Mass General Brigham

Title:	Reporting Unapproved Deviations in Human Subject Research
Department:	Human Research Affairs
Policy Type:	Mass General Brigham System-Wide
Applies to:	Employees, Professional Staff or Other Agents of Mass General Brigham
Approved by:	Chief Academic Officer
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Next Review Date:	October 1, 2022
Contact Person:	Director, Human Research Office

KEYWORDS:

IRB, Institutional Review Board

PURPOSE:

The purpose of this policy is to define the requirements for reporting to the Mass General Brigham IRB any unapproved deviation in Mass General Brigham IRB-approved research.

DEFINITIONS:

See Definition of Human Subjects Research

POLICY STATEMENT:

Investigators are responsible for conducting human-subjects research in accordance with all applicable federal and state regulations, Mass General Brigham IRB policies and procedures, and the requirements of the Mass General Brigham IRB. 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 [45CFR46.108(a)(3)(iii) and 21CFR56.108(a)(4)]. Planned changes to the Mass General Brigham IRB-approved protocol are to be submitted to the Mass General Brigham IRB as formal protocol amendments or protocol exceptions and must be approved prior to initiation or implementation of the change. See policy *Proposed Changes in IRB -Approved Research and Exceptions*.

The Mass General Brigham IRB considers reports of unapproved deviations under its policies and procedures forreview 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 Mass General Brigham IRB-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, they must report the deviation to the Mass General Brigham IRB as follows:

1. Unapproved **major deviations** must be reported to the Mass General Brigham IRB 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

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 Mass General Brigham IRB-approved protocol is major or minor and to ensure proper reporting to the Mass General Brigham IRB. 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 Mass General Brigham IRB 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
- Use of a consent document that has never been approved by the IRB
- Informed consent for IND/IDE studies obtained by someone other than individuals authorized by the IRB to obtain consent
- Enrollment of a subject who did not meet all inclusion/exclusion criteria
- Performing study procedure not approved by the IRB
- Failure to report an Unanticipated Problem to the IRB and/or failure to comply with sponsor reporting requirements regarding events
- 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)

- Missing original signed and dated consent form (only a photocopy available)
- Missing pages of executed consent form that do not contain any optional items or required signatures
- Inappropriate documentation of informed consent, including
    - 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 as approved by the IRB
- 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, unless it is a systemic problem
- Over-enrollment
- Failure to submit continuing review application to the IRB before study expiration

REFERENCE:

45 CFR 46
21 CFR 56

OTHER APPLICABLE Mass General Brigham POLICIES:

Reporting of Unanticipated Problems Review of Unanticipated Problems in Human-Subject Research Proposed Changes in Mass General Brigham IRB-Approved Research and Exceptions

Noncompliance in Human-Subjects Research
Minor Deviations/Violations Tracking Log

DEVELOPMENT AND CONSULTATION

Human Research Office
Human Research Affairs Compliance and Education Office