

IRB Policy 10: Modification Policy

Revision Date: April 16, 2008, revised November 11, 2009, revised January 27, 2011, revised May 28, 2013, revised February 9, 2015, revised 4/2/18, revised Feb 7, 2019

I. 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 ETSU IRB and the 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 received by the Coordinator and presented it to the Chair for his/her review. The Chair is responsible for evaluating the change in procedures and risks, and determining whether full IRB review of the modification is necessary.

Proposed changes for previously approved research that are classified as minor modifications may be reviewed and approved in an expedited manner by the IRB Chair or, in the case of the Chair's absence or conflict of interest, his/her Designee. The designee should be one or more experienced reviewers

designated by the chairperson from among the IRB membership. Examples of minor modifications may include, but are not limited to, the following:

1. Administrative changes, such as correction of typographical error(s)
2. Revision of phone number(s)

VI. Non-Minor Modifications

When a modification is determined to be non-minor, the Chair or his/her 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 (*meeting at which a majority of the members are present, including at least one member whose primary concerns are non-scientific). 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 his/her 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 in an exempt study must be submitted to the IRB for approval prior to initiation of the change. The IRB Chair will determine if the modification renders the study ineligible for continuing exempt status; and if so, the modification will not be approved. The investigator will be notified in writing that he may withdraw the modification request and continue the study as previously determined to qualify under exemption guidelines or submit the study for appropriate review and approval through an expedited or full board review.

For studies subject to the 2018 Common Rule, when a modification is submitted on an exempt study that underwent limited IRB review, the IRB Chair must determine in the modification request impacts the determinations made during the limited review. If so, then the IRB Chair must determine if the modification renders the study ineligible for continuing exempt status and if so, the modification will not be approved. The investigator will be notified in writing that

he may withdraw the modification request and continue the study as previously determined to qualify under exemption guidelines or submit the study for appropriate review and approval through an expedited or full board review.

VIII. VA Studies

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

IX. Changes in Study Sites or Investigators

Changes in study sites, investigators or revisions in study staff must also be submitted to the IRB. The newly assigned investigator of a full review study, must show proof of having obtained required education and submit a current CV for the purpose of assessment of qualifications. If the PI is unknown to the IRB, the PI must also attend a convened IRB meeting. The change will be noted in the minutes.

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)