UNIVERSITY OF TENNESSEE GRADUATE SCHOOL OF MEDICINE
INSTITUTIONAL REVIEW BOARD
CONTINUING REVIEW AND REAPPROVAL OF RESEARCH

I. PURPOSE

This document outlines the required elements of University of Tennessee Graduate School of Medicine Institutional Review Board (UTGSM IRB) procedures concerning continuing review and re-approval of research.

II. SCOPE

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

Personnel Responsible:

UTGSM IRB members, investigators

III. BACKGROUND

UTGSM IRB has the authority to perform the following functions:

- Conduct initial and continuing review of any research activities involving drug, device, biological, behavioral, psychosocial, educational or other studies involving human subjects prior to the start of the research.
- Report findings and actions to investigator and sponsor, when applicable.
- Determine which studies need more than annual review.
- Determine which studies need verification from sources other than the investigator that no material changes have occurred since previous IRB review.
- Insure prompt reporting to the IRB of changes in research activities.
- Insure that changes in previously approved human subject research are not initiated without IRB review and approval.
- Insure prompt reporting to the IRB of unanticipated problems or scientific misconduct involving risks to subjects or others.
- Review and ensure the adequacy of the informed consent document and process.
- Review and consider requests for HIPAA waivers, and HIPAA language incorporated into the informed consent form.
- Suspend or terminate the research or revoke approval of any study under its review.

Continuing review is conducted at defined intervals appropriate to the degree of risk as determined by the IRB, but at least annually. Continuing review must be substantive and meaningful in order to fulfill the requirements of federal regulations. Continuing review and approval is required for all studies reviewed by UTGSM IRB until a termination request has been granted.

Should an investigator fail to obtain re-approval of a clinical study prior to expiration date of the preceding approval period, all research activity must cease until re-approval is

established. Re-approval may not be done under expedited review unless the original study was approved under expedited review criteria.

In Accordance With:

38 CFR 16.103(b)(4) and (5); 38 CFR 16.109(e); 45 CFR 46.103(b)(4) and (5); 45 CFR 46 108(b); 45 CFR 46 109(e); 45 CFR 46.111; 45 CFR 46.115(a); 21 CFR 56.108(a) and (b); 21 CFR 56.109(f); OHRP Common Findings and Guidance #5, #7, #8, #9, #10, #11, #16; OHRP Guidelines for Formulating Written IRB Policies and Procedures; OHRP Guidance on Continuing Review 1/15/07; OHRP Guidance on Written IRB Procedures, 7/11/02. ICH Guidelines 3.1.2, 3.2.3; FDA Information Sheet – Self Evaluation Checklist for IRBs, OPRR Letter: IRB Approval Periods and Continuing Review of Research (January 20, 2000).

OHRP IRB Guidebook located at:
http://www.hhs.gov/ohrp/archive/irb/irb_chapter3.htm#e8

Additional information is also located at
http://www.hhs.gov/ohrp/policy/continuingreview2010.html

FDA Guidance for Institutional Review Boards and Clinical Investigators 1998 Update 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 UTGSM IRB shall conduct continuing review of research at intervals appropriate to the degree of risk (set at the initial review), but not less than one calendar year. There is no provision for a lapse or grace period.

2. The date by which continuing review must occur is determined by the date of the convened meeting at which the initial IRB approval was granted (even if approval was granted with conditions).

3. Should a protocol require review by other committees (Biosafety, Radiation Safety Committee, etc.), copies of those reviews must be submitted to the IRB when received.

4. At the time of initial IRB approval, the letter of the UTGSM 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 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. In addition, it will be explained that IRB approval is required prior to implementing any changes or amendments in the protocol, regardless how minor, except to eliminate apparent immediate hazards to subjects.

5. Approval periods for clinical research studies begin on the date of the IRB meeting in which the last approval was granted. The expiration date of IRB approval will be documented in the IRB correspondence for the study.

6. Re-approval cannot be expedited unless the initial approval met expedited criteria and was approved in that manner, except in limited circumstances described by 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 in accordance with section 36.110 will have changed or will change, such that expedited review would no longer be permitted for continuing review.
   A. Category 8: an expedited review procedure may be used for the continuing review of research previously approved by the convened IRB 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.
   B. Category 9: an expedited review procedure may be used for the continuing review of research not conducted under an investigational new drug application (NDA) 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.

7. Requests for continuing review and (re)approval are required to be submitted through the electronic system, iMedRIS.

8. The IRB staff will check the consent to assure that it is the most current approved version and meets with the IRBs current standards. The reviewer will notify both the investigator and the IRB Director when the consent review is complete

9. Upon receipt of the UTGSM IRB, the IRB Director or designee will review the submission for completeness. All IRB members will have access to all pertinent information for the continuing review.

10. During the review, the following will be discussed:
    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 to the risk / benefit assessment based on study results and / or Adverse Event reports:
    i. Consideration of the changes to the research including, but not limited to any relevant recent literature, interim or significant new findings, multi-site trial reports, amendments or modifications since last review
    ii. Summary of adverse event reports or unanticipated problems involving risks to subjects or others
    iii. Consideration of safety reports, including IND and IDE
    iv. Consideration of any updated Investigator Brochures
    v. Consideration of any DSMB reports or reports from a similar body
d. Consideration of any reports of injuries, unexpected events or unanticipated problems involving risks to subjects or others
e. Consideration of protocol violations and / or deviations
f. Consideration of investigator non-compliance
g. Consideration of any complaints or subject phone calls
h. Consideration of any reports from employees, staff and faculty
i. Management of protocols with lapsed approval
j. Consideration of any IRB audit reports
k. Consideration of any FDA or sponsor audits since last report
l. Consideration of whether the monitoring plan is adequate for the risk
m. Consideration of any changes in community or state laws relating to clinical research
n. Consideration of any changes in community attitudes concerning research
o. Recruitment, including the following:
    i. Total Enrolled
    ii. Demographic information on subjects enrolled
    iii. Total subjects withdrawn
p. New conflict of interest information:
    i. Investigator Financial Disclosure Documents
    ii. Report of non-financial conflicts of interest
q. 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.
r. 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.
s. Other information provided by the site for the IRB's consideration.

12. UTGSM IRB may require verification from other sources that no material changes have occurred since the previous IRB review. This may include, but is not limited to:
    a. Contacting the sponsor / CRO for verification of submissions
    b. Contacting the FDA reviewer for the study for verification of submissions
    c. IRB audit of the site prior to the expiration of approval
    d. Randomly selected projects
    e. Complex projects involving unusual levels or types of risk to subjects
    f. Projects conducted by investigators who have previously failed to comply with the requirements of the IRB, HHS or FDA regulations

g. Projects where concern about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports and other sources.

13. All members of the IRB will receive a copy of the complete project descriptors including any modifications previously approved by the IRB. In addition, any IRB member will have access to the complete IRB File(s) and relevant IRB minutes prior to the convened meeting.

14. Upon receipt of the complete continuing review form and attachments (current informed consent must be attached), the IRB administrative staff will place the request on the IRB agenda.

15. The continuing review will be reviewed, deliberated and discussed in the same manner as the original review and approval, and the minutes will reflect separate deliberations, actions and votes for each protocol undergoing continuing review by the convened IRB.
    a. Criteria for renewal
        i. The risks to subjects continue to be minimized and reasonable in relation to anticipated benefits
        ii. The selection of subjects continues to be reasonable in relation to anticipated benefits
        iii. The informed consent process continues to be adequate and appropriately documented
        iv. Provisions for safety monitoring of the data are in place
        v. Protections to ensure the privacy of subjects and confidentiality of data are adequate
        vi. Appropriate safeguards are in place for vulnerable populations
        vii. There are no issues of noncompliance or conflict of interest that have not been appropriately addressed.
        viii. Other issues as the IRB members feel appropriate to the study and information at hand.

16. When reviewing research under an expedited review procedure, the IRB Chair, (or designated IRB Member(s)) should receive and review all of the above referenced documentation. Documentation for initial and continuing reviews conducted under an expedited review procedure includes (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 chairperson or designee and any findings required under the HHS regulations.

17. Based on its review of the information submitted at continuing review, the IRB will take one of the following actions for each individual protocol:
    a. Approve the protocol for continuation
    b. Approve the protocol with modifications (interval for continuing review, monitoring plan activities, changes to the consent, etc.).
    c. Suspend the protocol

d. Terminate the protocol.

18. Block voting (voting on a group of proposals) is not allowed. IRB actions taken without a quorum or without a non-scientific member present do not satisfy the requirements for continuing review.

19. 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.

20. If the investigator fails to comply with the UTGSM 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 interest of the individual subjects to do so.
    c. On a case-by-case basis, the IRB will review those instances where failure to enroll would seriously jeopardize the safety or well-being of an individual prospective subject.
    d. The investigator will be notified of this action in writing within 48 hours of the vote. Correspondence will include the terms of the suspension according to the three regulatory categories (screening, enrollment of new subjects, and continuation of interactions/ interventions in previously enrolled subjects).
    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.
    g. UTGSM IRB will also notify the FDA of this action by calling, or faxing / emailing a copy of the correspondence to the FDA reviewer for the study. This person's name is obtained from the sponsor.

21. 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 by certified mail or other traceable means.

22. A copy of all correspondence concerning continuing review will be kept in the IRB files for the study.