Institutional Review Board

University of Missouri-Columbia

Standard Operating Procedure

Amendments

Amendments

Effective Date: January 21, 2019
Original Approval Date: January 21, 2019
Revision Date: March 1, 2020
June 15, 2021
August 15, 2022
November 11, 2022

Approved By: Michele Kennett, JD, MSN, LLM
Associate Vice Chancellor for Research

Michele Kennett

1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the requirements for submission and review of amendments to non-exempt research.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the University of Missouri Institutional Review Board.

3.0 Policy/Procedure

Submission Process

45 CFR 46.103(b)(4)(iii) requires that the IRB review and approve all proposed changes in a research study, prior to the initiation of such changes, as new or corrected information is obtained. Submission of all amendments is also required for IRB record keeping and to permit the reconstitution of the history of the project.

If the investigator initiates changes to eliminate apparent immediate hazards to the participant prior to IRB approval, the change must be submitted to the IRB as soon as possible as an

Amendment with justification. This is the only time a change can be initiated prior to IRB approval and not be classified as non-compliance.

The Amendment process is also used to submit reports and documentation relevant to the study and determinations of the IRB. For example, when the study has a Data Safety Monitoring Board, the reports from these reviews need to be submitted for review. If changes are requested by a committee or individual external to the IRB, this must be promptly (within 30 days) communicated to the IRB via the Amendment for review. No changes should be made to the study without prior IRB approval unless it meets the exception noted previously to eliminate immediate hazards. If the sponsor or sponsor-investigator consults the FDA or other federal agency regarding or affecting determinations made by the IRB, the IRB needs to be notified and an Amendment may be required if changes are necessary. Depending on changes requested, when applicable, enrollment and other study activities may need to halt until IRB review is complete.

Amendments may dictate that revisions be made to more than one project document. For example, a protocol amendment may affect both the protocol and the consent document. Two copies of all revised documents must be submitted for review and approval, in addition to the amendment form being submitted. One copy should be tracked changes indicating the changes and the other copy should be clean. An exception to the required tracked changes would be for administrative changes noted below.

There are 2 amendments available for submission on expedited and full board studies:

1. Amendment Form: This is the main amendment and includes a feature that requires investigators to edit the original application where necessary. Each approved version of the application is saved and should describe the current version of the project.
2. Amendment for External Sites: This must be submitted when MU IRB is the IRB of Record for multiple, external sites. External sites can be added or removed with this form. Also, any site-specific changes must be submitted on this form for external sites relying on the MU IRB.

<u>Review Process</u>

The amendment request will be processed by the IRB office in the order in which it is received. The IRB staff will review the amendment and will request further information as necessary for the board’s consideration in addressing all regulatory and institutional requirements.

There are three categories of changes that must receive prior IRB approval. If prior approval is not obtained, it may result in a deviation which will need to be submitted on an Event Report. See Non-Compliance SOP.

If expedited or full board review is required, the IRB will determine the study continues to satisfy the criteria set forth by 45 CFR 46.111, 21 CFR 56.111 and 38 CFR 16.111. Subjects will be informed if there are any significant new findings that may relate to the subject's willingness to continue to participate in accordance with HHS regulations at 45 CFR 46.116(b)(5)

1. Administrative Changes

Administrative changes may be approved by the Chair or IRB staff designated by the Chair. Administrative changes may be made on an Amendment Form or Continuing Review Report.

Examples may include:

a. Personnel changes (except for PI changes)
b. Changes to improve the clarity of statements or to correct typographical errors provided the requested changes do not alter the content or intent of the statement/document.
c. Title change that does not change the overall purpose of the study
d. Data safety monitoring reports allowing the research to continue as approved with no concerns noted.

2. Minor Changes

The regulations allow for expedited review of minor changes in previously approved research in accordance with 45 CFR 46.110(b)(1 and 2). Minor changes are defined as those which do not involve procedures that increase risk more than minimally or add procedures that would make the protocol ineligible for initial review using the expedited procedure.

Examples may include:

a. Request inclusion of activities that fall under the categories of allowable expedited review set forth in 45 CFR 46.110.
b. Changes to minimal risk projects that remain minimal risk with the proposed changes.
c. Changes to greater than minimal risk projects, which do not alter the risk/benefit ratio (a sponsor memo/protocol update documenting no changes to the risk/benefit ratio will be taken into consideration).
d. Changes to the anticipated enrollment number greater than 20%.

Minor changes will be reviewed by the Chair, Vice-Chair, or other qualified board member. The reviewer of an expedited amendment has access to and is expected to review all materials on file for the study. The reviewer will document that the amendment is a minor change and qualifies for expedited review by completing the reviewer checklist. The board member always has the option, upon further review of the request, to request review of the amendment by the full board. If disapproval of the amendment request is imminent, the amendment must be reviewed by the full board.

Amendments to research previously approved using the expedited procedure will again be reviewed through the expedited review process unless, upon review of all study materials, the IRB reviewer determines that the changes are to the extent that the research no longer qualifies under 45 CFR 46.110 for expedited review.

3. Major Changes

In accordance with 45 CFR 46.108(b), all amendment requests which do not meet the criteria set forth in the expedited categories (45 CFR 46.110) are considered major and must be reviewed by the full board.

Full board amendment requests will be reviewed using the primary reviewer system and will be placed on the next available agenda after which a complete submission was received. See Initial Review SOP for additional information regarding the full board review process.

If there are new anticipated risks, all new enrollment must halt until the IRB has reviewed and approved the amendment unless the modified risk information represents a minor alteration of the risk such as a clarification. The investigator receives notification of this requirement to halt enrollment in the Amendment Received Notification Memo.

The IRB always has the option to request that amendments that substantially change the conduct of the study be presented as separate new proposals.

IRB Amendment Actions

The IRB may take the following actions upon review of an amendment:

- approve
- approve with minor modifications
- defer
- disapprove

Participant Notification and Re-Consent Requirements

If the changes are a result of significant new findings which may relate to the participants' willingness to continue participation, re-consent or participant notification is required.

If the IRB requires re-consent or notification of participants, this must be accomplished at the next study visit or within a timeframe required by the IRB. The IRB determination will be documented in the IRB approval letter.

If re-consent or notification was not obtained as required, the issue will be reviewed as non-compliance. See the Non-Compliance SOP for more information.

Amendment Approval

The date of approval of an amendment does not change the original approval date or the date by which the regularly scheduled continuing review of the project will be performed.

An electronic copy of all materials will be stored in eCompliance as documentation of the action taken. Investigators will receive an electronic approval letter for their records as well.

The Board will be notified of all approved amendments in the board meeting packet. See Board Meeting Procedures and Minutes for more information about what is included in the packet.

Additional Review Requirements

Several other institutional reviews may be necessary because of the proposed changes. The description of requested amendment changes will allow the IRB office to determine whether additional reviews are required. See the Initial Review SOP regarding additional reviews.

References:

Policy Revision Dates Prior to January 21, 2019:
June 1, 2001; May 1, 2004; September 1, 2004; June 2, 2005; February 24, 2006; December 1, 2006; May 5, 2008; December 24, 2009; June 10, 2010; July 1, 2011; March 1, 2015; July 1, 2015; June 8, 2017