

**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. In order to re-approve research at the time of continuing review, the IRB must determine that all of the following requirements are satisfied:

- Risk to subjects are minimized (i) by using procedures which are consistent with sound research design and which do not necessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes;
- Risks to subjects are reasonable in relation to anticipated benefits, if any, to the subjects and the importance of the knowledge that may reasonably be expected to result;
- Selection of subjects is equitable;
- Informed consent will be sought from each prospective subject or the subject's legally authorized representative, and appropriately documented;
- When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects;

- When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data;
- Appropriate safeguards are included to protect subjects likely to be vulnerable to coercion or undue influence; and
- When the research involves pregnant women, fetuses, neonates, prisoners, or children, the research satisfies the additional requirements for IRB approval

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, including adverse events, are pertinent to these assessments. When conducting continuing review and evaluating whether research continues to satisfy the criteria for IRB approval of research, IRBs must pay particular attention to the following four aspects of the research:

- Risk assessment and monitoring;
- Adequacy of the process for obtaining informed consent;
- Investigator and institutional issues; and
- Research progress.

Continuing review for research initially approved by the convened IRB must be conducted at defined intervals appropriate to the degree of risk as determined by the IRB, but no less than annually. Exceptions to the continuing review requirement, including studies initially eligible for expedited under the revised Common Rule, are outlined in item 1 below.

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:**

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

45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) and (8); 45 CFR 46.108(a)(3) and (4); 45 CFR 46.108(b); 45 CFR 46.109(e) and (f); 45 CFR 46.111; 45 CFR 46.115(a)(3); 45 CFR 46.204-207; 45 CFR 46.305; 45 CFR 46.404-409;

**For studies approved under the Pre-2018 Common Rule:**  
[45 CFR 46.103\(b\)\(4\)](#)

**For FDA-regulated studies:**  
21 CFR 56.108(a) and (b); 21 CFR 56.109(f)

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

OHRP Guidance on Continuing Review located at  
<http://www.hhs.gov/ohrp/policy/continuingreview2010.pdf>

FDA Guidance on Continuing Review After Study Approval located at  
<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM294558.pdf>

***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 previous (pre-2018) Common Rule and the FDA-regulations (21 CFR 56.109(f)) state that the UTHSC IRB shall conduct continuing review of research approved by the convened IRB 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. However, under the revised Common Rule (45 CFR 46.109(f)(iii)), continuing review is not required for projects granted initial approval or approval pending provisos on or after 01/21/19 unless the IRB determines otherwise, in either of the following circumstances:
  - a. The initial research application was eligible for expedited review in accordance with 45 CFR 46.110; or
  - b. The initial research application was reviewed by the IRB in accordance with the limited IRB review requirements for exempt categories (2)(iii), (3)(i)(C), (7) or (8)

Further, if a Full Board project granted initial approval or approval pending administrative provisos on or after 01/21/2019 has progressed to the point that

it only involves one or both of the following, which are part of the IRB-approved study, then it will not require annual continuing review unless the IRB determines otherwise:

- a. Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
- b. Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

For studies that meet the criteria above, the UTHSC IRB may determine that a study still requires a continuing review, for which the IRB will provide a rationale in the IRB records (45 CFR 109(a)(3)). Items that may prompt a continuing review where it otherwise would not be required include but are not limited to : unanticipated problems, changes in the investigator's status with the university, problems consenting subjects, or any other changes since the previous review that would alter the risk-benefit ratio.

Studies that fall under the FDA IRB regulations (including both expedited and Full Board) will still be required to undergo a continuing review and approval until the study is closed with the IRB.

2. When continuing review is conducted annually for full board studies, the annual expiration date (anniversary date) by which continuing review must occur will be set in the following manner:
  - a. the *first* continuing review must occur no more than one year after the date of the convened meeting at which the initial IRB approval was granted (including approval pending satisfaction of administrative provisos);
  - b. if approval of a continuing review application (including approval pending satisfaction of administrative provisos) occurs *within* 30 days prior to the anniversary date on which the current approval expires, the IRB will retain that anniversary date as the expiration date for the subsequent one-year approval period;
  - c. if approval of a continuing review application (including approval pending satisfaction of administrative provisos) occurs *more than* 30 days prior to the anniversary date on which the current approval expires, then the subsequent continuing review must occur no more than one year after the date of the convened IRB meeting at which IRB approval of the continuation was granted (including approval pending satisfaction of administrative provisos); and
  - d. for studies that do not receive re-approval (including approval pending satisfaction of administrative provisos) until after the current expiration

date, the IRB will retain the prior anniversary date as the expiration date of the new one-year approval period.

However, the IRB retains the right to conduct continuing review more often than annually. (See paragraph #19.) In the event that the approval period is less than one year, the expiration date by which continuing review must occur will be set in the following manner:

- a. the *first* continuing review must occur by the end of the specified period of approval as determined from the date of the convened meeting at which the initial IRB approval was granted (including approval pending satisfaction of administrative provisos);
- b. if approval of a continuing review application (including approval pending satisfaction of administrative provisos) occurs *within* 30 days prior to the expiration date for the current approval period, the IRB will calculate the new expiration date for the new approval period from the current expiration date;
- c. if approval of a continuing review application (including approval pending satisfaction of administrative provisos) occurs *more than* 30 days prior to the date on which the current approval expires, the IRB will calculate the new expiration date for the new approval period from the date of the convened IRB meeting at which IRB approval of the continuation was granted (including approval pending satisfaction of administrative provisos); and
- d. for studies that do not receive re-approval (including approval pending satisfaction of administrative provisos) until after the current expiration date, the IRB will calculate the new expiration date for the new approval period from the current expiration date.

The expiration date of IRB approval will be documented in correspondence regarding the study.

3. To assist the investigators and research staff, the investigator will receive renewal notices 45-, 30-, 20-, 10-, and 5-days in advance of the expiration date of the study via IRBNet. However, it is the responsibility of the principal investigator to ensure that the continuing review of an ongoing research study or project is approved prior to the expiration date.
4. For all studies requiring a continuing review, investigators must submit the request for continuing review utilizing UTHSC IRB Continuing Review Submission Form (Form D) via IRBNet with the appropriate signatures and with all the appropriate attachments outlined in the Checklist for Submission located under the Library Tab, such as results

from the research that have not been previously reported, informed consent forms, and other supporting documents.

Investigators may wish to revise or amend their approved protocols at the time of continuing review. Investigators may submit the Continuing Review Submission Form (Form D) at the same time a Change Request and Amendments (Form C) is submitted for IRB review. The UTHSC IRB shall review both submissions by either Expedited Review or Full Board Review, as appropriate, in accord with applicable federal regulations and policies.

5. At the time of initial IRB approval of FDA-regulated studies, DHHS-regulated studies approved or approved pending response to administrative provisos prior to 01/21/2019, and DHHS-regulated Full Board studies approved or approved pending response to administrative provisos on or after 01/21/2019, 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, unless the investigator obtains prior written approval from the IRB.

At the time of initial IRB approval of DHHS-regulated expedited studies approved or approved pending response to administrative provisos on or after 01/21/2019, the letter of the UTHSC IRB to the principal investigator will include the date on which the study was approved, but will not contain an expiration date. Rather, the investigator will receive an annual reminder notice to submit revision requests, unanticipated problem reports, communications from the study sponsor, etc., and a study closure request to the IRB. Similarly, for DHHS-regulated Full Board studies that have reached the point that continuing review is no longer required as determined by the IRB under the revised Common Rule, the investigator will receive an annual reminder notice to submit revision requests, unanticipated problem reports, communications from the study sponsor, etc., and a study closure request to the IRB. Further, as with any other IRB-approved study, the IRB may perform random or for-cause audits at any time.

6. Continuation approval cannot be expedited unless the initial approval of the study satisfied criteria for expedited review under categories (1) to (7), except in limited circumstances described in expedited review categories (8) and (9) at 63 FR 60364-60367, November 9, 1998. Please note that categories (8) and (9) can only be used for studies that fall under the FDA IRB regulations and

studies approved or approved with provisos before 01/21/2019. It is also possible that research activities that previously qualified for expedited review will have changed such that expedited review is no longer permitted for continuation approval.

Under Category (8), an expedited review procedure may be used for the continuing review of research previously approved by the IRB at a convened meeting as follows:

- (a) Where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
- (b) Where no subjects have been enrolled and no additional risks have been identified; or
- (c) Where the remaining research activities are limited to data analysis.

Under Category (9), an expedited review procedure may be used for the continuing review of research previously approved by the IRB at a convened meeting that meets the following conditions:

- The research is not conducted under an investigational new drug application (IND) or investigational device exemption (IDE);
- Expedited review categories (2) through (8) do not apply to the research;
- The IRB has determined and documented at a convened IRB meeting that the research involves no greater than minimal risk to the subjects; and
- No additional risks of the research have been identified.

7. Upon receipt of the UTHSC IRB (Form D): Continuing Review Submission Form, the IRB Administrator will review the submission for completeness and determine whether the application qualifies for expedited review or should be reviewed by the IRB at a convened meeting. As part of this preliminary review, the IRB Director or designee may perform the following functions, among others:

- Confirm that all documents required by the IRB have been submitted by the investigator;
- Assess whether the information and documents submitted by the investigator match the current IRB-approved informed consent document;
- Aid the IRB in identifying important issues and concerns that the IRB may wish to consider;
- Provide technical assistance and guidance to the IRB at convened meetings and to the IRB chair (or designated IRB member(s)) during an expedited review process.

8. 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. In order for research undergoing continuing review to be approved by the IRB at a convened meeting, it will receive the approval of a majority of those members present at the meeting. All members voting on a continuation application must be free of conflicts of interest, and any member having a conflict of interest shall disqualify himself/herself from a given review. IRB members who are listed as key project personnel on the application or have a conflict of interest will recuse themselves from the deliberation and voting. For more information on conflicts of interest, see SOP: UTHSC IRB Conflicts of Interest. Should the quorum fail during the meeting, the IRB will not take further actions or votes for research projects undergoing continuing review unless the quorum can be restored.
9. Upon receipt of the complete continuing review form and appropriate attachments, the IRB Administrator will place the submission on an IRB agenda at least 3 weeks prior to the meeting date, unless it is determined that the submission requires review at an earlier scheduled meeting.
10. The renewal application is finalized on the agenda and becomes available to all board members, including pre-review recommendations and PI Response Form prior to the meeting.
11. At the meeting, the primary reviewer will present a synopsis of the progress of the research, any significant issues and his/her recommendation to the convened IRB.

12. In conducting continuing review of research not eligible for expedited review, all IRB members will have access via IRBNet to 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 from the research since the last IRB review, and the reasons for withdrawal, if known;
  - d. a summary of any complaints about the research from subjects or others 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 new and relevant information, published or unpublished, since the last IRB review, especially information about risks associated with the research;
  - i. any changes in the investigator's situation or qualifications and any changes in institutional commitments; and
  - j. a copy of the current consent document.
  
13. All members will have access via IRBNet to:
  - a. the Form D application and any attachments to the Form D;
  - b. a copy of the latest version of the IRB-approved protocol and informed consent documents;
  - c. any proposed modifications to the informed consent document or protocol;
  - d. for FDA-regulated research, the current Investigator's Brochure, if available, including modifications; and
  - e. any significant information related to subject risk, such as the reports of the DSMB or DMC monitoring the research, if available.
  
14. 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's Brochure; and
    - 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, and 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.
15. 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. Studies for which verification is required include, but are not limited to, the following:
- a. Randomly selected projects;
  - b. Complex projects involving unusual levels or types of risk to subjects;
  - c. Projects conducted by investigators who have previously failed to comply with the requirements of the HHS or FDA regulations or the requirements or determinations of the IRB; or
  - d. Studies where concern about possible material changes occurring without IRB approval have been raised based on information provided from other sources, such as audits or reports from research staff.
16. The IRB shall make a determination of the approval period, as well as the need for additional supervision or oversight on a project-by-project basis and will use the same criteria used for the initial approval of research as specified

at 45 CFR 46.111 and 21 CFR 56.111. The IRB will take into consideration the following factors when deciding on an appropriate interval for continuing review:

- a. the nature of and risks posed by the clinical investigation;
- b. the degree of uncertainty regarding the risks involved;
- c. the vulnerability of the subject population;
- d. the experience of the clinical investigator in conducting clinical research;
- e. the IRB's previous history with the investigator and/or sponsor;
- f. the project's rate of enrollment; and
- g. whether the study involves novel therapies.

In addition to specifying a time interval for determining an approval period, the IRB also may specify a subject enrollment number as a threshold for determining when continuing review is to occur. Also, the IRB will consider whether the current frequency of continuing review is appropriate or should be adjusted.

17. 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 without any provisos;
  - b. Approve the protocol with provisos;
  - c. Defer approval of the protocol pending resolution of substantive conditions requiring further review by the convened IRB; or
  - d. Disapprove the research study.

Approval with provisos will only occur when the convened IRB stipulates specific revisions requiring simple concurrence by the investigator. The investigator must respond to the provisos specified by the convened IRB within 30 days of the IRB meeting. If the investigator misses such a deadline, the IRB will consider the study/project inactive and reactivation may require re-submission of the original application for review by the convened IRB. The 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.

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. In the latter case, subsequent review and approval by the convened IRB is required.

18. 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 #15, #16 and #17. 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 an IRB Chairman or designee.
  
19. When continuing review is conducted annually under an expedited review procedure, the expiration date (anniversary date) by which continuing review must occur will be set in the following manner:
  - a. the *first* continuing review must occur no more than one year after the date on which the chair or other senior reviewer granted initial IRB approval (including approval pending satisfaction of administrative provisos);
  - b. if approval of a continuing review application by the chair or other senior reviewer (including approval pending satisfaction of administrative provisos) occurs *within* 30 days prior to the anniversary date on which the current approval expires, the IRB will retain that anniversary date as the expiration date for the subsequent one-year approval period;
  - c. if approval of a continuing review application by the chair or other senior reviewer (including approval pending satisfaction of administrative provisos) occurs *more than* 30 days prior to the anniversary date on which the current approval expires, then the subsequent continuing review must occur no more than one year after the date on which the chair or other senior reviewer granted IRB approval of the continuation (including approval pending satisfaction of administrative provisos); and
  - d. for studies that do not receive re-approval (including approval pending satisfaction of administrative provisos) until after the current expiration date, the IRB will retain the anniversary of the prior expiration date as the expiration date for the new one-year approval period.

However, the IRB retains the right to conduct continuing review more often than annually. (See paragraph #19.) In the event that the approval period is less than one year, the expiration date by which continuing review must occur will be set in the following manner:

- a. the *first* continuing review must occur by the end of the specified period of approval as determined from the date on which the chair or other senior reviewer granted initial IRB approval (including approval pending satisfaction of administrative provisos);
- b. if approval of a continuing review application (including approval pending satisfaction of administrative provisos) occurs *within* 30 days prior to the expiration date for the current approval period, the IRB will calculate the

- new expiration date for the new approval period from the current expiration date;
- c. if approval of a continuing review application (including approval pending satisfaction of administrative provisos) occurs *more than* 30 days prior to the date on which the current approval expires, then the IRB will calculate the new expiration date for the new approval period from the date on which the chair or other senior reviewer granted IRB approval of the continuation (including approval pending satisfaction of administrative provisos); and
  - d. for studies that do not receive re-approval (including approval pending satisfaction of administrative provisos) until after the current expiration date, the IRB will calculate the new expiration date for the new approval period from the current expiration date.

The expiration date of IRB approval will be documented in correspondence regarding the study.

20. 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.
21. If the IRB has not reviewed and approved a research project by the end of the approval period specified by the IRB, the study will be considered in non-compliance and the IRB approval will automatically expire.
  - a. All research activities must stop, including recruitment of subjects, enrollment of new subjects, consent, interventions, interactions, data collection, and data analysis.
  - 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. Further, the IRB Chair will determine what and how data collected during the lapse may be used. The principal investigator will be advised in writing if the request is approved.
  - d. The investigator will be notified of expiration of approval
  - 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 the appropriate federal agency head as a suspension of IRB approval. However, if the IRB notes a pattern of non-compliance

- with the requirements for continuing review, the IRB will determine the reasons for the non-compliance and take appropriate corrective actions.
- f. If the study is federally funded, suspension or termination of a protocol for reasons other than (e) will be reported to the appropriate federal agency head.
  - g. The IRB will document why the lapse in approval occurred and identify any steps that need to be taken to prevent future lapses in approval.
22. 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.
  23. A copy of all correspondence concerning continuing review will be kept in the IRB files for the study.
  24. For full board continuations, the IRB meeting minutes will document the following:
    - a. Separate deliberations, actions, and votes for each protocol undergoing continuing review;
    - 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;
    - c. Conditions of approval or reasons for deferral for each action taken by the IRB.
  25. For full board continuations, pre-review recommendations for changes in renewal applications provided to the investigator prior to the meeting 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.
  26. For continuations reviewed under an expedited review procedure, the satisfaction by the investigator of conditions for IRB approval, including the date when an IRB Chair, or other qualified IRB administrative staff determines that all conditions of IRB approval have

been satisfied, the date when re-approval becomes effective, and the date by which continuing review must occur 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.