UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER
INSTITUTIONAL REVIEW BOARD
REVIEW OF REVISIONS IN APPROVED STUDIES

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 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 application, protocol, and consent form, 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 the status of the study as either expedited or exempt. Under an expedited review procedure, the review may be carried out by an IRB Chairperson or one or more experienced reviewers designated by a Chairperson or Director to conduct the review. An experienced IRB staff member may review revisions that consist solely of changes in key study personnel listed on the study application. 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.

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

Conditions for IRB Use of Expedited Review
http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidancesInformationSheetsandNotices/ucm118099.htm

Expedited Review: Categories of Research that may be Reviewed Through an Expedited Review Procedure
http://www.hhs.gov/ohrp/policy/expedited98.html

OHRP Guidance on Written IRB Procedures
https://www.hhs.gov/ohrp/regulations-and-policy/guidance/institutional-issues/institutional-review-board-written-procedures/index.html

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 the following documents:
   a. Completed Form 2: Change Request/Amendment application;
   b. Complete copy of the original protocol (if applicable);
   c. Revised protocol (if applicable);
   d. Updated investigator's brochure and/or package insert (if applicable);
   e. Revised grant application (if applicable);
   f. Revised Form 1 application (if applicable);
   g. Revised informed consent document(s) (if applicable); and
   h. Other pertinent documents.

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

2. Upon receipt of a study revision application, the following procedures will be utilized:
   a. The Form 2 application 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 other senior member of the IRB is assigned the responsibility for reviewing the application. If the revisions consist solely of changes in key study personnel listed on the study application, an experienced IRB staff member may review the revisions in lieu of a Board member.
   c. The assigned reviewer(s) will review the application and consent documents according to applicable ethical principles, federal regulations and local IRB policies, and will complete the reviewer's form. If the revisions consist solely of changes in key study personnel listed on the study application, completion of a reviewer form is not necessary.
   d. If the study revision does not qualify for expedited review, it will be placed on the agenda for the next convened meeting of the Board.

3. Revisions in previously approved research that may qualify for expedited review include, but are not restricted to, the following:
   a. Amendments or modifications to a previously approved protocol/project descriptors 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. Minor amendments or revisions to a previously approved consent form;

d. Change of an investigator who will conduct the study protocol, provided such individual has standing as a faculty member, resident or fellow, and is otherwise qualified to conduct the study; and
e. Non-English translations of informed consent documents submitted after initial approval.

4. 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, 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 criteria for initial approval of the study will continue to be satisfied if the proposed revisions are implemented. The reviewer must 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 reviewers and administrative staff in Pre-review recommendations, which are sent to the principal investigator, study contact, 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.

5. Based on its review of the information submitted with the revision application, the 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.

6. 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 senior 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.

7. 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.

8. A copy of all correspondence concerning the revision will be kept in the electronic IRB files for the study.

9. 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/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.

10. For full board revisions, pre-review recommendations for changes in renewal applications will be provided to the investigator prior to the meeting when possible.

11. 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.

12. 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.

13. When a study revision involves the designation of a new principal investigator, the Form 2 must be routed to the new principal investigator in order to sign the statement of investigator responsibilities. Further, the Form 2 must be routed to the new principal investigator's UTHSC Department Chair for approval and signoff.

14. 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.

15. 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.

16. A copy of the approved minutes and the finalized agenda is provided to 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).