Mass General Brigham

Title:	Review of Unanticipated Problems in Human-Subjects 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
Original Approval Date:	December 6, 2007
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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 procedures the Mass General Brigham Institutional Review Board follows when determining whether a report of a problem or other information about the research is an Unanticipated Problem which includes either unanticipated problems involving risks to subjects or others (UPIRTSOs) and Unexpected Adverse Device Effects (UADEs).

POLICY STATEMENT:

The Mass General Brigham IRB is responsible for determining whether an event meets the definition of a UPIRTSO and for reporting according to the policy on *Reporting to Institutional Officials and Regulatory Agencies*. The Mass General Brigham IRB reviewers and Human Research Office (HRO) staff are subject to the Mass General Brigham policy on *IRB Member Conflicts of Interest* when reviewing and making determinations about Unanticipated Problems.

PROCEDURES:

1. Investigators relying on the Mass General Brigham IRB for IRB review of human subject research are required to report unanticipated problems to the Mass General Brigham IRB via the Insight system according to the Mass General Brigham IRB policy *Reporting Unanticipated Problems in Human Subject Research* using the appropriate Insight form and within the required time frame.
2. The HRO staff assign reports to an IRB Chairperson (or designee) for review. The Chairperson (or designee) reviews the report and corresponds with the research team to resolve any questions or

collect missing information. The IRB Chairperson (or designee) can:

1. Determine that the report meets the definition of a Unanticipated Problem
2. That the event does not meet the definition of a Unanticipated Problem
3. Refer review to the Other Event Committee (OEC)
4. Refer the event to the Senior IRB Chair for immediate action such as suspension.

3. In conducting reviews, the Chairpersons and the OEC have access to the entire protocol record maintained in Insight.

4. Review by the OEC:
   The OEC is comprised of the Senior IRB Chair, the HRO Director, the Human Research Affairs Compliance and Education Office (C&E Office) Director, other IRB Chairs or Vice Chairs as applicable, and HRO Assistant Directors as appropriate. The Senior IRB Chair (or designee) and/or OEC will evaluate whether events meet the definition of Unanticipated Problem and make the following determinations:

   a. If the event does not represent an unanticipated problem involving risks to subjects or others, the event is noted and no further action is required.

   b. If the event is determined to be a serious Unanticipated Problem, it is referred to the IRB for review.

   c. If the event is determined to be a Unanticipated Problem but not serious, the OEC and/or Senior IRB Chair (or designee) complete the review through the expedited review process and may take actions that include (but are not limited to):
      a. Accept the report and approve the proposed changes, if any, with no further action required;
      b. Require additional information from the investigators and/or others (e.g., pharmacy, legal, privacy, or departmental chairpersons);
      c. Require modifications in the protocol and/or consent form;
      d. Require that subjects currently on protocol be notified of the problem;
      e. Require that subjects whose participation has ended be notified of the problem;
      f. Require that subjects currently on protocol be re-consented;
      g. Request a directed audit by the C & E Office;
      h. Other actions as appropriate; or
      i. Refer the problem for review by the Mass General Brigham IRB at a convened meeting.

   d. If the problem suggests possible serious or continuing noncompliance, the OEC and/or Senior IRB Chair (or designee) will also follow the policy on *Noncompliance in Human Subject Research*.

5. When the OEC and/or Senior IRB Chair or designee 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 Mass General Brigham IRB at a convened meeting. The Senior IRB Chair or designee may also, at his or her discretion, suspend the research to protect the safety of subjects. In the event that the Senior IRB Chair or designee suspends the research, such suspension will be reported to and reviewed by the convened IRB.

6. Unanticipated Problem Review by the IRB:

   Unanticipated Problems may be reviewed by any Mass General Brigham IRB, however reports are routinely reviewed by IRB 02 which meets monthly or as needed.

   The Senior IRB Chair (or designee) assigns a primary and secondary reviewer with appropriate experience or expertise to review the unanticipated problem. IRB members are provided access in

Insight and/or are provided a copy of the report, 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). Any revised materials in response to the report are provided to members as well as a proposed corrective and preventative action plan as applicable.

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.

The IRB may take actions that include (but are not limited to):

1. Accept the report and approve the proposed changes, if any, with no further action required;
2. Require additional information from the investigators and/or others (e.g., pharmacy, legal, privacy, or departmental chairpersons);
3. Require modifications in the protocol and/or consent form;
4. Require that subjects currently on protocol be notified of the problem;
5. Require that subjects whose participation has ended be notified of the problem;
6. Require that subjects currently on protocol be re-consented;
7. Require observation of the consent process by a member of the IRB or the C&E Office;
8. Modify the continuing review schedule;
9. Suspend the research;
10. Terminate the research;
11. Request a directed audit by the C&E Office; or
12. Any other action deemed appropriate by the IRB.

The IRB may, when applicable, suspend or terminate the research. Reports to other entities are made in accordance with the policy *Reporting to Institutional Officials and Regulatory Agencies*.

The review by the IRB, the OEC or Senior IRB Chair (or designee) and associated determinations and recommendations are documented via the Insight checklist and/or meeting minutes.

The IRB sends written notification of determinations and actions taken to the PI through the Insight system. Reports to other entities are made in accordance with the policy *Reporting to Institutional Officials and Regulatory Agencies.*

OTHER APPLICABLE MASS GENERAL BRIGHAM POLICIES:

Reporting Unanticipated Problems including Adverse Events

Noncompliance in Human Subject 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