Mass General Brigham

Title:	Noncompliance 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:	June 11, 2007
Original Effective Date:	June 11, 2007
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Current Revision Effective Date:	October 1, 2021
Next Review Date:	October 1, 2022
Contact Person:	Director, Human Research Office

KEYWORDS:

IRB, Institutional Review Board

DEFINITIONS:

See Definitions in Human Subjects Research

PURPOSE:

The purpose of this policy is to define the duty and responsibility of individuals to report to the Mass General Brigham IRB (IRB) observed or potential noncompliance with federal, state and local laws and regulations or the requirements or determinations of the IRB and the procedures the Human Research Office (HRO) and IRB follow when reviewing reports of observed or potential noncompliance.

This policy is established to comply with the 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)(2) that require IRBs to have written procedures which the IRB will follow for ensuring prompt reporting to the IRB, appropriate institutional officials, Office for Human Research Protections, and, when applicable, the Drug FDA, of any serious or continuing noncompliance with the regulations or the requirements or determinations of the IRB.

This policy applies to investigators and others employed by, on staff at, or otherwise affiliated with Mass General Brigham who observe or otherwise become aware of potential noncompliance in connection with human subject research and clinical investigations subject to review by the IRB and to investigators who are the subject of a report of observed or potential noncompliance.

POLICY STATEMENT:

Mass General Brigham provides and maintains a culture characterized by integrity, responsible behavior and a commitment to the highest legal and ethical standards of human subject protection. Consistent with these principles, all human subjects research and clinical investigations conducted by Mass General Brigham employees or agents will be conducted in accordance with all applicable federal, state, and local laws and regulations and the highest ethical standards.

Any investigator or other individual employed by, on staff at, or otherwise affiliated with Mass General Brigham who observes or otherwise becomes aware of potential noncompliance with applicable federal, state, and local laws and regulations or the requirements or determinations of the IRB in connection with human subjects research and clinical investigations has the duty and responsibility to report the noncompliance to the Mass General Brigham IRB. This responsibility includes but is not limited to reporting noncompliance that is associated with or becomes apparent from protocol deviations, complaints or concerns of researchers or subjects, other problems in the research, or from results of audits of the research.

The IRB has the responsibility to: (1) fully investigate any reports of noncompliance and any audit results or reports of protocol deviations, complaints, or other problems that it receives that indicate observed or potential noncompliance; (2) have a process for determining appropriate actions for any findings of noncompliance; and (3) report any findings of serious or continuing noncompliance as required by DHHS and FDA regulations. When reviewing reports of noncompliance, the Senior IRB Chair, IRB Chairs, members of the IRB and HRO staff are subject to the Mass General Brigham policy on *IRB Member Conflicts of Interest.*

PROCEDURES:

1. Reporting Observed or Potential Noncompliance

   Reports/allegations of noncompliance or suspected non-compliance in the conduct of research or the operation of the IRB may be submitted to the HRO by a PI, study team, HRO staff, IRB members, the Human Research Quality Improvement program, other organization groups tasked with auditing, a research participant or any other person who has a concern.

   The applicable Mass General Brigham entities intend to protect, to the extent possible, the privacy of an individual who in good faith reports noncompliance on the part of another individual. Reports of noncompliance made in good faith will not reflect negatively on the individual reporting such noncompliance and, when applicable, will not affect his/her employment, in accordance with *Mass General Brigham Non-Retaliation Policy*.

   Reports may be made through Insight submission of an Other Event in accordance with the policy for *Reporting Unapproved Deviations in Mass General Brigham-Approved Research,* to the Human Research Office, to the Senior IRB Chair, IRB Chair or other organizational officials.

   Reports of noncompliance, whether written or oral, and whether made directly to the IRB through Insight or as part of another report to the IRB, should include a complete description of the noncompliance, of the observed circumstances and, the names of the individuals involved, if known. Whenever possible, the report should contain sufficient details to allow an assessment of noncompliance.

2. Allegations of Noncompliance

Reports of alleged noncompliance related to conduct of research are routed to the Senior IRB Chair (or designee) and/or the Other Event Committee (OEC). Reports of alleged noncompliance of the IRB are routed to the Vice President, Human Research Affairs (VP HRA.)

The OEC is comprised of the Senior IRB Chair, the HRO Director, the Compliance and Education 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 can make the following determinations:

1. The facts do not support a finding of noncompliance. The report of noncompliance is dismissed and no further action is required.

2. The allegation has a basis in fact and meets the definition of noncompliance. The remainder of this procedure for non-compliance is followed.

3. If unable to resolve whether the allegation has a basis in fact, the Senior IRB Chair (or designee) may engage other organizational leadership in the investigation or may refer the matter to the IRB for further investigation.

    a. If these entities determine that the allegation has no basis in fact, the report of noncompliance is dismissed and no further action will be taken.
    b. If these entities determine that the allegation involves noncompliance in fact, the remainder of this procedure for a report of noncompliance is followed.

3. Handling Reports of Noncompliance

Investigation of research noncompliance may include contact with the PI, research team members, and other individuals involved in the initial report as applicable. The OEC may also consult with the Office of General Counsel, Research Compliance and other institutional officials.

The PI may voluntarily place the research on hold in whole or in part while the investigation into reports of noncompliance is being conducted. Such holds are not subject to the reporting requirements in 45 CFR 46.108(4)(i) and 21 CFR 56.108(b)(2). At any point during the initial fact gathering process or later, the Senior IRB Chair or IRB Chair may suspend in whole or in part the research or refer the research to the IRB for suspension or termination. Such suspensions or terminations will be reported in accordance with IRB policy on *Suspension or Termination of Human Subjects Research*.

Once the investigation has been completed, OEC makes an initial determination regarding whether the noncompliance constitutes potential serious or continuing noncompliance.

- If the noncompliance is determined not to be serious and/or continuing and the proposed corrective action plan is appropriate, the Senior IRB Chair (or designee) will document review in the Insight expedited review checklist. If the proposed corrective action is not appropriate, the Senior IRB Chair (or designee) will require modification to the corrective action plan and once determined to be appropriate, the Senior IRB Chair (or designee) will document review in the Insight expedited review checklist.
- If the noncompliance is determined to constitute potential serious or continuing noncompliance, the report is referred to the IRB.

Reports of IRB noncompliance are investigated by the VP HRA and may include discussions with HRO Staff, IRB members, and/or IRB leadership.

4. Noncompliance Review by the IRB

Research noncompliance may be reviewed by any Mass General Brigham IRB; however, reports are routinely reviewed by IRB 02 which meets on a monthly basis or as needed.

The Senior IRB Chair (or designee) assigns a primary and secondary reviewer with appropriate experience or expertise to review the noncompliance. IRB members are provided access in Insight and/or are provided a copy of the report, any correspondence related to the report, the protocol, approved consent form and any other documents or information submitted by the investigator for review of the problem, (e.g., monitoring reports.) Any revised materials in response to the report are provide 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 noncompliance and associated materials. All other members are responsible for review of the report and any other materials sufficient for determining how to vote at the meeting. The IRB determines whether an event constitutes serious or continuing noncompliance, and may require corrective actions as noted (but not limited to):

- Approve the research to continue with no further action required
- Defer action pending additional information
- Require modifications in the research and/or consent form
- Require that subjects who are still participating in the research be re-consented or notified in writing of the noncompliance
- Require observation of the consent process by a member of the IRB or the Human Research Affairs Compliance and Education Office.
- Require that subjects whose participation has ended be notified in writing of the noncompliance
- Modify the continuing review schedule
- Suspend the research
- Terminate the research
- Require periodic audits by the Human Research Affairs Compliance and Education Office
- Require remedial education
- Require oversight by a senior investigator
- Restrict the conduct of research
- Restrict research privileges.
- Any other action the IRB deems appropriate to resolve the noncompliance.

The review by the IRB, the OEC or Senior IRB Chair (or designee) and associated findings, 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.*

The VP HRA reviews IRB noncompliance and may require corrective actions to prevent future occurrences including, but not limited to:

- Revision of standard operating procedures
- Retraining and education of HRO staff, HRO leadership, IRB members, IRB leadership
- Auditing by the Human Research Affairs Compliance and Education Office.

The VP HRA will determine whether the noncompliance represents serious or continuing noncompliance. If the noncompliance is determined to be serious or continuing, the VP HRA will report according to the policy *Reporting to Institutional Officials and Regulatory Agencies.*

OTHER APPLICABLE MASS GENERAL BRIGHAM POLICIES:

Suspension or Termination of Human Subjects Research
Reporting to Institutional Officials and Regulatory Agencies
Mass General Brigham Non-Retaliation Policy
IRB Member Conflicts of Interest Policy

REFERENCE:

45 CFR 46
21 CFR 56

DEVELOPMENT AND CONSULTATION:

Human Research Office
Office of General Counsel

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