Modifications to Previously Approved or Exempt Research Procedure

Scope

Applies to research personnel involved in human subjects research and to the Mayo Clinic Institutional Review Board (IRB) when Mayo Clinic IRB is the Reviewing IRB.

Purpose

To describe the process and responsibilities for Investigators and the IRB when modifications are made to the IRB approved research activity.

Equipment/Supplies

N/A

Procedure

- 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). Modifications may include premature completion of the research project due to an unanticipated problem or determination by an oversight entity.
- Modifications must be submitted to the IRB within the following timelines. Refer to guidance: Reporting Timelines for IRB submission when Mayo Clinic is serving as the IRB of Record.
    - Changes necessary to eliminate apparent immediate hazards to the human subject may be initiated without prior IRB approval, and must be reported to the IRB within 5 working days.
    - Changes involving Significant New Information must be reported to the IRB within 5 working days.
    - All revised Investigator Brochures that do not meet the 5-day reporting requirement must be submitted within 30 calendar days.
    - Changes involving an increase in risk (newly identified or increase in severity) that does not meet the 5-day reporting requirement must be submitted within 30 calendar days.
    - Changes not involving risk or changes due to risks that have previously been reported to the Mayo Clinic IRB must be submitted within 60 calendar days.
    - Modifications not meeting the submission timeline must include a justification.
- Any modification to an exempt research project must be submitted to the IRB for 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 the IRB finds:
    - The revision(s) do not pose an increased risk to subjects; and
    - The revision(s) 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 (Expedited Review: Categories of Research That May Be Reviewed by the Institutional Review Board [IRB] through an Expedited Review Procedure).
- Modifications to applications previously approved by the expedited review process may be reviewed via expedited review if the IRB finds:
    - 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 (Expedited Review: Categories of Research That May Be Reviewed by the Institutional Review Board [IRB] through an Expedited Review Procedure).

Investigator Responsibilities

- Promptly (**within 5 working days**) report to the IRB, using the IRB electronic (IRBe) Modification form, any research activity modifications which were made in order to avoid apparent immediate hazards to a subject and were implemented prior to IRB approval. The Modification will be titled 'Urgent Action' and include the Subject Notification form attachment.
- Promptly (**within 5 working days**) report to the IRB any Significant New Information requiring urgent action using the IRBe Modification form. The Modification will be titled 'Urgent Action' and include the Subject Notification form attachment.
- Evaluate 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.
- Revise research project documents accordingly. Describe each proposed modification and the justification for the change in the IRBe Modification form.
- Submit an IRBe Modification form (within the timelines listed above) to the IRB and attaches a revised protocol, consent form (if applicable), and other documents associated with the requested change. A Subject Notification Form is attached in all modifications involving an increase or significant change in risk.
- Re-consent or notify subjects as directed by the IRB.
- Assure that any change to conflict of interest has been disclosed and reviewed by the Conflict of Interest Committee.

IRB Responsibilities

The IRB:

- Determine the level of review (expedited or convened IRB) required for the proposed modification(s).
- Review the proposed modification(s) in accordance with approval criteria and determine whether modifications(s) are consistent with ensuring the subject's continued protection.
- Review modifications initiated without prior IRB approval that eliminate apparent immediate hazards to the human subjects, and determine whether each change was consistent with ensuring the participant’s continued welfare.
- Determine 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.
- Determine 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.
- Determine 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.
- Determine if the modifications warrant re-consenting or notification of subjects including those who have completed research interventions.
- Consider whether the interval for continuing review as last determined by the IRB should be adjusted based on the modifications.
- Determine 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.*
- Notify the Principal Investigator of IRB findings and determinations.

Troubleshooting

N/A

Procedural Notes

N/A

Related Documents

Expedited Review of Human Subjects Research

Exempt Human Subjects Research

Verification of No Material Changes since Previous IRB Review

Reporting Timelines for IRB Submission when Mayo Clinic is Serving as the IRB of Record

Subject Notification Form

Definitions

Minor Change: The IRB may use expedited review procedures for "minor" changes to research previously approved by a convened IRB. A proposed change in research is deemed “minor” if the IRB assesses it to have no effect on the risks and benefits to subjects or improves the acceptability of the risks, and it does not substantially change the aims or design of the study. A modification cannot be deemed "minor" if it involves: 1) the addition of procedures that involve more than minimal risk or that do not fall into categories (1) - (7) of research eligible for expedited review as published by the Secretary of the Department of Health and Human Services (DHHS); 2) decreases the acceptability of the risks in relation to the benefits; or 3) removes a direct benefit to the subjects enrolled if the overall risk to benefit ratio is adversely impacted due to the change.

Examples of "minor" changes to a research study include, but are not limited to, the following:

- Addition or deletion of study team members;
- Addition of research locations (sites), including Relying Organizations for which Mayo Clinic IRB is the Reviewing IRB, provided there are no local context considerations that warrant convened IRB review, including significant differences in the conduct of the research that have the potential to adversely impact the risk to benefit ratio;
- Addition of procedures that do not significantly increase risk to participants, considering the original purpose and study design of the approved study;
- Removal of research procedures that would thereby reduce the risk to no more than minimal (i. e. all research procedures now meet expedited research categories);
- Addition of non-sensitive questions to a survey or interview, and procedures;
- Changes to improve the clarity of statements or to correct typographical errors provided that such changes do not alter the intent of the statement.

Significant New Information: Information that indicates a significant new serious risk or increased severity of known risk, or a safety issue which requires immediate action.

References

Expedited Review: 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

Owner

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Revision History

Date	Synopsis of Change
08/29/2023	AHHRPP recommended addition of Minor Change definition, including when the addition of research locations can be subject to expedited review or is considered to be a “minor change". Edited title of "Expedited Review: …(1998)" reference. Added clarification that modifications to research may include premature completion of the research project due to an unanticipated problem or determination by an oversight entity. Clarified scope and purpose. Updated owner and contacts.
06/04/2021	Scheduled review. Updated to current template. Updated Owner and Contact. Minor changes.
06/01/2018	Updated to new template. IRB submission timelines added. Minor changes for clarification. Removed examples of major/minor modifications to be consistent with Reportable Event policy.
02/17/2016	Scheduled review – no changes
Unknown	Approval for need to establish document: Unknown

Content Information Stamp

Title:
Modifications to Previously Approved or Exempt Research Procedure

Content ID:
DOCMAN-0000047810

Effective Date of Current Version:
08/30/2023 04:07:35 PM

Applicable Sites

Arizona Sites:
Arizona

Florida Sites:
Florida

Rochester Sites:
Rochester

Reviewer(s):

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