

## **IRB Policy 10: Modifications**

**Revision Date: April 16, 2008, November 11, 2009, January 27, 2011, May 28, 2013, February 9, 2015, Apr 2, 2018, Feb 7, 2019, October 16, 2019, October 22, 2021**

### **I. Pertinent Definitions**

- A. Modification:** Any change to an IRB-approved study regardless of the level of initial review.
- B. Non-Minor Modification:** Any proposed change in research related activities that impacts the risks or benefits associated with the study or changes the purpose or design of the study.
- C. Minor Modification:** A proposed change in research related activities that does not impact the risks or benefits associated with the study or change the purpose or design of the study, does not add procedures involving more than minimal risk to participants, and does not add procedures that do not fall into categories (1)-(7) of research that can be reviewed using the expedited procedure.
- D. Substantive:**
  - a. With regard to modification requests, a proposed change that is non-minor, i.e., any proposed change in research related activities that impacts the risks or benefits associated with the study or changes the purpose or design of the study
  - b. With regard to approval pending modifications, a clarification or revision which makes a substantial alteration in risks to subjects, selection of subjects, informed consent process, informed consent documentation, safety or monitoring, or subjects' privacy or data confidentiality. Examples include requesting additional information regarding study endpoints, or requiring submission of a data safety monitoring plan. To be eligible for expedited review, changes requested by the full board must be directive or non-substantive.

### **II. Summary Policy**

It is the policy of both the East Tennessee State University Campus Institutional Review Board (ETSU IRB) and the East Tennessee State University/ Veterans Affairs Institutional Review Board (ETSU/VA IRB) to review all requests for modifications to any previously approved research study (including exempt studies) to determine if the change will alter the risk/benefit ratio of the study. A complete description of the modification must be received prior to review. Modifications may include, but are not limited to, protocol amendments, changes in the number of subjects, changes in the informed consent, etc. All requested changes in the conduct of a study and/or changes to study documents must be

approved by the IRB prior to implementation of that modification. The only exception is a change necessary to eliminate apparent immediate hazards to the research subjects [21 CFR 56.108(a)(4)]. In such a case, the IRB will be promptly informed of the change following its implementation (within 10 working days) and will review the change to determine that it is consistent with ensuring the subject's continued welfare. IRB members with a conflict of interest may provide information requested by the IRB, but may not participate in the deliberation or vote of the IRB on the involved modification. A modification is only given approval to the expiration date that was received at the most recent review.

### **III. Modifications Requested by Sponsor**

If the modification is requested by the sponsor, a copy of any pertinent correspondence from the sponsor must be submitted with the Modification Request xForm. In addition, investigators must submit any proposed revised documents with the Modification Request xForm.

### **IV. Reconsenting/Notification of Participants**

If the modification warrants changes to the informed consent document, the investigator must address whether the information needs to be communicated to currently or previously enrolled participants, and if so, how it will be communicated. This may be accomplished by using an addendum to the initial ICD or by re-consenting the subject using the modified ICD. While the investigator is responsible for making the initial decision regarding any necessary document changes, the IRB will make the final determination of whether the modification requires a change to the ICD or other study documents. The IRB will also make the final determination of the necessity of re-consenting of currently enrolled participants or notification of participants who have completed research interventions.

### **V. Minor Modifications**

The initial determination as to whether a modification alters risks to the participants is made by the Principal Investigator. The modification is reviewed by the IRB Coordinator for completeness and assigned to the Chair for review. The Chair is responsible for evaluating the change in procedures and risks and determining whether full IRB review of the modification is necessary.

Minor changes to previously approved research may be reviewed and approved in an expedited manner by the IRB Chair or Designee. The designee should be one or more experienced reviewers designated by the chairperson from among the IRB membership. Modifications to research previously approved by the full

board may be reviewed by the expedited procedure if they meet the following criteria:

1. Modifications that do not materially affect the assessment of risks and benefits.
2. Modifications that do not pose an increased risk to subjects; AND
3. Any additional procedures fall within expedited categories 1-7.

## **VI. Non-Minor Modifications**

When a modification is determined to be a non-minor change to previously approved research, the Chair, or designee, serves as a primary reviewer. The IRB Committee receives a synopsis of the primary reviewer's findings at the convened meeting. The IRB must review and approve changes at a convened meeting before changes can be implemented. At the Chair's discretion, the Principal Investigator may be required to present the non-minor modification to the convened board.

Examples of non-minor modifications may include, but are not limited to, the following:

1. Change in protocol procedures, such as increasing the number of times a test is performed or adding additional procedures
2. Deletion or decrease in tests performed as part of safety evaluations
3. The addition of serious unexpected adverse events or other significant risks to the ICD
4. Changes, which, in the opinion of the IRB Chair or Designee, do not meet the definition of a minor modification
5. Any change that increases the risk of the study

## **VII. Exempt Research**

Any changes to an exempt study must be submitted to the IRB for approval prior to initiation of the change. The IRB Coordinator will determine if the modification renders the study ineligible for exempt status; and if not, the modification will be administratively approved. If the requested change(s) appear to increase risk, decrease safety, or renders the study ineligible for exemption, the investigator will be notified in writing that the modification request can be withdrawn to continue the study as previously determined to qualify under exemption guidelines, or submitted for appropriate review and approval through an expedited or full board review. If changes to the study change the previously determined review level, the approval letter will document the review level, including the appropriate expedited category(ies), as applicable.

## **VIII. VA Studies**

For VA studies, PIs must submit modification requests using the VA Modification Request xForm, which routes through the VA Research Office before IRB review. The VA R&D Office electronically signs the modification request xform to document their review. Any change in authorized prescribers of an investigational drug requires the submission of a revised 10-9012.

## **IX. Changes in Study Sites or Investigators**

Changes in study sites, investigators, or study staff must also be submitted to the IRB. All newly assigned principal investigators of previously approved studies must show proof of having completed required education and submit a current CV for the purpose of assessment of qualifications. Modifications to PIs will be reviewed by the IRB Chair or Vice Chair. All other study staff changes will be reviewed and administratively approved by qualified IRB staff. IRB Staff may refer study staff changes to the IRB Chair for review if the changes require assessment of qualifications of the new investigators (i.e., interventional research or federally-funded research). Modifications that propose changes in addition to study staff will be reviewed by the IRB as detailed in this policy.

### **References:**

45 CFR 46.110(b)(2)

21 CFR 56.110(b)(2)

45 CFR 46.108(b)

OHRP Compliance Activities: Common Findings and Guidance

21 CFR 56.108(a)(4)