PARTNERS HEALTHCARE | FOUNDED BY BRIGHAM AND WOMEN'S HOSPITAL AND MASSACHUSETTS GENERAL HOSPITAL

Title:	Reporting Unapproved Deviations in PHRC-Approved Research
Department:	Human Research Affairs
Policy Type:	☑ Partners System-wide ☐ Partners System-wide Template ☐ Partners Corporate ☐ Partners Corporate Departmental ☐ Entity
Applies to:	Employees, Professional Staff or Other Agents of Brigham and Women's Hospital (BWH), Faulkner Hospital (FH), Massachusetts General Hospital (MGH), McLean Hospital (McLean), and North Shore Medical Center (NSMC)
Approved by:	Chief Academic Officer
Approval Date:	January 14, 2004
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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 requirements for reporting to the Partners Human Research Committees (PHRC) any unapproved deviation in PHRC-approved research.

DEFINITIONS:

See Definition of Human-Subjects Research

Deviation means any alteration/modification to the PHRC-approved research without prospective PHRC approval. The term *research* encompasses all PHRC-approved materials and documents including the detailed protocol, protocol summary, consent form, recruitment materials, questionnaires, and any other information relating to the research study.

Major Deviation means any alteration/modification to the PHRC-approved research that has the potential to negatively impact subject safety or integrity of study data (ability to draw conclusions from the study data), or affect the subject's willingness to participate in the study.

Minor Deviation means any deviation from the PHRC-approved research that does not have the potential to negatively impact subject safety or integrity of study data (ability to draw conclusions from the study data), or affect subject's willingness to participate in the study.

POLICY STATEMENT:

Investigators are responsible for conducting human-subjects research in accordance with all applicable federal and state regulations, Partners and Partners Human Research Committee (PHRC) policies and procedures, and the requirements of the PHRC. Federal regulations specifically require the IRB to review proposed changes in a research activity, and to ensure that such changes in approved research are not initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject [45CFR46.103(b)(4)(iii) and 21CFR56.108(a)(4)]. Planned changes to the PHRC-approved protocol are to be submitted to the PHRC as formal protocol amendments or protocol exceptions and must be approved prior to initiation or implementation of the change. See policy *Proposed Changes in PHRC-Approved Research and Exceptions*.

Unapproved deviations in PHRC-approved research are to be reported to the PHRC as unanticipated problems. The PHRC considers reports of unapproved deviations under its policies and procedures for review of reports of unanticipated problems and noncompliance. See policies *Review of Unanticipated Problems in Human-Subjects Research* and *Noncompliance in Human-Subjects Research.*

PROCEDURES:

Unplanned or unintentional deviations in PHRC-approved research may occur during the conduct of a research study or be discovered during routine data monitoring activities of the sponsor or investigator. When an investigator discovers or is made aware of an unapproved deviation, s/he must report the deviation to the PHRC as an unanticipated problem as follows:

1. Unapproved **major deviations** must be reported to the PHRC within five (5) working days of the date the investigator becomes aware of the unapproved deviation.
2. Unapproved **minor deviations** are to be recorded by the investigator in a protocol-specific Minor Deviation Log and submitted to the PHRC at continuing review. For **research limited to the use of medical records or excess human material**, in lieu of a Minor Deviation Log, unapproved minor deviations may be described in the Protocol Deviations section of the continuing review form.

Unapproved deviations should be reported to the sponsor as outlined in the sponsor's protocol or research or investigative plan.

It is the responsibility of the Principal Investigator (PI) to determine whether an unapproved deviation from the PHRC-approved protocol is major or minor and to ensure proper reporting to the PHRC. When making the determination of whether the unapproved deviation is major or minor, the Principal Investigator should consider whether the deviation negatively affected any of the following:

- The rights or welfare of the subject
- Risk benefit assessment
- The integrity of the data (the ability to draw conclusions from the study data)

The Principal Investigator is responsible for reviewing the Minor Deviation Log periodically to monitor compliance with the approved research. Frequent minor deviations of a similar nature should be reported to the PHRC as a major deviation.

Major Deviations

Examples (the list of examples is intended as a guide and is not all-inclusive)

- Changes necessary to eliminate apparent immediate hazards to the subject
- Failure to obtain informed consent, i.e., there is no documentation of informed consent
- Informed consent obtained after initiation of study procedures
- Informed consent for IND/IDE studies obtained by someone other than individuals authorized by the IRB to obtain consent, e.g. someone other than a licensed physician investigator
- Enrollment of a subject who did not meet all inclusion/exclusion criteria
- Performing study procedure not approved by the IRB
- Failure to report serious adverse event to the IRB and/or sponsor
- Failure to perform a required lab test that, in the opinion of the PI, may affect subject safety or data integrity
- Drug/study medication dispensing or dosing error
- Study visit conducted outside of required timeframe that, in the opinion of the PI, may affect subject safety
- Failure to follow safety monitoring plan

Minor Deviations

Examples (the list of examples is intended as a guide and is not all-inclusive)

- Implementation of unapproved recruitment procedures
- Missing original signed and dated consent form (only a photocopy available)
- Missing pages of executed consent form
- Inappropriate documentation of informed consent, including
    - missing subject signature
    - missing investigator signature
    - copy not given to the person signing the form
    - someone other than the subject dated the consent form
- Use of outdated/expired consent form that contains all required information and elements of informed consent
- Failure to follow the approved study procedure that, in the opinion of the PI, does not affect subject safety or data integrity
    - Study procedure conducted out of sequence
    - Omitting an approved portion of the protocol
    - Failure to perform a required lab test
    - Missing lab results
- Failure of subject to return study medication
- Over-enrollment
- Enrollment of subjects after IRB-approval of study expired
- Failure to submit continuing review application to the IRB before study expiration

REFERENCE:

45 CFR 46
21 CFR 56

OTHER APPLICABLE PARTNERS HEALTHCARE POLICIES:

Reporting of Unanticipated Problems Including Adverse Events
Review of Unanticipated Problems in Human-Subject Research
Proposed Changes in PHRC-Approved Research and Exceptions
Noncompliance in Human-Subjects Research
Minor Deviations/Violations Tracking Log

DEVELOPMENT AND CONSULTATION

Human Research Office
Human Research Quality Improvement Program

Reviewed by:	Original Review Date:	Revision Approval Dates: