

Section 22:

Amendments to Previously Approved Research

22.1 Overview

Once a study has been IRB approved (and activated), the associated study documents (submission forms, protocol document, consent forms, alert page, front sheet, study diaries, recruitment materials, questionnaires, etc.) dictate how the study will be conducted. Changes in approved research, including changes to informed consent documents, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the participant (45 CFR 46.103(b)(4)(iii) and 21 CFR 56.108(a) (3)-(4)). When applicable, activation requirements must also be met prior to the amendment being implemented.

Proposed amendments must be sent to the OHRS electronically via OHRS submit for review by the IRB. Minor changes to previously approved research may qualify for an expedited IRB review (review carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among the members of the IRB). In reviewing the proposed amendment, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the proposed changes. The proposed amendment can only be disapproved after review by the convened IRB. If a proposed amendment is not eligible for expedited IRB review procedures it will be routed directly to the convened IRB for their review. If there are significant scientific changes proposed P/SRC review may be required prior to IRB review. If the scientific changes proposed are minimal a biostatistician review may be requested prior to IRB review.

After IRB review the study team will be contacted as to the outcome of the review. The possible review outcomes described earlier in section 20.9 “Review Outcomes” of this guide are also applicable to the review of amendments. If a response is required to the IRB conditions (and P/SRC if applicable) the study team is expected to provide a point-by-point response as soon as possible after the review outcome is disseminated to the study team.

Once any conditions are satisfied, the study team will be notified of the IRB approval by the OHRS Online Communications Team. If there are no activation requirements the study team will receive an approval/activation memo and the revised study documents will be posted on OncPro for use by the study team. If the amendment is only IRB approved, and activation requirements are required, the study team will receive only an IRB approval memo and the amendment will be routed for activation. Activation sign offs for amendments are similar to the sign offs required for new protocol submissions and are further described in section 20.7 “Review and Approval of Other DF/HCC Departments/Committees” of this guide. Once all activation requirements have been met, the amendment will be activated and the OHRS Online Communication Team will notify the study team of the amendment’s activation and post the revised documents on OncPro. At the time of approval/activation amendment changes are considered implemented and the study team may conduct the research using the revised study documents.

22.2 Types of Amendment Submissions

General Amendments

General amendments (including CTEP amendments, Dose Escalation Amendments and Updated Investigational Brochures) may include one or more of the following changes to the previously approved research and are submitted using the Amendment form:

- Increased Risk to Participants: New Risk is Identified; Changes are made as a result of an updated Investigational Brochure, Serious Adverse Event or IND/IDE Safety Report necessitate changes to the study;
- Dose Escalation Amendment: Change in Cohort;
- Status Change: Moving from Phase I to Phase II; Closing or Opening a Arm; Temporary Suspension or Hold; re-opening the study along with other study changes;
- Scientific Changes: Adding a New Arm; Changing Objectives; Changing Statistical Analysis; Adding Correlative Studies; Increase or Decrease in Overall Accrual Goal;
- Eligibility Changes: Changes to the Inclusion or Exclusion Criteria;
- Therapy Changes: Change in Dose; Change in Administration; Change in Route of Administration; Change in Pre-Medications; Change in Drug Preparation; Change in Surgical Procedures or Radiation Administration;
- Recruitment of Subjects: Change in the way subjects are recruited; New or revised study advertisement;
- Data, Data Collection and Data Collection Materials: Revised documents given to participants including study diaries, questionnaires and QOL surveys; Adding new data points;
- Editorial, Administrative Changes: Change in contact information; Change in site participants; Typographical errors corrected; Clarifications made to previously approved research;
- Other changes, as specified in the amendment form.

Change in Participating Study Staff or Site Participants

Changes in participating study staff or site participants are submitted using the Research Team Update form, the Change in PI/Site PI form or the Request to Add/Remove Site form:

- Change in the Principal Investigator or Site Investigator, including additions and removals;
- Change in Research Team members including Co-Investigators, Research Nurses, Clinical Research Coordinators, including additions and removals;
- Addition or Removal of a participating site.

Change in Study Status

Changes in study status are submitted using the Closure/Re-Open form:

- Permanent Closure to Accrual;
- Temporary Closure to Accrual;

- Closure of part of a study to Accrual;
- Request to Re-open a Study to Accrual.

22.3 Amendment Submission Requirements

General amendment submissions require a justification for the changes made to the study. Without a sufficient justification within the amendment form review of the amendment may be delayed. The IRB requests that the justification be in lay terms and within the amendment form in order for the non-scientist IRB members to be able to understand the rationale for the proposed study changes.

All proposed changes to study documents must be clearly identified for the reviewers within the amendment form and/or submitted as a supplemental document such as a “summary of changes”. Clean and underlined revised documents are also strongly recommended. Without appropriate documentation of the proposed changes review of the proposed amendment may be delayed.