Mass General Brigham

Title:	Review of Human Subject Research Using Expedited Review
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 procedures the Mass General Brigham Institutional Review Board follows when conducting initial and continuing review of non-exempt human-subjects research and clinical investigations and review of proposed minor changes in approved research using the expedited review procedure.

This policy is established to comply in part with the regulatory requirements 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 may use the expedited review procedure for review and approval of certain categories of human subject research that involve no more than minimal risk, for certain categories of exempt research, and for review and approval of minor changes in approved research during the period of IRB approval [DHHS in 45 CFR 46. 104, 45 CFR 46.110 and FDA in 21 CFR 56.110]. When reviewing non-exempt human subject research and clinical investigations using the expedited review procedure, the Mass General Brigham IRB Chairpersons and designees are subject to the Mass General Brigham IRB policy on *IRB Member Conflicts of Interest.* The Senior IRB Chair is responsible for designating IRB members to conduct expedited review. Only experienced IRB members may be designated to conduct expedited. reviews. The Senior IRB Chair and Director, Human Research Office (HRO) determine when an IRB member has sufficient training and experience to be designated to

conduct expedited reviews.

PROCEDURES:

Investigators relying on 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 HRO for review by the Mass General Brigham IRB as described on the IRB Navigator website. Required documents include, but are not limited to, the recruitment materials including advertisements, detailed protocol, instruments and questionnaires and consent forms.

Initial Review and Continuing Review

All of the required forms and documents submitted by the investigator for review are reviewed administratively by the HRO staff, and when accepted, are assigned to an expedited reviewer. The expedited reviewer has access to the entire protocol record maintained by the HRO.

For research approved under the pre-2018 Common Rule and/or FDA-regulated research, continuing review of the research is required until the research has been completed, has transitioned to the 2018 Common Rule, or has been closed prior to completion. The investigator must submit the Insight Continuing Review or Expedited Check-In 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.

Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the Mass General Brigham IRB using the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110 [Source: 63 FR 60364- 60367, November 9, 1998]. The categories in this list apply regardless of the age of subjects, except as noted:

Research Categories:

(1) Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
    (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increase the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
    (b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
(2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
    (a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

(b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than 2 times per week.

(3) Prospective collection of biological specimens for research purposes by noninvasive means. Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

(4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)
Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). [Note: Research involving materials that have been collected includes materials collected for both research and nonresearch purposes per personal communication with Julie Kaneshiro of OHRP April 2003].

(6) Collection of data from voice, video, digital, or image recordings made for research purposes.

(7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

(8) Continuing review of research previously approved by the convened IRB as follows:
(a) where (i) the research is permanently closed to the enrollment of 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.

(9) Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply

but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

Research in any of these categories may require review at a convened meeting of the Mass General Brigham IRB if the circumstances of the proposed research involve more than *minimal risk*.

Research activities that are not FDA regulated and meet the requirements for Limited Review under 45 CFR 46.104(d)(2)(iii) or 45 CFR 46.104(d)(3)(i)(C) as follows may be reviewed using the expedited procedure:

1. Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §46.111(a)(7).
2. Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §46.111(a)(7).

The expedited review procedure may <u>not</u> be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that the risk related to invasion of privacy and breach of confidentiality is no greater than minimal.

The Mass General Brigham IRB expedited reviewers are responsible for reviewing and determining whether the research is eligible for review using the expedited review procedure. The reviewers use an Insight reviewer checklist that includes the applicability of expedited review and the categories of research eligible for expedited review to document that:

- The research is applicable for expedited review;
- The research is minimal risk (when applicable);
- The research activities fall within one or more of the research categories eligible for expedited review; and
- The consent form includes the basic elements of informed consent or a waiver or alteration of informed consent is approved, or no consent is required under Limited Review.

If the proposed research is not eligible for review using the expedited review procedure, the expedited reviewer provides a rationale for referral and requests the research activity be scheduled for full board review at a convened meeting of the Mass General Brigham IRB.

The expedited reviewer may approve or require modifications pending receipt of additional information from the Principal Investigator (PI). The expedited reviewer may not disapprove a research activity using the expedited review procedure; a research activity can only be disapproved by the Mass General Brigham IRB at a convened meeting.

The expedited reviewer may consult another Mass General Brigham IRB member(s) or a non-Mass General Brigham IRB member consultant with special scientific or scholarly expertise in the scientific area or discipline or special population being studied; however, the reviewing expedited reviewer is responsible for the review and approval of research using the expedited review procedure. When a

consultant is used, the expedited reviewer is responsible for communicating with the consultant and for verifying that the consultant does not have a conflict of interest as defined in the *Mass General Brigham IRB Member Conflicts of Interest Policy*.

When the expedited reviewer requires modifications in the research to secure approval the required modifications or additional information required for review is communicated via the Insight system. The PI is asked to submit a point-by-point response and revised documents as applicable to the Mass General Brigham IRB.

When received, expedited reviewer assesses the PI's response, including revised documents, and determines whether the modifications have been made as requested and the research can be fully approved. The expedited reviewer may continue to request additional modifications or information until the research is approved or referred for full board review at a convened meeting of the Mass General Brigham IRB.

When the human subjects research is reviewed using the expedited review procedure, the expedited reviewer is responsible for determining that all of the requirements set forth in 45 CFR 46.111 and, when applicable, 21 CFR 56.111 are satisfied as well as any applicable regulatory requirements for inclusion of vulnerable populations.

When human subject research is reviewed using the expedited review procedure, the date of expiration of Mass General Brigham IRB approval is set as follows:

1. No continuing review, but administrative Expedited Check-In in 2 years (expedited research or 3 years (exempt research under Limited Review.)
2. One year (or sooner as designated by the reviewer) from the date the expedited reviewer fully approves the research initially. The expiration date is the first date the research is no longer approved by the Mass General Brigham IRB.

Independent verification of information provided at initial or continuing review, or for review of proposed changes in research during the period of approval may be requested by the expedited reviewer in the course of conducting the review. Such independent verification may be considered in the following situations:

- 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 the following sources of information:

- audits by the Human Research Affairs Compliance and Education Office;
- 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 collaborating IRBs.

<u>Minor Changes in Approved Research</u>

The reviewing Mass General Brigham IRB Chairperson or designee is responsible for reviewing and determining whether the proposed change (or amendment) is minor, and if minor, may review and approve the change using the expedited review procedure described above.

The proposed change is considered minor when the research meets <u>all</u> of the following criteria:

- the proposed change does **not** significantly alter the risk to benefit assessment the Mass

General Brigham IRB relied upon to approve the research;

- the proposed change does **not** significantly affect the safety of subjects;
- the proposed change does **not** involve the addition of procedures, interactions or interventions that add significant medical, social or psychological risks;
- the proposed change does **not** involve the addition of a vulnerable population in research not otherwise eligible for expedited review; and
- the proposed change does **not** significantly alter the scientific question or the scientific quality of the research.

The expedited reviewer documents approval using an Insight reviewer checklist that documents the rationale and basis for approving the change using the expedited review procedure. The expedited reviewer may request additional information from the PI to make this determination.

Notification of Principal Investigators, Mass General Brigham IRB Members, and Institution

The HRO 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 via the Insight system. The approval letter includes the date of expiration of Mass General Brigham IRB approval.

The HRO is responsible for preparing and distributing a report of all human subject research approved using the expedited review procedure, including initial and continuing review, and proposed changes in approved research during the period of Mass General Brigham IRB approval. Reports are distributed on a monthly basis to the members of the Mass General Brigham IRB.

OTHER APPLICABLE MASS GENERAL BRIGHAM POLICIES:

IRB Member Conflicts of Interest
Review of Human-Subjects Research at a Convened Meeting of the Mass General Brigham IRB
Proposed Changes in Mass General Brigham IRB-Approved Research and Exceptions Continuing Review and Expiration of Mass General Brigham IRB Approval

REFERENCES:

45 CFR 46
21 CFR 56

DEVELOPMENT AND CONSULTATION:

Human Research Office