

<b>Title:</b>	Review of Human Subject Research at a Convened Meeting
<b>Department:</b>	Human Research Affairs
<b>Policy Type:</b>	Mass General Brigham System-wide
<b>Applies to:</b>	Employees, Professional Staff or Other Agents of Mass General Brigham
<b>Approved by:</b>	Chief Academic Officer
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<b>Contact Person:</b>	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 conducting initial and continuing review of human subject research and clinical investigations and review of proposed changes in approved research at a convened meeting of the Mass General Brigham IRB. Non-exempt human subject research and clinical investigations reviewed by the Mass General Brigham IRB at a convened meeting are subject to this policy.

This policy is established to comply in part with the regulatory requirement in 45 CFR 46.108(a)(3)(i) and 21 CFR 56.108(a)(1) requiring IRBs to have “written procedures which the IRB will follow for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution.”

**POLICY STATEMENT:**

The Mass General Brigham IRB must review all non-exempt human subject research and clinical investigations at a convened meeting at which more than half the members, including at least one physician-scientist member and one nonscientist member, are present unless the research is eligible for review using the expedited review procedure. When reviewing non-exempt human subject research and clinical investigations, the Mass General Brigham IRB Chairpersons and Mass General

Brigham IRB members are subject to the Mass General Brigham IRB policy on *IRB Member Conflicts of Interest*. Applications for initial review, continuing review and amendments to previously approved research are reviewed in accordance with regulatory criteria, 45 CFR 46.111 or 21 CFR 56.111, as applicable.

## **PROCEDURES:**

### Meeting Dates

The Mass General Brigham IRB meeting dates and times are posted on the Research Navigator website. Meetings are held with sufficient frequency to accommodate the volume of reviews.

### Quorum

Human subject research and clinical investigations that cannot be reviewed using the expedited review procedure are reviewed at a convened meeting of a quorum of the membership of the Mass General Brigham IRB. A quorum is the minimum number and type of IRB members that must be present at a convened meeting. In order to review research at a convened meeting, a majority of the members of the IRB must be present, including at least one physician-scientist and one member whose primary concerns are in nonscientific areas. In addition, reasonable efforts will be made to ensure that at least one unaffiliated member and at least one member representing the general perspective of subjects are present at each meeting. The unaffiliated member, the member representing the general perspective of subjects, and the non-scientific member may be the same person, or may be represented by two or three different persons.

The Chair or designee and Full Board Analyst are responsible for ensuring that quorum is achieved before the meeting begins and is maintained throughout the meeting. The Full Board Analyst or designee is responsible for recording attendance and vote on each agenda item.

### Determining Agenda, Attendance and Assigning Reviewers

IRB members sign up to attend meetings starting 3 months prior to meeting dates. HRO staff assign protocols that have been screen by HRO staff to scheduled meetings based on expertise available to appropriately review the protocol.

Agendas are typically capped at 8 agenda items however, the IRB Chair or HRO Staff may reduce or increase the number of protocols based on the nature or complexity of the protocols scheduled for review in order to allow sufficient time for discussion of each protocol at the meeting, or based on the availability of members for review. Generally, protocols are scheduled for review by receipt date; however, the Mass General Brigham IRB reserves the right to reschedule protocols for review based on other factors, such as the experience and expertise of the members planning to attend the Mass General Brigham IRB meeting or the expiration date of Mass General Brigham IRB approval.

The HRO staff is responsible for ensuring that at least one member attending the meeting has the necessary knowledge and expertise to review each of the protocols listed on the agenda.

When the agenda includes protocols that involve vulnerable populations, the HRO Staff are responsible for ensuring that at least one member attending the meeting has knowledge of and/or experience in working with the study population.

When making reviewer assignments, the HRO Staff takes into consideration the scientific discipline, the study population, and study procedures described in the protocol and the experience and expertise of the members attending the meeting.

The qualifications, experience, and expertise, as well as representative capacity of each member, are documented in the Mass General Brigham IRB roster. Member CVs are also maintained by the Human

Research Office in a secure area on the Mass General Brigham network. The HRO Staff have access to the Mass General Brigham IRB roster and member CVs when making reviewer assignments.

The primary reviewer is typically a physician-scientist or other scientist with experience in working with the population being studied and/or expertise in the type of research under consideration, although this is not an absolute requirement, depending upon the type of study.

The secondary reviewer is typically an individual who can provide another perspective, for example, a layperson, genetic counselor, nurse or other community member. The secondary reviewer, therefore, complements the scientific or scholarly expertise of the primary reviewer.

Reviewers are required to notify the IRB Chair and HRO staff prior to the meeting if they have questions about the study, particularly if they have significant concerns about the study or believe additional information is needed for the Mass General Brigham IRB to be able to assess the regulatory Criteria for Approval.

#### Use of Consultants

The Mass General Brigham IRB may use consultants to supplement or provide expertise not available on the Mass General Brigham IRB. When the HRO Staff reviews the draft agenda to make primary and secondary reviewer assignments, s/he is responsible for determining whether the membership includes the necessary expertise to review the protocol.

When, in the opinion of the presiding Chairperson or Full Board Analyst, the membership lacks the expertise needed to review the protocol, the presiding Chairperson or Full Board Analyst, in consultation with the Director and/or Senior IRB Chair or designee, identifies potential expert consultants.

Additionally, the Mass General Brigham IRB may vote to defer action on a protocol and may require an expert in the scientific area or discipline to review the research and provide consultation to the Mass General Brigham IRB. Potential consultants will be identified and agreed upon by the Mass General Brigham IRB, or as indicated above.

Consultants are subject to the Mass General Brigham IRB policy on *IRB Member Conflicts of Interest* and must confirm in writing that they have no conflict of interest. If the consultant agrees to review the research and the consultant has no conflict of interest, s/he is provided with all forms and documents submitted to the Mass General Brigham IRB for review.

Consultants are asked to attend the meeting to present their findings relative to any of the regulatory Criteria for Approval and to answer questions; however, if the consultant is unavailable to attend the meeting, s/he may provide written comments for distribution or communication to the Mass General Brigham IRB members. Consultants are not voting members at the meeting, and their attendance is recorded in the minutes as guests (consultant).

#### Distribution of Materials and Review by Members

Investigators who rely upon the Mass General Brigham IRB for IRB review of human subject research and clinical investigations are required to complete Insight application forms and provide all required information and documents to the Mass General Brigham Human Research Office for review by the Mass General Brigham IRB.

The meeting agenda and Insight application, forms and documents submitted for Mass General Brigham IRB review for each item on the agenda are made available in Insight to all members planning to attend the meeting at least 5 days prior to the meeting (unless an emergent need for priority review is agreed

upon by the HRO staff and IRB meeting Chair). All members are provided with links to guidance documents that include the regulatory criteria for approval and requirements for informed consent. For initial review and review of proposed changes in approved research, the agenda also includes references and links to relevant regulatory documents and Mass General Brigham IRB policies and procedures.

Members and reviewers are provided with the Guide to Review of Non-Exempt Human Research, Review Worksheet, and Consent Form Worksheet for reference and, when assigned to review, to prepare assigned reviews. Assigned reviewers are responsible for an in-depth review of all of the materials provided to them relevant to the research. Members who are not assigned to review the protocol are expected to review all of the materials provided to them relevant to the research in sufficient depth to vote on the research at the convened meeting.

### Initial Review

For initial review, all members attending the meeting receive the required Insight application forms and documents submitted by the investigator for Mass General Brigham IRB review, which include, but are not limited to, the protocol summary, recruitment materials including advertisements, detailed protocol, instruments and questionnaires, consent forms, and drug/device brochure.

### Continuing Review

For continuing review, all members attending the meeting receive the required Insight application forms and documents submitted by the investigator for Mass General Brigham IRB continuing review. The entire protocol file and minutes of prior meetings at which the protocol was reviewed are available to all members.

### Proposed Changes

For review of proposed changes (amendment) to approved research during the period of IRB approval, all members attending the meeting receive the required Insight application forms and documents submitted by the investigator for Mass General Brigham IRB review of the proposed change. The entire protocol file and minutes of prior meetings at which the protocol was reviewed are available to all members.

### Conflicts of Interest

Mass General Brigham IRB members are subject to the Mass General Brigham IRB policy on *IRB Member Conflicts of Interest*. The agenda for every meeting includes a reminder about the conflicts of interest policy. Any member with a conflict of interest is asked to recuse him/herself and leave the room while the protocol is being reviewed, except to provide information to the Mass General Brigham IRB, after which the member must leave the room for the discussion and vote on the protocol. The names of those voting members who were recused from voting due to a conflict of interest are recorded in the minutes. Recused members are not counted towards the quorum requirement; therefore, if a quorum of the membership is not present for the review of any protocol, no vote is taken and the protocol is held over for review at the next meeting of the same Mass General Brigham IRB panel.

### Discussion and Vote

The Mass General Brigham IRB administrator takes attendance at the meeting and records voting members present and absent for each review. Late arrivals, early departures, and individuals recused or out of the room for one reason or another during the discussion and vote on each protocol are recorded in the minutes.

The IRB meeting Chair and assigned reviewers lead the discussion of each new protocol, continuing review, or amendment listed on the meeting agenda.

The primary reviewer presents a brief synopsis of the research protocol, with the expectation that the

other members have reviewed the protocol materials. The primary reviewer is responsible for presenting information about the criteria for IRB approval and, when applicable, additional protections for pregnant women, human fetuses, and neonates; children; and individuals with impaired decision-making capacity.

Secondary reviewers are asked to present any additional clarifications or commentary on the study plan, and any questions or concerns, or modifications s/he would require for approval.

Reviewers are encouraged to provide written comments to ensure that the Mass General Brigham IRB convey the modifications required and/or questions and concerns raised by the Mass General Brigham IRB completely, accurately and precisely.

After the primary and secondary reviewers have presented the study and their review comments, the IRB meeting Chair opens the protocol up for discussion by the membership. The meeting Chair and members may direct specific questions to the assigned reviewers or to other members with specific expertise or viewpoints (e.g., a layperson, nurse or other member who may bring a different perspective to the discussion).

At the end of the discussion, the meeting Chair makes a motion to approve, require modifications in the research (to secure approval), defer action on (pending receipt of additional information), or disapprove the protocol. A vote on the motion is taken (for, against, or abstain) by show of hands or voice vote and recorded in the minutes. All motions are decided by majority vote of the members present for the review. A quorum of the members of the Mass General Brigham IRB must be present in order for the Mass General Brigham IRB to take a vote.

#### Determining Frequency of Continuing Review

When the motion is to approve or require modifications in the research (to secure approval), the motion includes the duration of Mass General Brigham IRB approval (one year or less). When determining the duration of approval, the Mass General Brigham IRB considers the following factors:

- The nature of risks to participants;
- The degree of uncertainty regarding the risks involved;
- The vulnerability of participants;
- The experience of the clinical investigator in conducting clinical research;
- The IRB's experience with the researcher or sponsor;
- The projected rate of enrollment;
- Whether the study involves novel therapies.

When the risks to subjects related to participation in the research are greater than the risk associated with alternative treatments or procedures, if any, the Mass General Brigham IRB will consider requiring that continuing review be conducted in less than one year, or one year with case-by-case reporting.

Examples of research that may be considered for review more frequently than annually include:

- phase I studies of a challenging or novel new drug or biologic;
- research involving Category A significant risk devices;
- research in which healthy volunteers may undergo anesthesia or medical procedures involving sedation with no direct health benefits;
- research for which there is little external oversight or data safety monitoring;
- research involving gene transfer or xenotransplantation; or
- research involving infectious agents.

For initial review or continuing review, the approval period begins the date the Mass General Brigham

IRB voted to fully approve the protocol at the convened meeting or, if voted to require modifications to secure approval, the date the protocol is fully approved by the Full Board staff when s/he or an IRB-designated reviewer, reviews the principal investigator's response and determines that all of the required modifications have been made. The expiration date is based on the duration of approval voted on by the Mass General Brigham IRB (one year or less) and is set from the date the protocol is fully approved. The expiration date is the first date the protocol is no longer approved by the Mass General Brigham IRB.

### Continuing Review

Continuing review of the research is required until the research has been completed or has been closed prior to completion. The investigator must submit the continuing review form to document that the study has been completed or is being closed prior to completion. For multi-site research, the research may be considered completed or may be closed prior to completion when the investigator at this site is no longer collecting, receiving, or analyzing identifiable data.

Continuing review of research previously approved by the convened Mass General Brigham IRB may be conducted using the expedited review procedure as follows:

- a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
- b) where no subjects have been enrolled and no additional risks have been identified; or
- c) where the remaining research activities are limited to data analysis.

Additionally, continuing review of research previously approved by the convened Mass General Brigham IRB may be conducted using the expedited review procedure where the research is not conducted under an investigational new drug application (IND) or investigational device exemption (IDE) where categories two (2) through eight (8) do not apply but the Mass General Brigham IRB determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified since the last review.

### Determining Which Studies Need Verification from Sources Other Than the Investigators

Investigators are required to provide the Mass General Brigham IRB with all relevant information regarding the conduct of the research and fulfill all requirements for prompt reporting to the Mass General Brigham IRB of any reportable events.

In order to ensure that the research is conducted in compliance with all applicable regulations for the protection of human subjects, the Mass General Brigham IRB may require verification of information from sources other than the investigator. Such independent verification may be considered in the following situations:

- complex projects involving unusual levels or types of risk to subjects;
- research being conducted by persons who have previously failed to comply with all regulations or requirements of the Mass General Brigham IRB;
- research conduct that comes into question as a result of information provided at continuing review; or
- research in which substantial segments of the project are conducted off site by Mass General Brigham investigators or non-Mass General Brigham collaborators.

Independent verification may include, but is not limited to:

- audits by the Human Research Compliance and Education Office;
- communications between the FDA and the sponsor (IND/IDE holder);
- communications with the sponsor, collaborating institutions, coordinating centers, or regulatory

- agencies;
- communications from any monitoring group, e.g., DSMB or DMC
- NIH communications and reviews; and/or
- communications with IRBs at collaborating sites.

### Requiring Modifications, Deferring Action, or Disapproving Research and Responses to Review Notification Letters

#### Require modifications in research to secure approval

When the Mass General Brigham IRB votes to require modifications in the research (to secure approval), the Principal Investigator (PI) is notified in writing of the action voted on by the Mass General Brigham IRB and the required modifications to the research. The PI is asked to submit a point-by-point response and revised documents to the Mass General Brigham IRB.

When received, the presiding Mass General Brigham IRB Chairperson or Full Board Analyst reviews the PI's response, including revised documents, and documents on the review form and checklist whether the modifications required by the Mass General Brigham IRB have been made and whether the protocol can now be fully approved. If the modifications have not been made as required, the response is scheduled for review at the next convened meeting of the reviewing Mass General Brigham IRB.

Proposed changes submitted with the response are reviewed in accordance with the policies and procedures for review of proposed changes, i.e., either at a convened meeting or, if minor, using the expedited review procedure.

#### Defer research for more information

When the Mass General Brigham IRB votes to defer action pending receipt of additional information or due to substantive changes or requirements or other issues related to the criteria for approval, the PI is notified in writing of the action voted on by the Mass General Brigham IRB and any questions and concerns that need to be addressed as well as modifications required to the research. The PI is asked to submit a point-by-point response and revised documents to the IRB.

When received, the PI's response, including revised documents, is scheduled for review at a convened meeting of the reviewing Mass General Brigham IRB.

#### Disapprove

When the Mass General Brigham IRB disapproves the research, the PI is notified in writing of the action voted on by the Mass General Brigham IRB and the basis for the disapproval. Disapproval means that, as designed, the study cannot be approved and the Mass General Brigham IRB can think of no modifications or additional information that will likely result in an approval.

The decision of the Mass General Brigham IRB to disapprove the research cannot be overruled by any other institutional body or individual(s); however, an investigator may appeal the decision of the Mass General Brigham IRB in writing directly to the Senior IRB Chair who is responsible for reviewing the appeal with the IRB meeting Chair. The appeal is then scheduled for review at a convened meeting of the Mass General Brigham IRB that disapproved the research. The investigator may appeal the decision of the Mass General Brigham IRB in person at the convened meeting.

### Notification of Principal Investigator and the Institution

The Human Research Office is responsible for notifying the Principal Investigators in writing of Mass

General Brigham IRB approval of initial or continuing review, or proposed changes in research activities during the period of approval. The approval letter is provided through the Insight system and includes the date of expiration of Mass General Brigham IRB approval. The expiration date is the first date the research is no longer approved by the Mass General Brigham IRB.

Minutes of Mass General Brigham IRB meetings are made available to the Institutional Officials in a secure area on the Mass General Brigham IRB network. In addition, the Human Research Office provides individuals and/or departments within Mass General Brigham IRB with responsibility for some aspect of the human research protection program access to Mass General Brigham IRB review information and protocols via the Insight system.

Minutes and Meeting Attendance:

Full Board Analysts are responsible for documenting attendance at each meeting. Documentation of attendance shall include:

- Each member's full name.
- Each member's representative capacity (scientist, non-scientist, member who represents the general perspective of research participants, unaffiliated).
- The names of members who participated in the convened meeting via an alternative mechanism, such as telephone or video conferencing.
- If a consultant is present at the convened meeting, the name of the consultant, and a brief description of the consultant's expertise, and documentation that the consultant did not vote with the IRB on the study.
- The names of non-members and guests, such as IRB support staff, researchers and study coordinators.
- When an alternate member replaces a primary member, including the name of the alternate member.
- The names of IRB members who leave the meeting because of a conflict of interest, along with the fact that a conflict of interest is the reason for the absence.

Meeting minutes include actions taken by the IRB, with sufficient information to identify the research activities reviewed and voted on by the IRB at the meeting, including initial review, review of requested modification and continuing review. Minutes shall include the following information:

- Separate deliberations for each action.
- Votes for each protocol as numbers for, against or abstaining.
- The basis for requiring changes in research.
- The basis for disapproving research, when applicable.
- A written summary of the discussion of controverted issues and their resolution.
- For initial and continuing review, the approval period.
- Required determinations and protocol-specific findings justifying those determinations for:
  - Waivers or alterations of the consent process.
  - Research involving pregnant women, fetuses and neonates.
  - Research involving prisoners.
  - Research involving children.
  - Research involving participants with diminished capacity to consent.
  - For FDA-regulated research, the rationale for significant and non-significant risk device determinations.
  - Rationale for conducting continuing review on research that would otherwise not require continuing review.

**OTHER APPLICABLE MASS GENERAL BRIGHAM POLICIES:**



IRB Member Conflicts of Interest  
Review of Human Subject Research Using Expedited Review  
Proposed Changes in Mass General Brigham IRB-Approved  
Research and Exceptions  
Continuing Review and Expiration of IRB Approval, Expedited  
Check-In

**REFERENCES:**

45 CFR 46  
21 CFR 56

**DEVELOPMENT AND CONSULTATION:**

Human Research Office