Modifications to Previously Approved or Exempt Research

Content Applies To

Mayo Clinic Human Research Protection Program

Research for which Mayo Clinic is the IRB of Record

Policy

- Modification of a research activity, during the period for which IRB approval has already been granted, must be submitted to the IRB and approved prior to initiation of the modification(s) except when necessary to eliminate apparent immediate hazards to the human subject. (Changes initiated without prior IRB approval in order to eliminate apparent immediate hazards to the human subject, must be reported to the IRB within 30 calendar days.)
- Any modification to an exempt research project must be submitted to the IRB for re-review and re-determination of exemption status prior to initiating the changes to the research. In some circumstances, modifications to exempt research disqualify the research from the exempt status.
- Modifications to applications previously approved by a convened IRB may be reviewed using the expedited review process if they meet the following criteria:
    - Do not pose an increased risk to subjects; and
    - Constitute a minor change to previously approved research; and
    - Any added research activity falls within categories 1-7 of the Health and Human Services expedited review categories (45 CFR 46.110 - Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure).
    - Link to (45 CFR 46.110) for complete category details.
- Modifications to applications previously approved by the expedited review process may be reviewed via expedited review if they meet the following criteria:
    - The research continues to pose no more than minimal risk to subjects.
    - Any added research activity falls within categories 1-7 of the HHS expedited review categories (45 CFR 46.110 - *Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure*).
    - Link to (45 CFR 46.110) for complete category details

Investigator Responsibilities

The Investigator:

- Promptly (**within 30 calendar days**) reports to the IRB any research activity modifications which were made in order to avoid apparent immediate hazards to a subject and were implemented prior to IRB approval.
- Evaluates each proposed modification to the research activity to assess potential impact upon the risk/benefit ratio, severity or frequency of the previously described risk(s), safety, design, or execution of the research project.
- Revises research project documents accordingly. Describes each proposed modification and the justification for the change in the IRB modification application.
- Submits an IRB modification application to the IRB and attaches a revised protocol, consent form (if applicable), and other documents associated with the requested change.
- Includes the justification for each modification listed in the application.
- Re-consents or notifies subjects as directed by the IRB.
- Assures that any change to conflict of interest has been disclosed and reviewed by the Conflict of Interest Committee.

IRB Responsibilities

The IRB:

- Determines whether the proposed modification is a minor modification or a major modification and conducts its review accordingly.
- Reviews the proposed modification(s) in accordance with approval criteria and determines whether modifications(s) are consistent with ensuring the subject's continued protection.
- Reviews modifications initiated without prior IRB approval that eliminate apparent immediate hazards to the human subjects, and determines whether each change was consistent with ensuring the participant’s continued welfare.
- Determines that any new significant findings arising from the review process, and possibly impacting the subject's willingness to continue participation are provided to the subject.
- Determines if any new information resulting from the modification or from other sources necessitates an adjustment to the IRB’s prior determination(s), such as inclusion of protected or vulnerable populations and findings regarding FDA-regulated products.
- Determines if the proposed modifications to the research require revision of the consent document(s). If so, the IRB will ensure that revised consent documents accurately reflect the modifications.
- Determines if the modifications warrant re-consenting of currently enrolled subjects or notification of subjects who have completed research interventions.

- Considers whether the interval for continuing review as last determined by the IRB should be adjusted based on the modifications.
- Notifies the Principal Investigator of IRB findings and determinations.
- Determines whether the modifications to the research activity may require verification from sources other than the investigator that no material changes have occurred. See *Verification of No Material Changes Since Previous IRB Review.*

Minor Modifications

A modification may be considered minor if it meets the following criteria:

1. Research that involves no more than minimal risk and meets the criteria for one of the Expedited Review Categories at 45 CFR 46.110;

   AND

2. Modifications that constitute a minor change to previously approved research and do not pose an increased risk to subjects.

   Examples of minor modifications include (but are not limited to):

   - Administrative or clerical changes;
   - Protocol revisions that entail no more than minimal risk;
   - Decrease in the number and volume of sample collections as long as they do not negatively alter the risk/benefit ratio of the research;
   - Changes to the informed consent documents that do not affect the rights and welfare of research subjects, or do not involve increased risk to subjects, or significant changes in the research procedures;
   - Minor changes to recruitment procedures, recruitment materials or submission of new recruitment materials to be used in accordance with approved recruitment methods;
   - Minor changes to research project documents such as surveys, questionnaires or brochures ;
   - New research project documents to be distributed to subjects that are similar in substance to those previously approved; and
   - Changes in payment to subjects that do not constitute undue influence or affect the risk/benefit ratio of the research.

Major Modifications

Major modifications are changes to the research project that would materially affect the assessment of risks and benefits or may alter prior IRB decisions or determinations.

Examples of major modifications include (but are not limited to):

- Changes in the Principal Investigator for research projects that have been deemed as greater than minimal risk;
- Changes in study design, population, or procedures that increase risk (e.g. revision of study purpose, broadening of eligibility criteria, addition of vulnerable populations, alteration of a data safety monitoring plan, change in drug dosage or frequency);

- Changes to the consent form(s) that have the potential to alter/affect the potential participant's understanding of the risk/benefit ratio of the study, the study requirements, or his/her rights, e.g. new study procedures, new risks or increase in severity or frequency of known risks, changes to subject remuneration, reimbursement, or out of pocket expenses, extended duration of study participation, and/or changes to the HIPAA authorization); and
- Premature completion of the research project due to an unanticipated problem or determination by an oversight entity.

Related Documents

Expedited Review of Human Subjects Research

Exempt Human Subjects Research

Verification of No Material Changes since Previous IRB Review

References

45 CFR 46.110 - Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure

21 CFR 56.110 - Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research

Effective Date

February 17, 2016

Revision History

Date	Synopsis of Change
2/17/2016	Scheduled review – no changes