

Title:	Reporting Unanticipated Problems
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
Original Approval Date:	June 4, 2007
Original Effective Date:	June 4, 2007
Revision Approval Date(s):	September 8, 2010; March 7, 2014; May 1, 2017
Current Revision Effective Date:	October 1, 2021
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 problems and adverse events that require prompt reporting to the Mass General Brigham IRB.

This policy complies with Department of Health and Human Services (DHHS) regulations 45 CFR 46.108(a)(4)(i) and the U.S. Food and Drug Administration (FDA) regulations 21 CFR 56.108(b)(1) that require IRBs to have written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head / FDA of any unanticipated problems involving risks to subjects or others and is consistent with Office for Human Research Protections (OHRP) and FDA guidance on reviewing and reporting unanticipated problems involving risks to subjects or others and adverse events.

DEFINITIONS:

See Definitions in Human Subject Research

POLICY STATEMENT:

Principal investigators are required to report to the Mass General Brigham IRB any event meeting one of the following definitions (as defined in the Definitions in Human Subject Research policy):

- Any Unanticipated Problem Involving Risks to Subjects or Others (UPIRTSO)
- Any Unanticipated Adverse Device Effect (UADE)

Events meeting either of these definitions are considered “Unanticipated Problems” and should be reported if they occur during the conduct of the study, after study completion, or after subject withdrawal

or completion.

Reports are to be submitted within 5 working days/7 calendar days of the date the investigator first becomes aware of the problem. Events meeting these definitions include unexpected or unanticipated drug or device adverse reactions attributable to the intervention and that place subjects at increased risk of harm, however other examples include (but are not limited to):

- Breach of confidentiality or violation of HIPAA (e.g., lost or stolen laptop)
- Medication, procedural or laboratory error (e.g., errors in drug administration or dosing, surgical or other procedure, or testing of samples or test results) regardless of whether subjects experienced any harm
- Interim analysis, safety monitoring report, publication in a peer-reviewed journal, or other finding that indicates that there are new or increased risks to subjects or others or that subjects are less likely to receive any direct benefits from the research
- Change in FDA labeling (e.g., black box warning), withdrawal from market, manufacturer alert from the sponsor, or recall of an FDA-approved drug, device, or biologic used in the research
- Complaint by/on behalf of a research subject that indicates that the rights, welfare, or safety of the subject have been adversely affected or that cannot be resolved by the investigator
- Incarceration of a research subject during participation in research that is not approved for involvement of *prisoners* as subjects
- Violation of applicable regulations or requirements or determinations of the IRB identified by the research team or others (e.g., FDA Form 483 or Warning Letter) that indicates that the rights, welfare, or safety of subjects have been adversely affected
- Suspension or termination of the research, in whole or in part, based on information that indicates that the research places subjects at an increased risk of harm than previously known or recognized (e.g., FDA *clinical hold*)
- Premature suspension, termination or hold of the research by the sponsor
- Suspension or disqualification of an investigator by FDA, sponsor, or others
- Scientific misconduct

PROCEDURES:

Reports of UPIRTSOs and UADEs are to be submitted through Insight within 5 working days (7 calendar days) of the date the investigator first becomes aware of the problem. Even if the investigator is still in the process of collecting outcome or other information about the event, the investigator is responsible for meeting the reporting timeline based on when the event is recognized as a UPIRTSO or UADE. Additional information can be submitted to the IRB when it becomes available.

1. Reporting

The investigator must provide the following information in the report:

- (1) a detailed description of the event;
- (2) the basis for determining that the event is unexpected in nature, severity, or frequency;
- (3) the basis for determining that the event is related or possibly related to the research procedures;
- (4) the basis for determining that the research places subjects at an increased risk of harm); and
- (5) whether any changes to the research or other corrective actions are warranted.

NOTE:

- The Mass General Brigham IRB does not accept, and researchers should not report expected adverse events or expected serious adverse events unless the sponsor and/or investigator has determined and provided justification that the event meets the definition of a UPIRTSO or UADE. This includes sponsor IND/IDE safety reports that do not meet one of these definitions.
 - Events that occur more frequently than expected or that represent a more severe instance of the event than has previously occurred may be considered a UPIRTSO or UADE.
- Events that are UPIRTSOs or UADES that occur at sites that are not under the oversight of the Mass General Brigham should only be submitted when they impact the Mass General Brigham subject's safety, rights or welfare, or the conduct of the research at Mass General Brigham. Such reports would likely warrant changes to the conduct of the research, consent process, or require notification to subjects.

Amendments

When making reports, investigators should take into consideration whether substantive changes in the research or informed consent document, or other corrective actions may be warranted to protect the safety, welfare, or rights of subjects or others. Changes to the protocol and/or the informed consent document are to be submitted through Insight as an Amendment.

Examples of substantive changes include:

- changes to the eligibility criteria
- changes to safety monitoring procedures
- changes to the informed consent document to describe newly identified risk or new information
- suspension of enrollment of new subjects
- suspension or termination of the research

OTHER APPLICABLE MASS GENERAL BRIGHAM POLICIES:

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

DEVELOPMENT AND CONSULTATION:

Human Research Office
Human Research Compliance and Education Program