or therapeutic activity that involves human subjects, but that does not meet the definition of human-subjects research.

4.1 Definitions

Human-subjects research means activities that meet the DHHS definition of *research* and involve a *human subject* as defined by DHHS or meet the FDA definition of *clinical investigation* and involve a *human subject* or *subject* as defined by FDA. The DHHS definition for *research* and *human subject* and the FDA definition for *clinical investigation*, *human subject*, and *subject* are provided below:

Research as defined by DHHS means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.
[45 CFR 46.102(d)]

Human subject as defined by DHHS means a living individual about whom an investigator (whether professional or student) conducting research obtains (1) Data through intervention or interaction with the individual, or (2) Identifiable private information. *Intervention* includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. *Interaction* includes communication or interpersonal contact between investigator and subject. *Private information* includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking

place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects. [45 CFR 46.102(f)(1)(2)]

Clinical investigation as defined by FDA means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of part 58 of this chapter, regarding nonclinical studies. The terms *research*, *clinical research*, *clinical study*, *study*, and *clinical investigation* are deemed to be synonymous... [21 CFR 50.3(c) and 21 CFR 56.102(c)]

Human subject as defined by FDA means an individual who is or becomes a participant in research, either as a recipient of the *test article* or as a control. A subject may be either a healthy human or a patient. [21 CFR 50.3(g) and 21 CFR 56.102(g)]

Test article as defined by FDA means any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product or any other article subject to regulation under the act or under sections 351 and 354-360F of the Public Health Service Act (42 U.S.C. 262 and 263b-263n).

Subject as defined by FDA means a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or have a medical condition or disease [21 CFR 812.3(p)].

ARTICLE V – SPECIFIC FUNCTIONS OF THE PARTNERS HRC

5.0 Specific Functions of the PHRC

The PHRC shall follow written policies and procedures for the following:

- (1) Determining whether a research activity submitted for PHRC review is human-subjects research within the meaning of DHHS, FDA or other applicable federal regulations;
- (2) Determining exemptions from 45 CFR 46 and 21 CFR 56;
- (3) Conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and to the institution;
- (4) Determining which projects require review more often than annually;
- (5) Determining which projects need verification from sources other than the investigators that no material changes have occurred since the last review;
- (6) Ensuring prompt reporting of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which PHRC approval has already been given, may not be initiated without PHRC review and approval except when necessary to eliminate apparent immediate hazards to the subject;
- (7) Ensuring prompt reporting to the PHRC, appropriate institutional officials and, when required or appropriate, to the department or agency head (regulatory agencies) of any unanticipated problems involving risks to subjects or others;
- (8) Ensuring prompt reporting to the PHRC, appropriate institutional officials and, when required or appropriate, to the department or agency head (regulatory agencies) of any serious or continuing noncompliance with federal regulations or the requirements or determinations of the PHRC;
- (9) Ensuring prompt reporting to the PHRC, appropriate institutional officials and, when required or appropriate, to the department or agency head (regulatory agencies) of any suspension or termination of PHRC approval; and
- (10) Except when an expedited review procedure is used, reviewing proposed research at convened meetings at which a majority of the members of the PHRC are present, including at least one member whose primary concerns are in nonscientific areas. In order for the research to be approved, it shall receive the approval of a majority of those members present and eligible to vote when the research activity is reviewed at the meeting.

ARTICLE VI – MEMBERSHIP

6.0 Membership

Each PHRC panel shall be composed of at least five (5) members with varying backgrounds to promote complete and adequate review of human-subjects research commonly conducted at the institutions. The membership shall include individuals with the necessary experience and scientific or scholarly expertise and knowledge of the local research context to review the scope of biomedical and behavioral research conducted at BWH, FH, MGH, McLean and NSMC. The membership

shall not include individuals who have responsibilities for negotiating grants or contracts with sponsors, or for developing the research enterprise through research ventures and licensing. Members shall include both men and women and members of minority groups. Each member shall have one vote and may have one or more designated alternates with similar scientific or scholarly expertise. Designated alternates (alternate voting members) shall be asked to attend meetings and vote when the primary voting member indicates that s/he does not plan to attend the meeting. Should both the primary voting member and alternate voting member attend the same meeting and be present for review of the same research activity, only one member shall vote on the specific research activity under review. The other shall be recorded in the minutes as attending, but not voting on the research activity.

The membership of each PHRC panel shall include:

- physicians;
- scientists;
- at least one member who is unaffiliated with any Partners HealthCare System, Inc. (Partners) entity or component of Harvard University (HU) and who is not part of the immediate family of a person who is affiliated with any Partners entity or HU component; and
- at least one member whose primary concerns are in nonscientific areas, such as lawyers, ethicists, and clergy.

6.1 Recruitment and Selection of Members

Affiliated physician, scientist, and nonscientist members shall be recruited by the Director and Chair of the PHRC through the chairs/chiefs/heads of the hospital departments or units or through current PHRC members. Non-affiliated physician, scientist, and nonscientist members shall be recruited through current PHRC members, through the volunteer department or various community agencies or groups. Additionally, individuals who are affiliated or non-affiliated may self-refer. New members shall be recruited as needed to ensure that the membership of each PHRC panel continues to include individuals with varying backgrounds and the necessary experience and scientific or scholarly expertise to review the scope of biomedical and behavioral research conducted at BWH, FH, MGH, McLean and NSMC. In addition, new members shall be recruited on an as needed basis to replace the scientific or scholarly expertise of members who resign and, when needed, to provide additional scientific or scholarly expertise to review new research programs.

6.2 Periodic Review of the Membership

The membership of the PHRC shall be reviewed at least annually to determine if the membership continues to include individuals with varying backgrounds and the experience and scientific or scholarly expertise needed

to review the scope of biomedical and behavioral research conducted at BWH, FH, MGH, McLean and NSMC. The Director and Chair of the PHRC shall conduct this review with the PHRC Chairpersons and the Director, Human Research Review and Compliance.

The Partners Human Research Office shall be responsible for compiling information about research protocols reviewed at convened meetings (full board review) to assess the scope of biomedical and behavioral research reviewed by the PHRC. The report shall include institution, department and unit, as well as special populations, such as pregnant women and fetuses, prisoners, children, and individuals with impaired decision-making capacity.

6.3 Term of Appointment

Appointments to the PHRC shall be made by the Director and Chair of the PHRC. There shall be no term limits; however, members may be removed by the Director and Chair for cause as described elsewhere in this document.

6.4 Equal Opportunity

The membership shall include individuals who can represent the perspective of the subjects who participate in research. No qualified individual shall be rejected from the membership on the basis of race, gender, creed, religion, color, national origin, age, disability, or sexual orientation.

6.5 Procedures for Appointment and Reappointment

Prospective members shall be asked to: (1) attend a meeting of the PHRC; (2) complete the *Partners Human Research Committee Member Information Sheet*; (3) provide a copy of their curriculum vitae or resume, (4) complete the Collaborative IRB Training Initiative program for biomedical research; and (5) complete the PHRC member orientation program. Based on the information provided and the membership requirements of the PHRC, the Director and Chair shall appoint individuals to the membership of one or more panels of the PHRC. The Human Research Office shall be responsible for notifying the individual in writing of his/her appointment and, when applicable, the relevant Department Chair/Chief. When the individual's membership is rejected, the Director and Chair of the PHRC shall be responsible for providing the individual with the basis for rejection.

6.6 Resignation

Any member may at any time resign from the PHRC by a written resignation submitted to the Director and Chair of the PHRC or Human Research Office.

6.7 Suspension or Removal of Members

The Director and Chair of the PHRC may suspend or remove for cause any member of the PHRC; provided, however, that such member shall have been given reasonable notice of the grounds for the suspension or removal and an opportunity to be heard. For this purpose, cause (with respect to a voting member) shall include the failure to attend more than one-third (1/3) of the convened meetings in a calendar year of the PHRC panel of which s/he is a member without excuse or the failure to perform reviews when assigned as a primary or secondary reviewer without prior notice or excuse.

6.8 Membership Records

The Partners Human Research Office shall maintain a roster of PHRC members for each PHRC panel to include the following information:

- Name;
- Earned degrees;
- Scientific status (i.e., physician-scientist, other scientist, or non-scientist);
- Experience and expertise, such as board certifications, licenses;
- Representative capacity (e.g., children, pregnant women, prisoners, economically disadvantaged, educationally disadvantaged, or cognitively impaired adults); and
- Affiliation, if any, with any Partners entity or with any component of HU.

The Partners Human Research Office shall be responsible for updating the membership roster and PHRC registration information as needed when membership changes and submitting the updated information to OHRP as required by the institutions' FWAs. PHRC rosters shall be retained for at least seven (7) years and shall be made available upon request, when applicable, to authorized representatives of DHHS, NIH, FDA and other federal agencies for inspection and copying onsite during normal business hours. Individual membership records shall be retained by the Human Research Office for at least seven (7) years from date of last service.

6.9 Member Designations

Members shall be designated as either: (1) physician-scientists, other scientists, or nonscientists; (2) affiliated or unaffiliated; and (3) primary voting member or alternate voting member.

6.9.1 Physician-Scientists

Members who have a medical degree shall be categorized as physician-scientists.

- 6.9.2 Other Scientists
Members who are not physicians, but whose training, background and occupation would incline them to view scientific activities from the standpoint of someone within a behavioral or biomedical research discipline shall be categorized as other scientist. [45 CFR 46.107(c) and 21 CFR 56.107(c)]
- 6.9.3 Nonscientists
Members whose training, background and occupation would not incline them to view scientific activities from the standpoint of someone within a behavioral or biomedical research discipline shall be categorized as nonscientists.
- 6.9.4 Affiliated
Members, or their immediate family members, who are affiliated with any Partners entity or any component of HU shall be considered affiliated. “*Immediate family member*” is defined as spouse, domestic partner, child, parent, or sibling. “*Affiliated*” members include, but are not limited to, individuals who are: part-time employees; current students; members of any governing panel or board of the institution; paid or unpaid consultants; healthcare providers holding credentials to practice at the institution; and volunteers working at the institution on business unrelated to the IRB.
- 6.9.5 Unaffiliated
Members, or their immediate family members, who are not affiliated with any Partners entity or component of HU shall be considered unaffiliated. “*Immediate family member*” is defined as spouse, domestic partner, child, parent, or sibling. “*Affiliated*” is defined as having an employment relationship with, a professional relationship with, a paid consultant relationship with, or a trustee/governing board member relationship with, or as being a student or volunteer of, any Partners entity or HU component.
- 6.9.6 Primary Voting Member
Primary voting members shall be required to vote or abstain from voting on each research activity considered by the PHRC panel when they are present for the discussion and vote unless the primary voting member’s alternate is present and is voting on the research activity.
- 6.9.7 Alternate Voting Member

Alternate voting members shall be required to vote or abstain from voting on each research activity considered by the PHRC panel when they are present for the discussion and vote and the primary voting member for whom they are a designated alternate voting member is not present or is not voting.

6.9.8 Massachusetts General Law 94C:8

A subset of the membership of each PHRC panel shall be designated as the Institutional Review Board with responsibility for the review of research protocols involving controlled substances M.G.L. 94C:8.

6.10 Use of Consultants

The PHRC shall have the authority to use consultants, when needed, to supplement or provide scientific or scholarly expertise not available on the PHRC. The PHRC Chairperson(s) or Administrative Chairperson(s) shall be responsible for determining that a consultant is needed when human-subjects research is scheduled for review. Additionally, members of the PHRC may vote to defer action and require an expert in the scientific area or discipline to review the research and provide consultation to the PHRC. In such cases, the PHRC Chairperson or Administrative Chairperson shall be responsible for identifying the consultant and for requesting such consultation, which may be provided in writing or orally at a convened meeting. Consultants shall not be considered members and, as such, shall not vote on human-subjects research before the PHRC; however, consultants shall be subject to the Partners policy on *IRB Member Conflicts of Interest*. Consultants shall be reminded that the discussions that take place at the meeting are confidential and should not be disclosed to others.

ARTICLE VII – MEMBER ORIENTATION, EDUCATION, TRAINING AND EVALUATION

7.0 Orientation, Education, Training and Evaluation

7.1 Orientation

The Administrative Chair of the PHRC shall provide new members with the access to online PHRC Governance and Operating Procedures, all PHRC policies, and relevant federal and state regulations. Members shall also be provided with access to the online PHRC Member Handbook.

7.2 Education and Training

Members shall be required to complete the Collaborative IRB Training Initiative (CITI) program for biomedical research.

7.3 Continuing Education and Training

Members shall be required to complete a CITI program for biomedical research refresher every three (3) years. The PHRC Office shall provide all members with new PHRC policies and guidance as well as any new and updated guidance documents from the FDA, OHRP, or other governing agencies. Additionally, members shall receive copies of various external IRB-related publications, e.g., *IRB, Human Research Report*. Members shall be encouraged to attend local, regional, or national conferences each year. The cost of attending conferences shall be covered by Partners Human Research Affairs when funds are available in the budget.

7.4 Evaluation

Members shall be evaluated annually to assess members' knowledge of regulations and ethical principles, preparedness for meetings, participation and attendance.

ARTICLE VIII – RESPONSIBILITIES OF MEMBERS

8.0 Responsibilities

Members shall be responsible for initial and continuing ethical and scientific review of all research activities involving human subjects as well as review of proposed changes in approved research, review of unanticipated problems involving risks to subjects or others, and review of reports of serious or continuing noncompliance that are on the agenda of the PHRC meeting they are attending and for considering whether:

- (1) Risks to subjects are minimized: (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) 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;
- (3) Selection of subjects is equitable;
- (4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116 and when applicable, 21 CFR 50.20;
- (5) Informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117 and when applicable, 21 CFR 50.27;
- (6) When appropriate, the research plan makes 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) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects;
- (9) When the research is a device investigation, the research is a significant risk device study or a nonsignificant risk device study; and
- (10) When applicable, the human research described in the grant or contract funding or supporting the research is consistent with the human research described in the protocol submitted to the PHRC.

Primary voting members (or their alternate voting members) shall be expected to attend at least two-thirds (2/3) of the scheduled PHRC meetings of which they are a member in each calendar year. Attendance records shall be reviewed annually. The Director and Chair of the PHRC shall consider suspension or removal of primary voting members who have not attended more than one-third (1/3) of the scheduled meetings during the past year or the appointment of an alternate voting member with similar scientific or scholarly expertise to provide the necessary expertise when the primary voting member is not present.

ARTICLE IX – CONFLICTS OF INTEREST

9.0 Conflicts of Interest

All members of the PHRC shall be required to disclose conflicts of interest and recuse themselves from participating in the discussion and vote on human-subjects research with which they have a conflict of interest as defined in the Partners policy on *IRB Member Conflicts of Interest*. In preparation for each meeting, the Human Research Office shall remind members that they must recuse themselves from the discussion and vote on protocols if they are involved in the conduct or evaluation of the research or have significant financial interests (i) that would reasonably be affected by the research for which PHRC approval is sought, and/or (ii) in entities whose financial interests would reasonably appear to be affected by the research. When members recuse themselves, they shall leave the room for the discussion and vote on the research, except to provide information at the PHRC's request prior to the discussion and vote. Recusals shall be documented in the minutes of the meeting as not present for the discussion and vote. Recusals shall not count towards the quorum requirement for the review.

Individuals who are asked to act as a consultant to the PHRC with respect to review of a particular research protocol shall be required to disclose any conflicts of interest as defined in the Partners policy on *IRB Member Conflicts of Interest*.

Individuals may not act as consultants if they are involved in the conduct or evaluation of the research or if they have significant financial interests (i) that would reasonably be affected by the research for which PHRC approval is sought, and/or (ii) in entities whose financial interests would reasonably appear to be affected by the research.

ARTICLE X – CHAIRPERSONS

10.0 PHRC Chairpersons and Administrative Chairpersons

10.1 Qualifications

The PHRC Chairpersons shall be selected and appointed by the Director and Chair of the PHRC. Chairpersons shall be selected from among PHRC members with three (3) or more years of experience. There shall be no term limits placed on length of service. The Chairpersons shall be provided with orientation and training by the Director and Chair of the PHRC and/or by an experienced Administrative Chairperson. PHRC Chairpersons shall be required to attend at least one human-subjects protection-related local, regional or national conference every three years.

The PHRC Administrative Chairpersons shall be selected by the Director, Human Research Review and Compliance, with input from the Director and Chair of the PHRC. Administrative Chairpersons shall have extensive knowledge of federal, state, and local laws and regulations governing human-subjects research acquired through at least three (3) years of direct IRB experience or experience in clinical research.

10.2 Periodic Review

The PHRC Chairpersons shall be reviewed at least annually by the Director and Chair of the PHRC, with input from the Director, Human Research Review and Compliance and the Administrative Chairpersons, who shall provide continuous objective feedback based on quality assurance activities that include review of PHRC minutes, and expedited and exempt reviews for compliance with regulatory requirements. The PHRC Chairpersons shall participate in ongoing educational activities coordinated by the Director and Chair of the PHRC and the Director, Human Research Review and Compliance.

The PHRC Administrative Chairpersons shall be reviewed annually by the Director, Human Research Review and Compliance, with input from PHRC Chairpersons in accordance with Partners Human Resources Policies and Procedures.

10.3 PHRC Chairpersons and Administrative Chairpersons Responsibilities

The PHRC Chairpersons and Administrative Chairpersons are voting members of the PHRC and shall be responsible for one or more of the following:

- determining whether a research activity submitted to the PHRC for review is human-subjects research within the meaning of the DHHS, FDA or other applicable regulations;
- determining exemptions from 45 CFR 46 and 21 CFR 56;
-
- presiding at convened PHRC meetings during which the PHRC conducts: (i) initial and continuing ethical and scientific review of research activities involving human subjects; (ii) review of proposed changes in approved research during the period of approval that are not minor; (iii) review of unanticipated problems involving risks to subjects or others, including adverse events that are serious, unexpected and related to the research; and (iv) review of reports of possible serious or continuing noncompliance;
- reviewing modifications in research required by the PHRC at convened meetings to secure approval, and confirming that modifications have been made as required by the PHRC;
- conducting initial and continuing ethical and scientific review of research activities involving human subjects that may be approved using the expedited review procedure;
- conducting review of proposed minor changes in approved research during the period of PHRC approval;
- conducting review of unanticipated problems involving risks to subjects or others, including adverse events that are unexpected and related to the research, but are not serious;
- conducting review of reports of minor noncompliance;
- participating in the development of human-subjects research policies and procedures;
- fulfilling triennial human-subjects protection continuing education requirements, including attendance at conferences, workshops, seminars, or lectures pertaining to human-subjects research; and
- performing other activities, as needed, to fulfill institutional responsibilities set forth in the FWAs or at the request of the Director and Chair of the PHRC or Director, Human Research Review and Compliance.

XI – REVIEW OF RESEARCH

11.0 Review of Research

The PHRC has the authority to and shall be responsible for determining whether a research activity submitted to it is human-subjects research within the meaning of 45 CFR 46, 21 CFR 50, 56 and 812, or other applicable federal regulations. When the research activity is human-subjects research, the PHRC shall determine whether non-FDA regulated research is exempt in accordance with 45 CFR 46.101(b)(1-6). When providing ethical review of exempt research, the PHRC shall be guided by the *Ethical Principles and Guidelines for the Protection of Human Subjects of Research* and the requirements of the Health Insurance Portability and Accountability Act (HIPAA) of 1996 and its implementing regulations as may be amended from time to time. The PHRC shall act as the HIPAA Privacy Board for research activities at BWH, FH, MGH, McLean and NSMC.

The PHRC shall conduct initial and continuing ethical and scientific review of non-exempt human-subjects research at intervals appropriate to the degree of risk and, when federally funded or otherwise subject to federal regulation, not less than once per year and shall review proposed changes in approved research during the period of PHRC approval either at a convened meeting of the PHRC or, when applicable, by use of the expedited review procedure authorized in 45 CFR 46.110 and, when applicable, 21 CFR 56.110. When conducting initial and continuing review or review of proposed changes in approved research, the PHRC shall determine that all of the requirements for approval of human-subjects research in 45 CFR 46.111 and, when applicable, 21 CFR 56.111 are satisfied.

Additionally, when conducting review using the expedited review procedure, the PHRC Chairperson, Administrative Chairperson or designated reviewer shall be responsible for determining whether the research is minimal risk and the applicability of the expedited review categories. The PHRC Chairperson, Administrative Chairperson or designated reviewer shall have the authority to approve, require modifications in the research to secure approval, or defer action for more information; however, they may not disapprove the research. Research may be disapproved only after review by the PHRC at a convened meeting.

The PHRC and relevant ancillary committees or departments shall approve all non-exempt human-subjects research prior to initiation of the research. Non-exempt human-subjects research cannot be approved by any other institutional body or individual(s) if the research has not been approved by the PHRC. Investigators may appeal the decision of the PHRC to disapprove human-subjects research in writing directly to the Director and Chair of the PHRC. The Director and Chair of the PHRC shall review the appeal with the Chair of the PHRC panel that disapproved the research. The appeal shall be scheduled for review at a convened meeting of the PHRC panel that disapproved the research initially. The investigator shall be given the opportunity to appeal the decision of the PHRC in person at the convened meeting.

XII – CONVENED MEETINGS

12.0 Meetings

The PHRC shall meet regularly. Meetings shall be scheduled in advance for the entire calendar year and shall be posted on the PHRC website. Members shall be informed of the meeting schedule prior to the end of the previous calendar year. The agenda shall be finalized by the PHRC Chairperson and/or Administrative Chairperson taking into consideration the nature and complexity of the human-subject research activities on the agenda and members attending the meeting. The agenda shall be limited as needed to allow sufficient time for discussion of each research activity before the Committee. Members shall be contacted prior to the meeting to determine attendance. From among those members planning to attend the meeting, the PHRC Chairperson and/or Administrative Chairperson shall assign a primary and secondary reviewer to each human-subjects research activity on the agenda. When making review assignments, the PHRC Chairperson and/or Administrative Chairperson shall take into consideration the experience and scientific or scholarly expertise and, when applicable, knowledge of and experience in working with individuals with impaired decision-making capacity, children, pregnant women and fetuses, or neonates, required to review the research. In general, protocols shall be scheduled for review by receipt date; however the PHRC reserves the right to reschedule protocols for review based on the experience and expertise of the members planning to attend the meeting or to request the use of a consultant to supplement or provide scientific or scholarly expertise not available on the PHRC. Research involving prisoners as subjects shall be referred to the Harvard School of Public Health (HSPH) IRB for review on behalf of BWH, FH or MGH, under an appropriate IRB Authorization Agreement. The agenda and materials related to the human-subjects research scheduled for review at the meeting shall be provided to members at least five (5) days in advance of the meeting to allow sufficient time for review.

12.1 Primary and Secondary Reviewers

The primary and secondary reviewers shall perform an in-depth review of all materials provided to them relevant to the human-subjects research they are assigned to review including, when applicable, any investigational drug brochure or investigational device information, or NIH or other federal grant application or proposal for funding. The primary and/or secondary reviewer shall be responsible for notifying the PHRC Chairperson and/or Administrative Chairperson if s/he has a conflict of interest as defined in the Partners policy on *IRB Member Conflicts of Interest*. In such cases, the PHRC Chairperson and/or Administrative Chairperson shall reassign review of the research activity to another member.

12.2 Members Not Assigned as Primary or Secondary Reviewers

Members who are not assigned as the primary or secondary reviewer shall perform review of, when applicable, completed Forms, Protocol Summary, Research Consent Form and recruitment materials in sufficient depth to vote on the research activity at the convened meeting.

12.3 Quorum

Human-subjects research that cannot be reviewed using the expedited review procedure shall be reviewed at a convened meeting of a quorum of the membership of the PHRC, including at least one physician-scientist and at least one member whose primary concerns are in nonscientific areas. At least one non-affiliated member should also be in attendance. The presence of more than one-half the voting membership shall constitute a *quorum*. Quorum shall be maintained for the discussion and vote on each research activity on the agenda. Members not present for or recused due to a conflict of interest from the discussion and vote on a research activity shall not be counted towards the quorum. When the primary voting member and alternate voting member are present for the discussion and vote on a research activity, only one member shall be counted towards the quorum for the specific research activity under review. The PHRC shall not vote on any research activity when a quorum of the membership is not present for the vote. The Chairperson and/or Administrative Chairperson shall be responsible for ensuring that at least one non-scientist member is in attendance and that quorum is achieved before the meeting begins and is maintained throughout the meeting when each research activity on the agenda is reviewed. The Administrative Chairperson or designee shall be responsible for recording attendance and vote on each research activity.

12.4 Guests

Normally, PHRC meetings are closed to the public, although on occasion and at the discretion of the PHRC, individuals (such as consultants or others) may attend PHRC meetings as guests. In such cases, guests shall be reminded that the discussions that take place at the meeting are confidential and should not be disclosed to others. Guests are not members of the IRB by virtue of their attendance and are not eligible to vote.

12.5 Discussion and Vote

The primary and secondary reviewers shall present their reviews and the PHRC Chairperson shall open the review for discussion by the members. At the end of the discussion, the primary and secondary reviewers or another member shall make a motion to approve, require modifications in the research (to secure approval), defer action for more information, or disapprove the research. When the motion is to approve or require modifications in the research (to secure approval), the motion shall include the period of approval (one year or less). A vote on the motion shall be

taken by show of hands or voice vote, and the number of votes for, against, and abstentions from voting shall be recorded in the minutes. All motions shall be decided by majority vote of the members present for the review and eligible to vote on the research activity.

12.6 Minutes of Meetings

The minutes shall include the following:

- Primary voting members (or alternate voting members) present;
- Primary voting members absent;
- Staff and guests, including consultants, present; and

For each human-subjects research activity and clinical investigation reviewed at the meeting:

- Action voted on by the PHRC;
- Number of votes for, against, and the number of abstentions from voting (documentation of quorum);
- Members attending the meeting but not present for the discussion and vote;
- Recusals of voting members due to conflicts of interest;
- Period of PHRC approval, (e.g., one year or less);
- When applicable, summary of information provided by consultant(s);
- Findings and determinations of the PHRC required by regulation including, when applicable, waiver or alteration of the consent process, additional protections for pregnant women, fetuses and neonates, and for children;
- When applicable, rationale for significant versus nonsignificant risk device determinations;
- Summary of the discussion of controverted issues and their resolution, if any;
- When applicable, justification of deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document;
- Modifications required and/or additional information requested by the PHRC; and
- Basis for requiring changes or disapproving the research.

Minutes shall be made available to the PHRC members for review and approval and shall not be altered once approved. Minutes shall be retained by the Partners Human Research Office for at least seven (7) years and shall be maintained in a secure area within the Human Research Office or in a secure area or application on the Partners network.

12.6.1 Access to Minutes of Meetings

Minutes of meetings shall be made available to the relevant IOs of BWH, FH, MGH, McLean and NSMC, as applicable, and, upon request, to IOs of other institutions who, by appropriate IRB Authorization Agreement, rely on the PHRC for IRB review. Minutes shall also be available upon request, when applicable, to authorized representatives of DHHS, NIH, FDA and other federal agencies for inspection and copying onsite during normal business hours. Minutes shall not ordinarily be available to others within or outside the institutions unless otherwise required by law. Subpoenas for meeting minutes shall be handled in consultation with the Partners Office of the General Counsel and the Risk Management Office of the involved institution(s).

ARTICLE XIII – RECORDS OF REVIEW ACTIVITIES

13.0 Records of Review Activities

In addition to minutes of convened meetings, the Partners Human Research Office shall maintain individual files of every research activity reviewed by the PHRC, whether at a convened meeting or through the use of the expedited review procedure, to include:

- All of the documents submitted with the research proposal for initial review and subsequently including, but not limited to, the application form, protocol summary, detailed protocol or research plan, recruitment materials (letters, flyers, advertisements, etc.), consent form(s), drug/device brochures, , NIH cooperative group protocol, NIH cooperative group sample consent form, ancillary committee/department review, scientific evaluations, if any;
- When applicable, the application for funding (e.g., NIH or other federal grant), in the secure Agreements application on the Partners network;
- When applicable, written reports from consultants to the PHRC;
- Checklists and review documentation, including review forms documenting, when applicable, justification for expedited review, exemption determination, findings required by applicable regulations and laws signed by PHRC Chairpersons/Administrative Chairpersons or designated alternate(s);
- PHRC-approved recruitment materials;
- PHRC-approved consent forms;
- Progress reports, interim analyses, safety reports, DSMB/DMC reports;
- Reports of injuries to subjects and/or adverse events;
- Reports of unanticipated problems involving risk to subjects or others;
- Reports of protocol deviations and noncompliance;

- Proposed changes to the protocol and revised documents (amendments);
- Copies of all correspondence between the PHRC and investigator;
- Continuing review activities and all of the documents submitted for continuing review including, but not limited to application form, protocol summary, detailed protocol, recruitment materials,; and
- Statements of significant new findings provided to subjects.

Individual files of research activities shall be retained by the Partners Human Research Office for at least seven (7) years from completion of the research or closure of the file. Files shall be maintained in paper format in a secure area within the Human Research Office or sent to an external vendor for long-term storage as needed, or in electronic format in a secure area or application on the Partners network.

13.1 Access to Records of Review Activities

Access to individual files of review activities shall be provided to the relevant IOs of BWH, FH, MGH, McLean and NSMC and to PHRC Chairpersons, PHRC Administrative Chairpersons, PHRC members, and Partners Human Research Office staff to carry out their human research protection responsibilities. Investigators may be provided reasonable access to files pertaining to their own research activities, subject to prior review by the Director and Chair of the PHRC or designee to ascertain whether the file contains any materials to which the investigator should not be granted access. Other institutional access to individual files of review activities is limited to those with a legitimate need for access, such as other institutional offices or departments within the Partners Human Research Protection Program. With respect to parties outside the institution, individual files of review activities shall be made available upon request to authorized representatives of the sponsor and, when applicable, to authorized representatives of OHRP, NIH, FDA and other federal agencies for inspection and copying onsite during normal business hours. Subpoenas for documents or materials maintained in the PHRC's files of review activities shall be handled in consultation with the Partners Office of the General Counsel and the Risk Management Office of the involved institution(s).

ARTICLE XIV – CONFIDENTIALITY

14.0 Confidentiality

PHRC review proceedings and records of review activities shall generally be considered confidential and protected from access except as provided in these Governance and Operating Procedures (see Articles XII and XIII). PHRC members or others with access to these proceedings or records shall not use them for any purpose other than to carry out their review responsibilities and shall not

disclose them to others who are not authorized under these procedures to have access. Such protection is essential to encourage open discussion by the PHRC in review of proposed research, maintain the integrity of the deliberative process, safeguard the privacy and confidentiality of participants in research and avoid disclosure of information that is proprietary to the research sponsor or other third party and which the institutions may be contractually obligated to keep confidential.

Without limiting any of the above, the Partners Human Research Office shall specifically prohibit distribution of documents and records containing confidential and proprietary information of the hospital or of a third party beyond the hospital research team and others within hospital/Partners with a need to know without prior written approval by the hospital or the third party involved, as applicable.

ARTICLE XV – INCIDENT REPORTING

15.0 Incident Reporting

Consistent with the federal regulations, the Director and Chair of the PHRC shall report any unanticipated problems involving risks to subjects or others; any serious or continuing noncompliance with Department of Health and Human Services (DHHS) or FDA regulations or the requirements or determinations of the PHRC; and any suspension or termination of PHRC approval in accordance with the PHRC policy *Reporting to Institutional Officials and Regulatory Agencies*.

ARTICLE XVI - POLICIES AND PROCEDURES

16.0 Policies and Procedures

The PHRC shall adopt such Policies and Procedures and develop such guidance as may be necessary for the review of human-subjects research in compliance with federal, state, and local laws and regulations. Policies implementing the authorities of the PHRC or concerning PHRC operations shall be developed by the Partners Human Research Office and approved by the Director of Human Research Affairs. Policies intersecting with or affecting other institutional offices or processes may be developed in consultation and coordination with those offices or institutional research leadership and are generally approved by the Partners Chief Academic Officer. All PHRC policies and procedures shall comply with Partners HealthCare Policy Management Process. The PHRC Policies and Procedures, including PHRC guidance documents and significant policy-related communications to the research community, shall be made available on the PHRC website and shall be maintained by the Partners Human Research Office for at least seven (7) years from the date of their adoption/distribution and shall be made available upon request to authorized representatives of the sponsor and, when applicable, authorized representatives of

OHRP, NIH, FDA and other federal agencies for inspection and copying onsite during normal business hours.