

**UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER
INSTITUTIONAL REVIEW BOARD
PROTOCOL WAIVERS AND DEVIATIONS**

I. PURPOSE

To provide a procedure for the accurate and timely reporting to the University of Tennessee Health Science Center Institutional Review Board of waivers and deviations from the requirements of approved research protocols.

II. SCOPE

This SOP applies to all personnel involved in the conduct of research approved by the UTCOMC IRB.

Personnel responsible:

IRB administrative staff, IRB members and investigators.

III. BACKGROUND

Federal regulations require that institutions develop written policies and procedures for prompt reporting of changes in research activities to the IRB. Protocol waivers and deviations represent unapproved changes in research activities. Protocol waivers must receive IRB approval prior to implementation. Protocol deviations must be reported by the investigator and reviewed by the IRB. Reports of these changes in a previously approved research study are utilized by the IRB to determine whether the risk-benefit ratio for the study, study procedures and the previously approved informed consent process/document remain acceptable. In some cases, protocol waivers or deviations may warrant substantive changes to assure that the rights and welfare of subjects continue to be adequately protected. Changes that may be necessitated by protocol waivers and deviations include, but are not limited to: modification of inclusion/exclusion criteria; implementation of additional monitoring procedures; suspension of enrollment of new subjects; suspension of research procedures for currently enrolled subjects; and modification of consent documents to acknowledge revision of study procedures.

In Accordance With:

For studies approved under the revised Common Rule:
45 CFR 46.108(a)(3)(iii); and

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

For FDA-regulated studies:
21 CFR 56.108(a)(4); and 21 CFR 812.150(a)(4)

IV. DEFINITIONS

Protocol Waiver (Eligibility Exception or Eligibility Waiver): A prospective decision by a sponsor or investigator to permit accrual of a subject who does not satisfy the approved inclusion/exclusion criteria for enrollment.

Protocol Deviation: The term “protocol deviation” is not defined by either the HHS human subjects regulations (45 CFR 46) or the FDA human subjects regulations (21 CFR 50). For UTCOMC purposes, a protocol deviation is a failure to follow procedures specified in the approved research protocol in the absence of a protocol waiver.

Minor Protocol Deviation: A protocol deviation that (a) has no substantive effect on the risks or benefits for the individual research subject, and (b) has no substantive effect on the value of the data collected, and (c) does not result from willing or knowing misconduct on the part of an investigator or study staff. Examples of minor protocol deviations include: follow-up visits that were performed outside of the required protocol window because of the subject’s schedule; or blood samples obtained at times slightly different than those outlined in the IRB approved protocol.

Major Protocol Deviation: A protocol deviation that (a) has harmed or has posed a significant risk of substantive harm to the individual research subject, or (b) has compromised the scientific integrity of the data collected for the study, or (c) appears to result from the willing or knowing misconduct on the part of an investigator or study staff, or (d) appears to involve some other serious or continuing noncompliance with federal, state or local research regulations.

IV. PROCEDURES

1. Protocol Waivers

- a. When a local investigator receives a protocol waiver from a study sponsor, or the principal investigator of an investigator-initiated study proposes to enroll a subject who does not meet the approved inclusion/exclusion criteria, the details of the proposed waiver, subject identification and all supporting documentation must be submitted to the UTCOMC IRB for

review and approval **prior to implementation**. The IRB will acknowledge receipt of such waiver requests.

- b. The principal investigator will use **Form I: Report of Protocol Waiver, Deviation, Violation** to submit (via IRBNet) a protocol waiver for IRB review.
- c. The principal investigator will apply his/her electronic signature to the form prior to submission to the UTCOMC IRB.
- d. Upon receipt of the protocol waiver, the IRB Administrator will electronically forward it to an IRB Chair or designee for review. If the reviewer determines that there are no relevant safety concerns and that the proposed waiver is not repetitive for the same exclusion criteria, the reviewer may approve the proposed waiver. However, if the reviewer determines that there are relevant safety concerns or that the waiver is repetitive for the same exclusion criteria, then the IRB will notify the investigator that the waiver may not be implemented without review by the full Board.
- e. If the IRB requires additional information, a letter will be sent to the investigator requesting the necessary information.
- f. Proposed waivers that present concerns about subject safety or that could reasonably be considered as reaching the threshold of “revision in the research activity” (because repetitive for the same exclusion criteria) must be approved by the full Board. A copy of the proposal and all supporting documents will be available to all board members at the next convened meeting for review and action by the Board.
- g. If a protocol waiver request might reasonably be considered to represent revision of the research activity, the IRB may require that the change be submitted as a request to revise the protocol.

2. Protocol Deviations

- a. The principal investigator is responsible for reporting all **Major Protocol Deviations** occurring at the local research site to the IRB. All deviations should be reported as soon as possible, but no later than five working days after the investigator becomes aware of the event.
- b. Protocol deviations that meet the definition of a **Minor Protocol Deviation** (outlined above) are not required to be submitted for review by the UTCOMC IRB. Sponsor reporting requirements for deviations may differ from UTCOMC reporting requirements. It is the responsibility of the principal investigator to comply with the reporting requirements outlined in the signed agreement.
- c. The investigator will use **Form I: Report of Protocol Waiver, Deviation, Violation** to submit (via IRBNet) all Major Protocol Deviations for IRB review. Information must include the facts of the case, including subject identifier, the date of deviation, impact on the subject’s safety, and plan for preventing the deviation in the future (if applicable).

- d. The principal investigator will apply his/her electronic signature to the form prior to submission to the UTCOMC IRB.
- e. Upon receipt of the Major Protocol Deviation, the IRB Administrator will electronically forward it to an IRB Chair or designee for review.
- f. If the IRB requires additional information, a letter will be sent to the investigator requesting additional information.
- g. All major protocol deviations will be reported to the full Board. A copy of the full report will be available via IRBNet to all board members at the next convened meeting.
- h. The IRB will determine if additional actions or follow-up are required. Further actions might include:
 - i. Stipulation of specific revisions in protocol procedures;
 - ii. Request for a corrective action plan from the principal investigator;
 - iii. Audit of investigator's study by the IRB;
 - iv. Increasing the frequency of the continuing review period for the study; and
 - v. Suspension or termination of the study.
- i. A copy of all correspondence / reports will be maintained in the electronic IRB files for the study.
- j. Correspondence regarding protocol deviations is included on the agenda of the IRB meeting at which the deviations are reported.