

**UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER  
INSTITUTIONAL REVIEW BOARD  
CONTINUING REVIEW OF RESEARCH**

**I. PURPOSE**

This document outlines the University of Tennessee Health Science Center Institutional Review Board procedures concerning continuing review and re-approval of research.

**II. SCOPE**

This SOP applies to all IRB administrative staff and board members.

**Personnel Responsible:**

IRB members, investigators

**III. BACKGROUND**

HHS and FDA regulations for the protection of human subjects require that IRBs create procedures for conducting continuing review of previously approved research and for reporting its findings to investigators and the institution. Continuing review must be substantive and meaningful. The IRB is responsible for determining that the criteria for initial approval of research studies are still satisfied at the time of continuing review. This process includes review of the risks of study participation, the potential benefits, the informed consent process and appropriate additional safeguards necessary to protect subjects. In particular, the IRB must determine whether any new information has emerged that would alter the acceptability of the risk-benefit ratio for the study, change the procedures necessary to protect the welfare of subjects, or necessitate revision of the informed consent disclosure. Reports regarding any unanticipated problems occurring since the last approval for the study are pertinent to these assessments.

Continuing review must be conducted at defined intervals appropriate to the degree of risk as determined by the IRB, but no less than annually. Continuing review cannot be performed under an expedited review procedure unless the original study was initially approved under expedited review criteria or the study satisfies other specific expedited review criteria (e.g., when no subjects have been enrolled and no new risks have been identified). Continuing review and approval is required for all studies reviewed by UTHSC IRB until a termination request has been granted.

If approval of a continuing review application is not received from the IRB prior to the expiration date of a study, then all research activities must stop. Enrollment of new subjects may not occur. In addition, interventions or interactions involving previously accrued subjects must cease, unless the IRB determines that it is in the best interests of individual

subjects to continue participation. A request to continue research interventions or interactions with previously accrued subjects after the expiration date must be submitted in writing to the IRB, and it must include a list of the affected subjects and an explanation of why it is in their best interests to continue participation in the research interventions or activities. The principal investigator is advised in writing if the latter request is approved.

**In Accordance With:**

45CFR46.103(b)(4) and (5); 45CFR46.108(b); 45CFR46.109(e); 45CFR46.111;  
45CFR46.115(a); 21CFR56.108(a) and (b); 21CFR56.109(f)

OHRP Guidance on Written IRB Procedures, 7/15/007 located at  
<http://www.hhs.gov/ohrp/humansubjects/guidance/irbgd107.pdf>

OHRP Guidance on Continuing Review located at  
<http://www.hhs.gov/ohrp/humansubjects/guidance/contrev0107.pdf>

FDA Guidance on Continuing Review After Study Approval located at  
<http://www.fda.gov/oc/ohrt/irbs/review.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. The UTHSC IRB shall conduct continuing review of research at intervals appropriate to the degree of risk, but not less than one calendar year. There is no provision for a lapse or grace period under federal regulations.
2. For studies requiring full board review, the date by which continuing review must occur is set from the date of the convened meeting at which the initial IRB approval was granted (including approval pending satisfaction of administrative provisos). If approval of a continuing review application (including approval pending satisfaction of administrative provisos) occurs within 30 days prior to the date on which the current approval expires, the IRB may utilize the previous expiration date in determining the subsequent expiration date, rather than using the date of the convened meeting at which IRB re-approval is granted. For studies that do not receive re-approval until after the current expiration date, the new expiration date must be calculated from the date of the convened meeting at which IRB approval of the renewal application is granted (including approval pending satisfaction of administrative provisos). The expiration date of IRB approval will be documented in correspondence regarding the study.
3. Investigators must submit the request for continuing review utilizing UTHSC IRB Continuing Review Submission Form (Form 3) and all required attachments. For studies conducted at Methodist Healthcare facilities, including Lebonheur Children's

Medical Center, an additional document listing subject names and medical record numbers must be included as one of the attachments.

4. At the time of initial IRB approval, the letter of the UTHSC IRB to the principal investigator will include the date on which approval of the study will expire and state that it is the responsibility of the principal investigator to initiate the request for continuation regardless of the time for which the activity has been approved by the sponsoring agency. It will also be explained that, if there is a failure to obtain re-approval prior to the expiration date of the preceding approval period, all research activity must cease until re-approval is established.
5. Continuation approval cannot be expedited unless the initial approval of the study satisfied criteria for expedited review, except in limited circumstances described in expedited review categories 8 and 9 at 63 FR 60364-60367, November 9, 1998. It is also possible that research activities that previously qualified for expedited review will have changed such that expedited review is no longer be permitted for continuation approval.
  - a. Category 8: an expedited review procedure may be used for the continuing review of research previously approved by the convened IRB when (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions and the research remains active only for long-term follow-up of subjects, (iii) no subjects have been enrolled and no additional risks have been identified, or (iv) the remaining research activities are limited to data analysis.
  - b. Category 9: an expedited review procedure may be used for the continuing review of research not conducted under an investigational new drug application (IND) or investigational device exemption (IDE) where categories (2) through (8) do not apply but the IRB has determined and documented at a convened IRB meeting that the research involves no more than minimal risk and no additional risks have been identified.
6. Upon receipt of the UTHSC IRB (Form 3): Continuing Review Submission Form, the IRB Director or designee will review the submission for completeness.
7. Except when an expedited review procedure is used, the IRB will review continuation applications at convened meetings at which a majority of the members of the IRB section are present, including at least one member whose primary concerns are in a nonscientific area. Upon receipt of the complete continuing review form and attachments (including the current informed consent document), the IRB Chairman will assign a reviewer and the administrative staff will place the request on the IRB agenda.
8. In conducting continuing review of research not eligible for expedited review, all IRB members will receive and review a protocol summary and a status report on the progress of the research that includes the following:

- a. the number of subjects accrued;
  - b. a summary of any unanticipated problems and available information regarding adverse events (such a summary may be a simple statement that there have been no unanticipated problems and that adverse events have occurred at the expected frequency and level of severity as documented in the research protocol, the informed consent document, and any investigator brochure);
  - c. a summary of any withdrawal of subjects since the last IRB review;
  - d. a summary of any complaints about the research since the last IRB review;
  - e. a summary of any recent literature that may be relevant to the research;
  - f. a summary of any amendments to the research since the last IRB review
  - g. any relevant multicenter trial reports;
  - h. any other relevant information, especially information about risks associated with the research; and
  - i. a copy of the current consent document.
9. The assigned IRB reviewer and all members of the section will have access via iMedRIS to the Form 3 application, attachments to Form 3, a copy of the complete protocol, including any modifications previously approved by the IRB, and all other study related documents.
10. During the review, any of the following considerations may be examined:
- a. Current status of the study with respect to whether enrollment remains open, the research remains active only for follow-up of current subjects, or remaining research activities are limited to data analysis;
  - b. The continuing review form and supporting documentation, including the current consent form;
  - c. Changes in the risk / benefit assessment based on factors such as:
    - i. Amendments or modifications in the research since the last review;
    - ii. Recent reports in the literature relevant to the conduct of the research;
    - iii. Summary of adverse events or other unanticipated problems involving risks to subjects or others;
    - iv. Safety reports;
    - v. Changes in the Investigator Brochure;
    - vi. DSMB reports or reports from a similar monitoring body;
  - d. Consideration of protocol violations and /or deviations;
  - e. Incidences of investigator non-compliance;
  - f. Any complaints received from subjects;
  - g. Reports from employees, staff and faculty regarding problems with the study;
  - h. Management of protocols with lapsed approval;
  - i. IRB audit reports;
  - j. FDA or sponsor audits since last report;
  - k. Consideration of whether the monitoring plan remains adequate for the risk;
  - l. New conflict of interest information;

- m. Evaluation of the current consent form in terms of accuracy and completeness, changes in the risk-benefit ratio, or the availability of new information that may affect the willingness of subjects to continue participation; and
  - n. Assessment of the continuing review period based on the materials presented at continuing review. The IRB will determine the continuing review period at the time of each continuing review.
11. UTHSC IRB may require verification from sources other than the investigator that no material changes have occurred in the research since the previous IRB review.
  12. The criteria for re-approval at continuing review will be the same criteria used for the initial approval of research as specified at 45CFR46.111 and 21CFR56.111. Decisions to re-approve studies for less than one year will be based on factors including, but not limited to: unusual risks of harm, uncertainties in estimating the degree of risk, and special vulnerabilities of subjects that may require more frequent review to determine whether their rights and welfare are adequately protected.
  13. Based on its review of the information submitted at continuing review, the IRB will vote separately on each continuation application and take one of the following actions:
    - a. Approve the protocol for continuation;
    - b. Approve the protocol with administrative provisos;
    - c. Defer approval of the protocol pending resolution of substantive provisos; or
    - d. Terminate the protocol.
  14. When reviewing research under an expedited review procedure, the IRB Chairman or designated IRB member should receive and review all relevant documents as specified in #8, #9 and #10. Documentation of the results of continuing reviews conducted under an expedited review procedure must include in the reviewer's form and the letter to the applicant (a) the specific permissible categories per 63 FR 60364-60367 justifying the expedited review; and (b) documentation of the review and action taken by the IRB Chairman or designee.
  15. Upon re-approval, the IRB correspondence will include the new approval period (dates), the time for submission of the next continuing review, and any conditions of re-approval.
  16. If the investigator fails to comply with the UTHSC IRB reporting requirements, the study will be considered in non-compliance and the IRB approval will automatically expire.
    - a. Enrollment of new subjects cannot occur after the expiration of IRB approval.
    - b. Continuation of research interventions or interactions in previously enrolled subjects should only continue when the IRB finds it is in the best interests of the individual subjects to do so.

- c. A request to continue research interventions or interactions with previously accrued subjects after the expiration date must be submitted in writing to the IRB, and it must include a list of the affected subjects and an explanation of why it is in their best interests to continue participation in the research interventions or activities. The principal investigator will be advised in writing if the latter request is approved.
  - d. The investigator will be notified of expiration of approval in writing within 48 hours of the expiration date.
  - e. With respect to expiration of IRB approval due to a failure to submit materials to the IRB prior to the expiration date, such expiration does not need to be reported to appropriate federal agency head as a suspension of IRB approval.
  - f. Suspension or termination of a protocol for reasons other than (e) will be reported to the appropriate federal agency head.
17. Written correspondence concerning any suspension or termination of IRB approval shall include a statement of the reason(s) for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, the sponsor and the appropriate federal agency department head within 48 hours.
18. The minutes of the IRB should document separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB. A copy of all correspondence concerning continuing review will be kept in the IRB files for the study.