



Institutional Review Board

University of Missouri-Columbia

Standard Operating Procedure

AMENDMENTS

Amendments

Effective Date:	June 1, 2004	
Original Approval Date:	January 22, 2001	
Revision Date:	May 1, 2004	February 24, 2006
	September 1, 2004	December 1, 2006
	June 2, 2005	May 5, 2008
	December 24, 2009	June 10, 2010
	July 1, 2011	March 1, 2015
	July 1, 2015	

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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.

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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

General Information

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. These amendment requests may be submitted to the IRB administrative office at any time using the online eIRB system.

All project amendments should be submitted to the IRB office regardless of whether the study sponsor indicated that the amendment requires IRB approval. It is the responsibility of the IRB office/chair(s) to determine whether the amendment is considered administrative in nature and how it should be processed. Submission of all amendments is also required for IRB record keeping and to permit the reconstitution of the history of the project and project-related actions from the IRB file. Investigators are required to submit sponsor amendments to the IRB office within thirty days of receiving the change.

If the Investigator changes approved research 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.

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. The IRB staff will request further information or additional submission requirements as necessary for the board's consideration in addressing all regulatory requirements. The following categories of review will be determined for each request:

- minor/administrative changes
- major changes

If the amendment requires full board review, the amendment will be placed on the next available agenda contingent if a complete submission has been received.

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

- approve
- approve with documented modifications
- defer

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- disapprove

If the board requires re-consent of the subjects, this must be accomplished within 60 days of notification. If not, the investigator must contact the IRB office to provide a justification as to why this has not occurred. This information will be reviewed by the board at the next available meeting.

Any member may request clarifications or changes to any project materials during the review of an amendment.

Specific revisions stipulated by the convened IRB requiring simple concurrence by the investigator or minor modifications or clarifications* as defined below may be reviewed using the expedited procedure.

*Minor Modifications or clarifications:

- Those modifications or clarifications that do not involve potential for increased risk or decreased benefit to the human subjects.
- Protocol revisions that entail no more than minimal risk to participants are considered “minor” modifications.
- Changes to informed consent documents that do not affect the rights and welfare of study participants, or do not involve increased risk, or significant changes in the study procedures
- New or revised recruitment advertisements or scripts.

The IRB administrative office will request the clarifications or revisions from the investigator in writing. This request and the written response will be documented in the file. The IRB staff will review for completeness, the clarifications or documented changes when they are received. The clarifications are subsequently reviewed and approved by the IRB chair or another designee in a timely fashion.

When the convened IRB requests substantive clarifications or modifications regarding the protocol or informed consent documents that are directly relevant to the determinations required by the IRB for research under the 45 CFR 46.111, the convened IRB must review the revisions. The board will try to contact the investigator by phone and ask the investigator to come to the meeting for discussion or have a discussion by speaker phone. If the investigator is not available the board will defer review of the amendment and the modifications will be requested of the investigator by the IRB office in writing. The request and response will be documented in the file. The project will be re-reviewed with the written documented modifications at the next convened board meeting to determine approval status. The investigator may request to attend the meeting to discuss the study under review and answer questions or provide explanation. In addition, the board may request that the investigator attend the meeting to address concerns of the study.

Under expedited review, if the request for modifications or clarifications is of such magnitude that they are directly relevant to the determinations required by the reviewer under 45 CFR 46.111, the IRB staff will contact the investigator and request the

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modifications or clarifications in writing. The request and response will be documented in the file. The reviewer will re-review the amendment once the modifications have been made and determine approval status.

The reviewer may request specific revisions requiring simple concurrence by the investigator or minor modifications or clarifications as defined in this policy. These revisions may be processed administratively and reviewed by the Chair or other designee.

Under expedited review, if the investigator is unwilling to make requested modifications and/or the reviewer will not approve the amendment it will be placed on the agenda for the next full board meeting. The investigator will be made aware of this in writing and this will be documented in the file.

Amendment requirements

Proposed modifications to any study documents must be reviewed and receive IRB approval before they can be implemented

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 is to be performed.

Types of changes include, but are not limited to:

- amendment to the study protocol
- amendment to the informed consent document
- amendment to study personnel
- amendment to the investigator brochure or drug brochure
- amendment to the recruitment material, surveys, questionnaires, etc.
- amendment to change the study status (ie. Closed to enrollment)
- amendment to report the results of the interim analysis

Amendments may dictate that revisions be made to more than one project document. For example, a protocol amendment may impact 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 through the online eIRB system. One copy should be highlighted indicating the changes and the other copy should be clean.

Requests for amendments should include the following information:

- Study title
- IRB project number
- Principal Investigator
- Contact person (if other than Principal Investigator)
- Complete description of the proposed changes. If the amendment request pertains to the protocol, the protocol amendment summary and the actual amended protocol pages must be submitted. If the amendment changes to the protocol are extensive, a complete new protocol must be submitted with the changes incorporated. A

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detailed summary of the amendment changes from the sponsor should be submitted, if available. If the protocol changes are a result of significant new findings and/or impact current participants' willingness to continue to take part in a study, information must be provided to the participant and a copy submitted to the IRB for review.

Once approved by the IRB, the approval will be indicated on the original amendment request which will be returned to the Principal Investigator or contact person for inclusion into the study files. An electronic copy of all materials will be kept in the IRB administrative office files as documentation of the action taken.

Minor/administrative changes

The regulations allow for expedited review of minor/administrative 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, such as procedures that involve exposure to ionizing radiation.

Administrative changes include but are not limited to:

- Change in/addition to study personnel
- Change in Principal Investigator
- Change in current advertisement or request for additional advertisement.
 - Additional advertisement requests will be considered administrative if the method of advertisement/recruitment was previously approved in the application.
 - If a new type of advertisement/recruitment is requested, the request will be reviewed on an individual basis to determine if it merits a higher level of review, based on the allowable expeditable categories and/or the minor changes to previously approved projects outlined in this SOP.
 - National advertising/recruitment materials will be reviewed in relation to the local context. The IRB understands the difficulty in requesting revisions to national recruitment materials; therefore, if the IRB requests revisions which are unable to be resolved with the sponsor, then the national recruitment materials may be disapproved from being played in the local market. As with any amendment which may be disapproved, it will first be reviewed by the full board.
- Changes to improve the clarity of statements or to correct typographical errors provided the requested change does not alter the content or intent of the statement
- Minor changes requested by the IRB
- Closing to enrollment for planned interim analysis

Additional minor changes include but are not limited to:

- Request inclusion of activities that fall under the categories of allowable expedited review set forth in 45 CFR 46.110.
- Changes to minimal risk projects which do not significantly alter the risk/benefit ratio.

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- Changes in inclusion/exclusion criteria making the population pool smaller
- Changes in the inclusion/exclusion criteria which do not significantly increase the possible study population pool
- Changes in the recruitment/advertising methods which are intended to increase enrollment in approved subject categories and in the context of approved inclusion/exclusion criteria
- New or changes in study documents to be distributed to or seen by subjects such as surveys, questionnaires, brochures, etc. which are not significantly changed or do not change the content or meaning of the previously approved versions.
- Alterations in reimbursement/compensation amount or changes to compensation method that are not so great as to change the risk/benefit ratio. Any request to add/change compensation to a study must obtain approval from the Accounting Department prior to approval from the IRB.
- Increase in study visits to increase safety monitoring
- Changes in or removal of perceived risks that improve the risk:benefit ratio
- Extension of study enrollment phase

Minor/administrative 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 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.

The Board will be notified of any approved amendments with a listing in the attachment pages of the agenda of each monthly meeting.

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 at a meeting in which a majority of the members are present, with at least one nonscientific member present.

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. All materials relevant to the agenda will be available for each Board member at least 5 working days prior to the scheduled IRB meetings, and IRB members are expected to review all of the information. The primary reviewer will conduct an in-depth

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review of all documentation of the assigned amendment to ensure compliance with the applicable regulations. Other board members receive all submission information for each amendment and are expected to have a working knowledge of each project so that they are able to engage in a meaningful discussion about the amendment. The lay reviewer will present any concerns or questions noted from their review of the consent document, or other materials, focusing particular attention to documents that will be seen by the research subject. Also, any board member may indicate for discussion any issues they found during their review of all supplied documentation for review.

Examples of amendment requests considered to be major include:

- Changes in the inclusion/exclusion criteria or recruitment method which would significantly increase the possible study population pool
- Alterations in the dosage or route of administration of an administered drug
- Addition/deletion of study arms or phases
- New or significantly revised study documents to be distributed to or seen by subjects such as surveys, questionnaires, brochures, etc.
- Deletion of study procedures, visits, or procedures that may adversely impact study safety
- Changes in radiation or biosafety
- Any new risks or an increase in severity or frequency of a risk*

* All new enrollment must halt until the board has reviewed and approved the amendment unless the modified risk information represents a minor alteration of the risk such as a clarification.

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

If disapproval of the amendment request is imminent, the Principal Investigator will be contacted to appear before the board to answer any questions the Board may have. If the amendment is disapproved the Principal Investigator will be notified in writing. The letter will include the reason(s) for disapproval and recommendations, if any, on how to proceed in an attempt to have the amendment approved. The investigator will be given the opportunity to respond. (see appeals policy)

The reviewer/Board always has the option to request revision of the informed consent or other study documents if, in their opinion, the amendment request impacts the study in such a way as to necessitate a revision.

Additional Review Requirements

Several other reviews are necessary for studies involving devices, drugs, conflict of interest, and radiation or biosafety. The description of requested amendment changes will allow the IRB office to determine whether additional reviews are needed. Most of

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the additional reviews will be required prior to IRB granting approval of the amendment. In many cases, the reviews take place prior to the amendment being reviewed by the full board; however, some reviews may take place after the IRB has conducted their review. Rarely is it necessary to prolong an approval for an amendment due to an additional review, however, it can occur. Documentation of each additional review will be entered into the eIRB database. Please refer to the individual SOPs for each type of review for additional information or requirements. Procedures for obtaining Accounting Services approval for research participant compensation are available at:

<http://www.missouri.edu/%7Emuacct/BPPM%20Research%20Participant%20Compensation.htm>

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