

<b>UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER          INSTITUTIONAL REVIEW BOARD</b>	
<b>REVIW OF REVISIONS IN APPROVED STUDIES</b>	
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**I. PURPOSE**

This document outlines the University of Tennessee Health Science Center Institutional Review Board procedures for review of revisions in approved studies.

**II. SCOPE**

This SOP applies to all investigators performing research under the auspices of the University of Tennessee Health Science Center IRB and its affiliated institutions.

**Personnel Responsible:**

IRB administrative staff, members, and investigators

**III. BACKGROUND**

HHS and FDA regulations for the protection of human subjects require that IRBs create written procedures for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval. Applications to implement revisions in approved studies must be reviewed by the convened Board, unless the revisions qualify for expedited review.

IRB review of proposed revisions involves the determination of whether the regulatory criteria for initial approval of research will still be satisfied if the revisions are implemented. The IRB must determine whether proposed revisions alter the acceptability of the risk-benefit ratio for the study, require other changes in procedures to assure that the rights and welfare of subjects remain adequately protected, necessitate amendment of the informed consent disclosure, and preserve the ability to select subjects equitably. Proposed revisions must be

incorporated into the *UTHSC IRB Form 1: Study/Project Application*, protocol, and consent form(s), as appropriate, in order to facilitate proper review.

Expedited review procedures may be used when the revisions constitute “minor changes” in previously approved research during the period for which approval is authorized. Expedited review of revisions is also permitted for research studies that were initially approved on an expedited basis or as exempt, provided that the revisions do not alter qualifying category of the study as either expedited or exempt. Under an expedited review procedure, the review may be carried out by an IRB Chairperson or by one of the experienced reviewers designated by a Chairperson or Director from among the members of the IRB . Designated reviewers will be professionally competent (i.e., experienced with and having demonstrated the ability to apply IRB review requirements and with appropriate scientific or scholarly expertise) to conduct expedited reviews. These reviewers may exercise the authority of the full Board, except that they may not disapprove the research.

The only exception to the requirement for prior IRB approval of revisions in research occurs when immediate changes in a study are necessary to eliminate apparent hazards to subjects (see #15 below for reporting requirements).

**In Accordance With:**

**For studies approved under the revised Common Rule:**

45 CFR 46.108(a)(3)(iii); 45 CFR 46.108(b); 45 CFR 46.110; and

**For studies approved under the Pre-2018 Common Rule:**

[45 CFR 46.103\(b\)\(4\)\(iii\)](#); and

**For FDA-regulated studies:**

21 CFR 56.108(c); and 21 CFR 56.110

[Categories of Research that May Be Reviewed by the Institutional Review Board \(IRB\) Through an Expedited Review Procedure](#)

[Expedited Review: Categories of Research that may be Reviewed Through an Expedited Review Procedure](#)

[Institutional Review Board Written Procedures: Guidance for Institutions and IRBs](#)

***Compliance with this policy also requires compliance with state or local laws or regulations that provide additional protections for human subjects.***

#### IV. PROCEDURES

1. For revisions of previously approved studies, the principal investigator will submit to the UTHSC IRB via iMedRIS the following documents:
  - a. Completed *Form 2: Change Request and Amendment*;
  - b.
  - c. Revised protocol (if applicable);
  - d. Protocol summary of changes (if applicable);
  - e. Updated investigator's brochure and/or package insert (if applicable);
  - f. Revised statement of work/study procedures from the grant application (if applicable);
  - g. Revised *UTHSC IRB Form 1: Study/Project Application* (if applicable);
  - h. Revised informed consent document(s) (if applicable); and
  - i. Other pertinent documents.

The originals for each document being revised are accessible for comparison in a tab available to Board members in iMedRIS at the time of their reviews.

2. Upon receipt of a *Form 2: Change Request and Amendment*, the following procedures will be utilized:
  - a. The *Form 2: Change Request and Amendment* is forwarded to the electronic queue of an IRB analyst for determination of whether the application qualifies for expedited review.
  - b. If the study qualifies for expedited review, a Chair or experienced reviewer is assigned the responsibility for reviewing the application.
  - c. The assigned reviewer(s) will review the submission according to applicable ethical principles, federal regulations and local IRB policies, and will complete the reviewer's form.
  - d. If the study revision does not qualify for expedited review, it will be placed on the agenda for an upcoming convened meeting of the Board.
3. Revisions in previously approved research that may qualify for expedited review (minor changes) include, but are not limited to, the following:
  - a. Amendments or modifications to a previously approved protocol that provide for a minor administrative or procedural change that does not alter or that decreases the risk to subjects;
  - b. Addition or modification of research activities that present no more than minimal risk to human subjects and involve only procedures listed in one or more of the categories outlined in 45 CFR 46.110 and 21 CFR 56.110.
  - c. c. Change in consent form wording that does not increase risk or decrease benefit;
  - d. A statistically small change to the number of subjects an investigator will enroll;
  - e. Change in an equally qualified investigator;
  - f. Change in equally qualified key study personnel (study coordinator, data analyst, etc.); and

- g. Non-English translations of informed consent documents including the translator's declaration submitted after initial approval.
4. The revisions of studies that qualify for expedited review will follow the review procedures outlined in the [SOP: IRB Expedited Review of New Studies](#).
5. For revisions of studies requiring full board review, the following procedures will be followed:
  - a. A primary reviewer will be assigned as appropriate to the subject matter of the application.
  - b. The revision application and all supporting documents will be provided to the reviewer after an initial review is conducted by the assigned IRB administrator, usually 19 days prior to the meeting of the full Board.
  - c. The reviewer will conduct a detailed review of the proposed revisions and will determine whether the regulatory criteria for initial approval of the study will continue to be satisfied if the proposed revisions are implemented including whether there are any changes in the level of risk (minimal risk, minor increase over minimal risk, more than a minor increase over minimal risk). The reviewer will usually complete the review no more than 13 days prior to the Board meeting using the reviewer form available in the iMedRIS system.
  - d. The assigned IRB analyst collates the comments of the reviewer and administrative staff in Pre-review recommendations, which are sent to the principal investigator, study contact(s), and Research Administrative Specialist (RAS) (as appropriate) via iMedRIS prior to the meeting.
  - e. The principal investigator must respond to questions and recommendations using the *PI Response Form* the Friday or Monday prior to the meeting.
  - f. At the meeting of the full Board, the primary reviewer will present a synopsis of the revisions, any significant issues, and his/her recommendation to the IRB.
  - g. At the meeting of the full Board, the IRB will consider whether the proposed changes might relate to the subjects' willingness to continue participation in the study and necessitate the reconsent of all currently enrolled subjects or whether subjects who have completed active participation should be notified of issues pertinent to their health, safety, and well-being. If such determination(s) are made, these instructions will be communicated to the investigator in the outcome letter issued via iMedRIS.
6. Based on its review of the information submitted with the revision application, the full convened IRB will vote separately on each revision application and take one of the following actions:
  - a. Approve the revisions without provisos;
  - b. Approve the revisions pending response to administrative provisos;

- c. Defer approval of the revisions pending resolution of substantive conditions requiring further review by the full board or convened IRB;
  - d. Disapprove the proposed revisions.
7. Approval pending response to administrative provisos will only occur when the full board or convened IRB stipulates specific revisions requiring simple concurrence by the investigator. The investigator must respond to the provisos specified by the full board or convened IRB within 60 days of the IRB meeting. If the investigator misses the deadline, the IRB will consider the study/project inactive and reactivation may require re-submission of the revision application for review by the full board or convened IRB. An IRB Chair, Director, other qualified IRB administrative staff person, or other designated experienced IRB member will review the responsive materials from the investigator required by the IRB, and determine whether the provisos stipulated by the IRB have been satisfied.
  8. Deferral of approval pending satisfaction of full board conditions will apply to applications for which the IRB requires the investigator to address substantive issues raised in the IRB deliberations. Subsequent review and approval by the full board or convened IRB will be required.
  9. A copy of all correspondence concerning the revision will be kept in the electronic IRB files for the study.
  10. For full board revisions, the IRB meeting minutes will document the following:
    - a. Separate deliberations, actions, and votes for each protocol submitting a *Form 2: Change Request and Amendment*;
    - b. The vote on all IRB actions including the number of members voting for, against, and abstaining, recorded in a manner that documents the continued existence of a quorum, with the votes recorded using the following format: Total = 15, Vote: For-14, Opposed-0, Abstained-1; When an IRB member is recused because of a conflict of interest, he/she will not be counted towards quorum, and the votes will be recorded using the following format: Total = 14, Vote: For- 14, Opposed-0, Abstained-0 ([Name] was not present for the deliberation or vote as he/she has a [conflict of interest briefly described]). For more information on conflicts of interest, see [SOP: UTHSC IRB Conflicts of Interest](#).; and
    - c. Conditions of approval or reasons for deferral for each action taken by the IRB.
  11. For full board revisions, pre-review recommendations for changes in renewal applications will be provided to the investigator prior to the meeting, when possible.

12. For revisions reviewed under an expedited review procedure, the satisfaction by the investigator of conditions for IRB approval, including the date when an IRB Chair, Director or other qualified IRB administrative staff determines that all conditions of IRB approval have been satisfied, will be placed on the electronic meeting agenda and sent electronically to Board members before the Board meeting each applicable week when the agenda is finalized.
13. The IRB will adopt the following procedures for assuring that investigators do not implement revisions to approved research studies prior to IRB review and approval:
  - a. In all approval letters for new applications, continuations, and revisions, investigators will be reminded that changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval;
  - b. At the time of initial submission for new applications, investigators will sign a statement of investigator responsibilities that includes the requirement that investigators must obtain prior approval from the IRB for any modifications of previously approved research, including modifications to the informed consent process and documents, except those necessary to eliminate apparent immediate hazards to subjects;
  - c. When random audits of studies are performed by the IRB, it will be determined whether any revisions have been implemented without prior review and approval by the IRB; and
  - d. Training materials available to the investigators on the IRB website will note the requirement that revisions may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to subjects.
- 134 When a study revision involves the designation of a new principal investigator, the *Form 2: Change Request and Amendment* must be routed to the new principal investigator in order to sign the statement of investigator responsibilities. Further, the *Form 2: Change Request and Amendment* must be routed to the new principal investigator's UTHSC Department Chair for approval and signoff.
15. When immediate changes in a study are necessary to eliminate apparent hazards to subjects, those changes may be implemented without prior IRB approval. Changes implemented to eliminate apparent hazards to subjects prior to IRB review and approval should be reported to the IRB as protocol deviations according to IRB policy. (See [SOP: UTHSC IRB Protocol Waivers and Deviations](#).) These revisions must be submitted within 48 hours of implementation for review and approval according to the usual procedure outlined above.
16. IRB review of a proposed change to a research project during the period for which approval is authorized does not constitute continuing review of the

project as a whole, and thus does not extend the date which continuing review must occur.

17. A copy of the approved minutes and the finalized agenda is provided to the Senior Associate Vice Chancellor for Research and the Vice Chancellor for Research in fulfillment of the regulatory requirement to communicate the IRB's findings and actions to the institution in writing (previously found at 45 CFR 103(a)(4)(i), now found at 45 CFR 46.108(a)(3)(i) in the revised Common Rule).