Protocol Amendments

**Introduction:**
The IRB reviews and approves all amendments (i.e., revisions, modifications, or addenda) to an IRB approved research protocol.

**Definition:**
*Amendment* is defined as a revision, a change, or an addition (addendum) to an approved research protocol.

**Minimal Risk** means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (*45 CFR 46.102 (i)*).

**Policy:**
The IRB policy states that any revisions, changes or additions in procedures, alterations of risk compared to the original protocol, or changes in subject population, must be reviewed by the IRB prior to continuation of the research. Prior approval by the IRB is required except when necessary to eliminate apparent immediate hazards to the subject (*21 CFR 56.108(a)(4) and 45 CFR 46.103 (b)(4)(iii)*).

Changes in approved research that are initiated without IRB approval to eliminate apparent immediate hazards to the participant must be to be promptly reported to the IRB. They are reported as unanticipated problems involving risks to participants or others, using the paper *Report Unanticipated Problem or Protocol Deviation Checklist (U/D)* (for paper-based studies) or the *electronic Unanticipated Problem or Protocol Deviation Checklist* (submitted via the iRIS system for electronic protocols). The IRB will review all changes to approved research, initiated without IRB approval to eliminate apparent immediate hazards to the participants, to determine whether the change are consistent with ensuring the participants’ continued welfare.

Major changes in study design or the application of a study to a very different population usually require a new protocol.

**A) Amendments Examples**
Examples of common amendments are:
- Changes to the IRB investigator checklists
- Revisions to a protocol including:
  - Sponsor amendments;
  - Administrative or editorial changes or addenda;
  - Changes or additions to eligibility criteria
  - Changes to a procedure
  - Addition of a procedure
Revisions to consent form or assent form
Changes to study investigators
Changes in study personnel
Change in recruitment practices including:
  Change in research population
  Letters to potential participants
  Bulletin boards flyers
  Media/internet advertisements, press releases
  Notifications and/or letters to research participants
  Advertisements
  Recruitment materials
  Use of recruitment registries (e.g. ResearchMatch)

B) Investigator Amendment Submission Requirements
Investigators who wish to make alterations to an active IRB protocol must submit a written addendum/amendment request to the IRB in a timely manner, prior to initiation of the alteration. The investigator must complete the paper Addendum Checklist (A) if the study is paper-based or the electronic Addendum checklist (submitted via the iRIS system) if the study is electronic. A written description of the proposed change(s) and the reason for the change(s) must be included. Attached to the addendum request must be all new or revised materials (i.e., consent form, questionnaires, scripts, revised protocol etc.). The exact text of the revisions must be submitted with the application.

The IRB will reassess the balance of risks to benefits in light of the proposed change, and may require the research to be modified or terminated. Only those individuals noted as Responsible Investigator or designee have the authority to submit addenda requests on his or her protocol.

The investigator must determine if the amendment significantly alters the basic design of the study or changes the risk/benefit ratio for participants. Amendments that alter the research method design, in particular the inclusion and exclusion criteria or the risk/benefit ratio, will be reviewed by the convened IRB. If the risk/benefit ratio has changed, the investigator must also determine whether participants currently and/or previously enrolled on the study will be re-consented. The investigator will need to amend the currently approved informed consent document(s) to reflect the change. In addition, when reviewing information relating to protocol changes, the IRB is required to assess whether the information should be provided to the participants, when such information might affect their willingness to continue to take part in the research.

The Department Review Committee and/or Department Chair or Clinical Director must approve amendments which alter the basic design of the study; increase the risk/benefit ratio; or those amendment determined by the IRB to require review by the convened IRB, prior to being reviewed at a convened IRB meeting.
If submitting paper-based amendment, the investigator must submit two copies of the currently approved document, two copies of the revised document with the changes highlighted, and two copies of the revised document without the changes highlighted. For amendments such as advertisements, flyers, etc., one original document and one copy must be submitted to the IRB office for review and approval.

C) IRB Review
The IRB Chair, Vice-Chair or experienced designated IRB member may utilize expedited procedures to review a proposed change/s to previously approved research if it represents a minor change to be implemented during the previously authorized approval period. The IRB defines a minor change to be one that makes no substantial alteration in any of the following:

- The probability or magnitude of risks to participants
- The research design or methodology
- The number of participants enrolled in the research
- The qualifications of the research team
- The facilities available to support safe conduct of the research
- The likelihood of participants’ willingness to participate
- Any factor that might warrant convened IRB review

If the IRB administrative office or expedited reviewer determines that the proposed change to previously approved research represents more than a minor change to be implemented during the previously authorized approval period, the request will be reviewed by the convened IRB.

All amendments that significantly alter the basic design of a study or increase the risk/benefit ratio must be reviewed and approved by a convened IRB. The primary and secondary reviewer will receive and conduct an in-depth review of the amendment application (investigator checklist), all modified documents all relevant currently IRB approved documents (approved consent, research plan), the investigator’s written explanation for the changes, and a clean copy of the revised documents. All other IRB members will have access to and review the amendment application (investigator checklist), all modified documents, and all relevant currently IRB approved documents (approved consent, current protocol) in enough depth to be familiar with them and be prepared to discuss them at the convened IRB meeting. For paper-based submission, before and after the meeting IRB members may come to the IRB office to obtain the complete IRB protocol file, meeting minutes, and information provided to the primary reviewers. IRB staff will make these items available to them upon request. During the meeting, IRB members may ask the IRB staff for a copy of the protocol file, meeting minutes, and information provided to the primary reviewers. IRB staff will make these items available.
When reviewing amendments using the expedited procedure, the reviewer will receive and review the same information, outlined above, provided to a primary reviewer.

Amendments that receive expedited review do not require Department Review or approval. The IRB requires that all amendments approved by expedited review are reviewed at the subsequent continuing review.

The IRB will determine whether re-consenting of currently enrolled participants is necessary. This determination should be based on new information regarding a change in the risk/benefit ratio that would possibly affect the participant’s decision to continue with the research activities. The IRB will also decide whether participants who have completed the study should be contacted and provided with additional information.

The minutes should reflect the IRBs determinations regarding whether the amendment has changed the risk/benefit ratio of the study and whether the approval period is appropriate to the level of risk.

Approval of an amendment to a protocol does not change the date of the protocol Continuing Review unless the IRB assigns an earlier review date based on the amended information.

Amendments that receive administrative approval are included in the monthly report to the IRB of administrative activities and are reviewed and approved by a vote of the Board.

References and/or Regulatory Citations:
21 CFR 56.108(a)(3 and 4)
45 CFR 46.103 (b)(4)(iii)

Related Forms:
IRB paper Checklist – Protocol Addendum (A)
Electronic Addendum Checklist in iRIS
IRB paper Checklist – Report Unanticipated Problem or Protocol Deviation (U/D)
Electronic Unanticipated Problem or Protocol Deviation Checklist in iRIS