Continuing Review

Full Continuing Review

Studies initially reviewed by the full, convened IRB undergo continuing review by the full convened IRB with recorded vote on each study, unless the study has been modified such that it meets the federal guidelines to be eligible for reclassification for expedited continuing review. For full continuing review, the IRB reviews proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in the nonscientific areas (45 CFR 46.108(b)).

In conducting full continuing review, a Primary Reviewer System is utilized. Consideration for the selection of Primary Reviewers to serve is based on area(s) of expertise in compliment to the research under review, term of IRB membership, dedication to continuing education and availability to accept new and continuing research proposals. The Chair, Vice Chair review each continuing review submission to determine which members have the relevant expertise to conduct an in-depth evaluation of the protocol. Primary Reviewers are responsible for analyzing the protocol and the complete IRB application in detail and are authorized to discuss any unanswered questions with the investigators, associated researchers or consultants prior to or during the convened meeting.

For continuing review of research that does not qualify for expedited review, all IRB members are responsible for reviewing:

1. Project Narrative, which serves as protocol summary or project narrative portion of xForm
2. Continuing Review/Study Closure Application (xForm 107), which serves as status report, and any attachments (complete documents as received from investigator).
3. Copy of the current approved informed consent document
4. Copy of any newly proposed consent document
5. Summary history of modifications reported to the IRB and list of interim adverse events, if applicable
6. Results of any IRB and, if appropriate, VA audits that have occurred since last review

For continuing review of research that does not qualify for expedited review, the primary reviewer(s) are responsible for reviewing:
1. Project Narrative, which serves as protocol summary or project narrative portion of xForm

2. Continuing Review/Study Closure Application (xForm 107), which serves as status report, and any attachments (complete documents as received from investigator).

3. Current approved informed consent document

4. Any newly proposed consent document

5. AE Reports and summary history of modifications done since the last review

6. HIPPA authorization, if applicable

7. Results of any IRB and, if appropriate, VA audits that have occurred since last review

8. Complete protocol, including any protocol modifications previously approved by the IRB

Upon request, any IRB member has access to the complete IRB protocol file and relevant IRB minutes prior to or during the convened IRB meeting. In addition, any IRB member has access to additional information provided to individual reviewers.

The full IRB Committee is informed of the Primary Reviewer’s findings at a convened meeting. Particular attention will be paid to the Risk/Benefit Ratio of the investigations and the adequacy of the Consent Forms in conveying the procedures, implications and full intent of each study. Problems identified by the Primary Reviewers or by other IRB members will be discussed and suggestions for any necessary changes will be agreed upon by the IRB.

After discussion, including an explanation of the important issues that were evaluated, the full, convened board makes its determination with a recorded vote. Any controverted issues will be recorded in the minutes. This process allows the IRB to conduct a more substantive review and discussion at convened meetings.

Minutes of IRB meetings document separate deliberation, actions, and votes for each protocol undergoing continuing review by the convened board.

**Expedited Continuing Review**

Expedited continuing review may be conducted if the study was initially eligible for, and approved by, an expedited mechanism, with the following exception: if an amendment or continuing review indicates changes in the study so that it is now ineligible for expedited continuing review as noted with submission of modification/continuing review. The IRB is only permitted to use expedited review for the continuing review of research...
that involves solely one or more of the activities published at 63 FR 60364-60367. If the study is modified such that it fails to meet expedited criteria for review, the study will undergo full continuing review.

When conducting research under an expedited review procedure, the IRB Committee Chair or designated Expedited Reviewers conduct the review on behalf of the full IRB Committee. When performing continuing review by the expedited procedure, the IRB Chair or designated Expedited Reviewers are responsible for reviewing all of the following documentation:

1. Project Narrative, which serves as protocol summary or project narrative portion of xForm
2. Continuing Review, Study Closure Application (xForm 107), which serves as status report, and all attachments (completed documents as received from investigator)
3. Current approved informed consent document
4. Newly proposed consent document
5. Current HIPAA Authorization document
6. Complete protocol, including any protocol modifications previously approved by the IRB

Exempt Studies

Studies that have been determined to meet exempt status do not undergo continuing review unless a change in the study renders it ineligible for exempt status per federal guidelines. Investigators are informed in the exempt status letter to inform the IRB of any change in the project prior to its implementation, and reclassification under expedited or full review would be determined at that time by the IRB Chair.

Approval Criteria

Approval, both initial and continuing, must meet HHS regulations at 45 CFR 46.111, including determinations by the IRB regarding risks, potential benefits, informed consent and participant safeguards. Criteria for both initial and continuing review approval are the same and therefore, IRB continuing review must include a determination by the IRB that risks to subjects continue to be minimized, risks to subjects continue to be reasonable in relation to anticipated benefits, selection of subjects continues to be equitable, informed consent continues to be adequate, and appropriately obtained and documented; where appropriate, the research plan continues to make adequate provision for monitoring the data collected to ensure the safety of subjects; there
continue to be adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data, appropriate safeguards continue to be included to protect vulnerable participants. If interim changes in IRB policy have occurred such that the proposal submitted for continuing review would not be approved if the same study were an initial submission, the IRB does not approve the continuing review of that protocol.

Changes/New Information

The IRB is also responsible for ensuring that changes in approved research are promptly reported to, and approved by, the IRB [21 CFR 56.108(a)(3-4)]. Continuing review will include an IRB determination of whether new information or unanticipated risks have been discovered since the previous IRB review. Based on new information or unanticipated risk, the IRB has the authority to reconsider its approval, require modifications to the study, and/or revise the continuing review timetable. Any significant new findings which may relate to the subject's willingness to continue participation should be provided to the subjects in accordance with 21 CFR 50.25.

Review Interval

The policy of ETSU IRB and ETSU/VA IRB is to determine appropriate continuing review interval for each review conducted by the IRB. The IRB will generally obtain review more often than annually if any of the following situations are true:

1. Recommendations by another committee, such as the VA Research and Development Committee, to obtain review more often than annually

2. Consent being given by legally authorized representatives

3. Identified conflict of interest of involved study personnel

4. Research for which participants would be exposed to additional risk (i.e., disproportionate number or severity of adverse events, Phase I study) and study does not have DMSB

5. Previous suspension of the study due to non-compliance

6. Recommendations by other IRB members that review be conducted more often than annually

Informed Consent

IRB continuing review will also include evaluation of the informed consent document currently in use. The currently approved informed consent, as well as any proposed
informed consent document, will be reviewed to determine if the information provided continues to be accurate and complete, and to determine if any new information needs to be added. The informed consent document will also be reviewed to ensure that any significant new findings that may relate to the subject's willingness to continue participation are provided to the subject in accordance with HHS regulations at 45 CFR 46.116(b)(5). Review of the informed consent document will take place not only at continuing review, but at other times when new information becomes available that needs to be communicated to participants.

**Source Verification**

When conducting continuing review, the IRB is responsible for determining which studies need verification from sources other than the investigator that no material changes in the research have occurred since the previous IRB review [21 CFR 56.108(a)(2)]. The need for additional verification will be determined by the IRB on a case-by-case basis. Source verification will be required when:

- Investigator is providing inconsistent information that cannot be resolved
- The IRB doubts the investigator's veracity
- IRB doubts that the investigator has sufficient relevant knowledge
- IRB perceives that investigator is intentionally not providing necessary information

**No Grace Period**

Per regulations, there is **no** grace period that allows the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of research must occur on or before the date when IRB approval expires. If any activity occurs or continues after the expiration date, the investigator is deemed to be out of compliance with both federal regulations and ETSU/VA policies.

The IRB may restrict, require modifications, or terminate a research project based on continuing review by the IRB Committee. All studies in which the IRB requests changes to current documents are assigned a pending status. IRB approval is not given until the requested changes are received and approved. **The expiration period is not extended.** If continuing review and re-approval fails to occur by the continuing date specified by the IRB, all research activities must **stop**, unless the IRB finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions.

If the IRB does not re-approve the research by the expiration date, the IRB approval expires. The PI, upon receipt of expiration letter, must immediately submit to the Chair...
a list of research participants that could be harmfully affected by expiration of the research. The IRB Chair, with appropriate consultation with (for VA) either the Chief of Staff (COS), or in his/her absence, the ACOS/R, or (for ETSU) the Vice Provost for Research (VPR), will determine if the subject(s) may continue in the research. If the ACOS/R or VPR is not a physician, they will designate a physician as a consultant. If the study is an FDA regulated study, the COS, ACOS/R or VPR and IRB Chair will follow FDA requirements in 21 CFR 56.108(b)(2) and (3) in making their decision.