



Title:	Review of Unanticipated Problems in Human-Subjects Research
Department:	Human Research Affairs/Research Management
Policy Type:	<input checked="" type="checkbox"/> Partners System-wide <input type="checkbox"/> Partners System-wide Template <input type="checkbox"/> Partners Corporate <input type="checkbox"/> Partners Corporate Departmental <input type="checkbox"/> Entity
Applies to:	Employees, Professional Staff or Other Agents of Brigham and Women's Hospital (BWH, Faulkner Hospital (FH), and Massachusetts General Hospital (MGH))
Approved by:	Chief Scientific 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 determining whether a report of a problem or other information about the research is an unanticipated problem involving risks to subjects or others and for reporting unanticipated problems involving risks to subjects or others as required by 45 CFR 46.103(b)(5) and 45 CFR 46.108(a) and 21 CFR 56.108(b)(1).

DEFINITIONS:

See Definition of Human-Subjects Research

Unanticipated problem involving risks to subjects or others means any incident, experience, information, outcome, or other problem that is *unexpected* given the research procedures and that indicates that the research places subjects at increased risk of physical, psychological, economic, legal, or social harm than was previously known or recognized.

Unexpected means that the incident, experience, or outcome in terms of nature, severity or frequency is not described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document or the characteristics of the study population being studied.

POLICY STATEMENT:

The PHRC is responsible for determining whether an unanticipated problem in human-subjects research involves risks to subjects or others and for reporting according to the policy on *Reporting to Institutional Officials and Regulatory Agencies*. The PHRC Chairpersons are subject to the Partners policy on *IRB Member Conflicts of Interest* when reviewing and making determinations about unanticipated problems involving risks to subjects or others.

PROCEDURES:

1. Investigators relying on the PHRC for IRB review of human-subjects research are required to report unanticipated problems to the PHRC according to the PHRC policy *Reporting Unanticipated Problems in Human-Subjects Research* using the appropriate forms and within the required time frame.
2. The Human Research Office staff is responsible for receiving reports of unanticipated problems and for providing the report with the protocol file containing the current PHRC-approved protocol and consent form to the PHRC Chairperson for review. The entire protocol file is available to the PHRC Chairperson.
3. The reviewing PHRC Chairperson is responsible for determining whether the problem is unexpected and indicates that the research places subjects or others at a greater risk of physical, psychological, economic, legal, or social harm than was previously known or recognized and, if so, whether subjects are placed at increased risk of serious harm.
4. When the reviewing PHRC Chairperson determines that the problem is not unexpected or does not indicate that subjects or others are at increased risk of harm, then the problem is determined not to be an unanticipated problem involving risks to subjects or others. The report is noted, and no further action is required under this Policy.
5. When the reviewing PHRC Chairperson determines that the problem suggests possible serious or continuing noncompliance, the PHRC Chairperson will also follow the policy on Noncompliance in Human-Subjects Research.
6. When the reviewing PHRC Chairperson determines that the problem is unexpected and indicates that subjects or others are at increased risk of harm, then the problem is determined to be an unanticipated problem involving risks to subjects or others.
7. Unanticipated problems that do not indicate that subjects or others are at increased risk of serious harm are reviewed using the expedited review procedure. The PHRC Chairperson reviewing the unanticipated problem will take one or more of the following actions:
 - Accept the report and approve the proposed changes, if any, with no further action required;
 - Require additional information from the investigators and/or others (e.g., pharmacy, legal, privacy, or departmental chairpersons);
 - Require modifications to the protocol and/or consent form;
 - Require that subjects currently on protocol be notified of the problem;
 - Require that subjects whose participation has ended be notified of the problem;
 - Require that subjects currently on protocol be re-consented;
 - Request a directed audit by the Human Research Quality Improvement Program; or
 - Refer the problem for review by the PHRC at a convened meeting.

8. Unanticipated problems that indicate that subjects or others are at increased risk of serious harm are referred for review by the PHRC at a convened meeting, including changes made to eliminate apparent immediate hazards to subjects.
9. When the reviewing PHRC Chairperson determines that the changes are necessary to protect the rights and welfare of subjects, the changes may be approved prior to additional review by the PHRC at a convened meeting. The PHRC Chairperson may also, at his or her discretion, suspend or terminate the research to protect the safety of subjects.
10. The presiding PHRC Chairperson assigns a primary and secondary reviewer with experience or expertise in the scientific discipline or area. The primary and secondary reviewers are provided with a copy of the report of the problem, the approved consent form, and, when applicable, the revised consent form, and the detailed protocol as well as any other documents or information submitted by the investigator for review of the problem, e.g., monitoring group reports.
11. Members not assigned to review the problem report are provided with a copy of the report of the problem and the approved consent form and, when applicable, the revised consent form.
12. The primary and secondary reviewers are responsible for an in-depth review of the report of the problem and materials provided. All other members are responsible for review of the report of the problem and the consent forms in sufficient depth to vote at the meeting.
13. By majority vote of a quorum of the membership present at the convened meeting, the PHRC will take one or more of the following actions:
 - Accept the report and approve the proposed changes, if any, with no further action required;
 - Require additional information from the investigators and/or others (e.g., pharmacy, legal, privacy, or departmental chairpersons);;
 - Require modifications to the protocol and/or consent form;
 - Require that subjects currently on protocol be notified of the problem;
 - Require that subjects whose participation has ended be notified of the problem;
 - Require that subjects currently on protocol be re-consented;
 - Require observation of the consent process by a member of the IRB or the Partners Human Research Quality Improvement (QI Program);
 - Modify the continuing review schedule;
 - Suspend the research;
 - Terminate the research;
 - Request a directed audit by the Human Research Quality Improvement Program; or
 - Any other action deemed appropriate by the PHRC.
14. The PHRC Administrative Chairperson is responsible for preparing a description of the problem and for recording the findings and actions of the PHRC and, when relevant, the discussion of controverted issues and their resolution, in the minutes of the meeting.
15. The Human Research Office staff is responsible for notifying the Principal Investigator in writing of the findings and actions of the PHRC.
16. Within thirty (30) days of the PHRC meeting, the Director and Chair of the PHRC or designee shall be responsible for submitting a report of any serious unanticipated problem involving risks to subjects or others and, when applicable, suspension or termination of the research in accordance with the policy *Reporting to Institutional Officials and Regulatory Agencies*.

17. The records of the review by the PHRC and associated findings of fact and determinations and recommendations will be maintained in the Human Research Office with the protocol file.

OTHER APPLICABLE PARTNERS HEALTHCARE POLICIES:

Reporting Unanticipated Problems including Adverse Events
Noncompliance in Human-Subjects Research
Suspension or Termination of Human-Subjects Research
Reporting to Institutional Officials and Regulatory Agencies

REFERENCE:

45 CFR 46
21 CFR 56

DEVELOPMENT AND CONSULTATION

Human Research Office

Reviewed by:	Original Review Date:	Revision Approval Dates: