



I. Background

IRB review is an ongoing process. Federal regulations require that IRBs have written procedures for ensuring prompt reporting to the IRB of any changes in approved research and for ensuring that such changes are not implemented without prior IRB approval, except when necessary to eliminate apparent immediate hazards to subjects. The IRB must be notified immediately of any changes made to protect subjects' immediate safety.

II. Policy

- A.** All changes to currently approved research must be approved by the IRB prior to implementation, except when necessary to eliminate apparent immediate hazards to the human subjects.
- B.** Minor changes to currently approved research may be reviewed by expedited review procedures. Examples of amendments that may be considered minor include advertisements, personnel changes and other, low risk changes. Additionally, changes to protocols that have previously been reviewed under the expedited review procedures may be reviewed under the expedited review procedures as long as these changes do not increase the risk level of the study.
- C.** The criteria for approval of changes to previously approved research are the same as those for initial review. The IRB must determine that, in light of the proposed changes, the research continues to satisfy 45 CFR 46.111 and/or 21 CFR 56.111, as applicable.

III. Memorandum of Understanding

In aspects where the MUSC IRB is being utilized by the Ralph H. Johnson VA Medical Center, both parties will abide by the agreements set forth in the current "Memorandum of Understanding Between The Ralph H. Johnson VA Medical Center And The Medical University of South Carolina Concerning Utilization of the Medical University of South Carolina's Institutional Review Boards".

IV. Procedures

- A.** Submitting a Modification to the IRB for Review

1. All proposed modifications to study submissions must be submitted via the amendment process in the appropriate electronic system (either eIRB or ERMA) prior to instituting the change.
2. Examples of modifications that must be submitted include, but are not limited to, changes in:
 - a) Study Personnel
 - b) Enrollment numbers
 - c) Duration of study
 - d) Recruitment methods
 - e) Consent form
 - f) Investigator Brochure or device information
 - g) Study design, methods, procedures, or randomization
 - h) Adding or dropping an arm of the study
 - i) Questionnaires, surveys, interview scripts, advertising
 - j) Funding
 - k) Data and Safety Monitoring plan
3. Investigators must provide the IRB with complete descriptions of the modifications, including the rationale(s) for the modifications and the anticipated impact upon current and future subjects, as well as revised versions of those study materials affected by the modifications. This could include modifications to the protocol, informed consent, HIPAA authorizations and eIRB/ERMA application as applicable. The Principal Investigator electronically submits requests for modifications. Changes in any document must be clearly marked in this submission and the appropriate associated paperwork uploaded with the submitted amendment.

B. Initial Review and Level of Review

1. Upon receipt of a modification request, IRB staff and/or a Chair will pre-review the submission to determine the appropriate level of IRB review required.
 - a) Modifications containing minor changes in previously approved research may be forwarded to the Chair or his/her designee for consideration under the expedited review procedures. The Chair has

discretion to forward such changes to the full board for review if appropriate.

- b) Modifications that represent more than a minor change will be forwarded to the full board for review. PI's should review the meeting deadlines prior to submitting a full board amendment. Modifications to research initially eligible for expedited review may be reviewed using expedited procedures. However, modifications that render a research study ineligible for expedited review under the applicable regulatory categories will be reviewed by the full board.
 - c) Some modifications, such as study staff changes (other than the PI) or fixing typos or formatting errors in study documents, are not considered changes in the research. They still must be submitted through the eIRB/ERMA for administrative purposes, but may be approved administratively by designated IRB staff. The following are considered administrative changes which can be approvable by designated IRB staff:
 - 1) deletion of study staff
 - 2) Addition of study staff other than principal investigators
 - 3) Change in contact information (ERMA only)
 - 4) Title change that does not reflect a change in the study
 - 5) Corrections of typographical errors/reformatting of unchanged text
 - 6) Errors in the eIRB smartforms as confirmed by the study team and IRB staff
2. All modifications will undergo initial evaluation by MUSC IRB staff to make sure the submission is complete and correct and the changes are consistent with the applicable administrative and regulatory requirements.
 3. The convened IRB, or the IRB Chair/designee using expedited review procedures, will determine whether the research, in light of the proposed changes, continues to satisfy the applicable criteria for approval. This includes determining whether the proposed changes reflect new information that may relate to a subject's willingness to continue participation, thus warranting re-consent or notification of subjects.
 4. Approval of a modification to a study does not result in a change to the approval period for the study.

5. The IRB or IRB staff will provide investigators with written notice of approval (including administrative approval where appropriate), required modifications to secure approval.

C. Full Board Amendment Review

1. Once the determination is made that the amendment requires full board review, the IRB Staff reviews the amendment for completeness and forwards the amendment to the Primary Reviewer (Chair, the Vice Chair, or Chair's designee). S/he reviews the amendment for compliance with the criteria for approval of research.
2. The amendment application is distributed to all IRB members by the IRB Staff prior to the convened meeting. The amendment application consists of the following items:
 - a) the amendment application;
 - b) a red-line version of the informed consent and protocol indicating changes as applicable
 - c) information which would relate to participant's willingness to continue participation; and
 - d) other supporting documents (summary request from sponsors, new surveys and questionnaires etc.).
3. All IRB members are expected to review all modified documents in sufficient depth to discuss the information at the convened meeting.
4. Using the designated review procedure, the IRB Staff will provide comments regarding the administrative review of the application. The Primary Reviewer (the Chair, Vice-Chair or the Chair's Designee) will enter his/her review comments and recommendation of approval, required changes, or disapproval to the on-line application. If the recommendation is for additional changes or disapproval, IRB Staff will send the reviewer's comments to the study communication leads for response prior to the Board meeting. In addition to the above material, the designated reviewers also receive a red-line version of the protocol indicating changes.
5. In addition to the above material listed in III.C.2. above, Board members will receive a red-lined version of the documents being revised by the amendment. Reviewing members can send any questions/concerns to the Administrator or Chair prior to the convened meeting.

D. Reporting of IRB Approval

1. Protocols approved by the expedited process will be reported to the full IRB board at a convened meeting. Any board member may request further consideration of any protocol approved by the expedited process.

E. IRB Convened Meeting

1. The Primary Reviewer's recommendations are included in the agenda distribution.
2. During the meeting, each full Board amendment is presented by the Chair and/or Primary Reviewer(s), discussed and voted on individually. The Principal Investigator will be present if requested by any Board member or if the Chair/Administrator thinks the Investigator needs to be present to clarify issues/concerns.
3. In evaluating the proposed amendment, IRB members and staff consider OHRP, FDA and, as relevant, VA regulatory criteria.
4. In addition to the application material submitted by the Principal Investigator, the IRB may request additional information, e.g. DSMB reports, sponsors reports, journal articles etc., which may be relevant to the participant's willingness to continue participation.
5. If the IRB determines that the information presented in the amendment application and associated documents would affect a participant's willingness to continue participation, the IRB will request the Principal Investigator contact and re-consent the participants.
6. When the amendment is the result of an immediate change initiated without IRB approval in order to eliminate apparent immediate hazards to participants, the IRB will review the facts surrounding the hazard in order to determine that the benefits of such change outweighed the risks inherent in instituting such change without IRB approval and that the change was consistent with ensuring the participants' continued welfare. An example would be the Principal Investigator reading a scholarly scientific article reporting the deleterious effects of a drug dose, which, had not been previously reported.
7. The Board may approve, require further modifications to secure approval, table, or disapprove an amendment to a study. If the Board requests minor changes which do not substantially impact the risk/benefit analysis, the Board may approve the amendment contingent on final review and approval by the Chair or the Chair's Designee.
8. Final review and approval of Board-requested changes to study documents may be deferred to the Chair's or Chair's Designee.

F. IRB Administration Responsibilities Post-Meeting

1. If the amendment is approved at the meeting, the IRB Staff releases the approval to the Principal Investigator.
2. If applicable, the new version of the informed consent/HIPAA authorization is date stamped with the amendment approval date. A new version of the amended informed consent/HIPAA authorization document, with an original IRB approval stamp, is released to the study contact. The previously approved version becomes "obsolete".
3. For amendments in which the Board has approved contingent upon completion of requested minor changes which do not substantially impact the risk/benefit analysis, the IRB Staff will notify the study contact electronically of any required changes. When revisions are received in the IRB office, they will be reviewed and if acceptable, the approval will be released.
4. If modifications are substantive in nature or if the Board tables or disapproves the amendment, the IRB Staff/Chair will notify the study contact in writing outlining the Board's requirements.

G. Substantive Modifications Required by the IRB

1. Principal Investigator's responses to an amendment tabled due to substantive modifications or rewrites are presented to the Full Board for review, discussion and vote at the earliest possible convened meeting. If approved, the IRB Staff will release the approval using the above outlined process.

H. Responsibilities and Assurances

1. It is the responsibility of the Investigator as attested in the Principal Investigator assurance, that no modification will be made to the approved research without IRB approval except in circumstances necessary to eliminate apparent immediate hazards to participants.
2. In addition, the University Compliance Office performs for cause and routine random audits of research records. One focus of these audits is the determination that study modifications either occurred subsequent to IRB approval or were initiated in order to eliminate apparent immediate hazards to participants with subsequent review and approval by the IRB.
3. Furthermore, the training completed by research staff emphasizes the need for IRB approval of all research activities.