

University of Kentucky Office of Research Integrity and Institutional Review Board Standard Operating Procedures			
Revision #9	TITLE: Modification, Deviations, and Exceptions - IRB Review of Changes		Page 1 of 5
Approved By: ORI Director	Signature	Date	Date First Effective: 05-15-05
Approved By: Nonmedical IRB Chair	Signature	Date	
Approved By: Medical IRB Chair	Signature	Date	Revision Date: 12-15-17

OBJECTIVE

To describe the policies and procedures for reviewing a modification or a deviation/exception to a previously approved protocol

GENERAL DESCRIPTION

Investigators may not initiate any changes in research procedures or consent/assent form(s) without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to the subject. Examples of modifications that require IRB review include, but are not limited to, changes in:

- Study personnel removal/replacement;
- Advertising materials (flyers, radio spots, etc.);
- Research procedures;
- Subject populations (e.g., age range);
- Location where research will be conducted;
- Consent/assent forms;
- Recruitment procedures; or
- Date for completion of study.

If the investigator makes protocol changes (i.e., modifications, exceptions or deviations) to eliminate apparent hazards to the subject(s) without prior IRB approval, the investigator must immediately report the changes to the IRB for review and a determination as to whether the changes are consistent with the subject's continued welfare. (See Protocol Violations SOP)

Investigators must promptly notify the IRB in writing of any change in a protocol's status, such as discontinuation or completion of a study. See the Continuation Review SOP and the Study Closure SOP for procedures on reporting an activity status change to the IRB.

University of Kentucky Office of Research Integrity and Institutional Review Board Standard Operating Procedures		
Revision #9	TITLE: Modification, Deviations, and Exceptions - IRB Review of Changes	Page 2 of 5

Definitions

Modifications are defined as changes that impact the overall protocol.

Exceptions or *deviations* are changes that impact individual subjects and do not change the overall protocol. Investigators may not initiate these changes without prior IRB review and approval, except where necessary to eliminate apparent hazards to the subject.

The IRB considers enrollment of a research subject in a protocol that fails to meet current IRB approved protocol inclusion criteria or falls under protocol exclusion criteria to be a protocol *exception*.

The IRB considers a departure from the current IRB approved procedures that impact an individual subject to be a protocol *deviation*.

RESPONSIBILITY

Execution of SOP: Principal Investigators (PI)/Study Personnel (SP), IRB Chair, IRB, Office of Research Integrity (ORI) Staff, ORI Research Privacy Specialist

PROCEDURES

Submission of Modifications, Deviations, and Exceptions

1. The PI is responsible for submitting a modification request (MR) or deviation/exception request prior to the implementation of any change.
2. The PI makes relevant changes to IRB application and provides documents associated with the MR.

Screening of Submissions and Approval of Administrative Changes

1. The ORI staff member for the applicable IRB team screens the MR.
2. If the request is incomplete, ORI Staff requests additional information from the PI. ORI staff assigns the MR to the IRB reviewer(s) once the MR is complete.
3. If the modification references a medical instrument, apparatus, reagent, machine, implement or device, ORI staff consults applicable sources to determine if the modification involves testing a medical device under FDA jurisdiction (i.e., collecting safety or efficacy data). If so, ORI staff screens the application to ensure the PI has provided all relevant materials,

University of Kentucky Office of Research Integrity and Institutional Review Board Standard Operating Procedures		
Revision #9	TITLE: Modification, Deviations, and Exceptions - IRB Review of Changes	Page 3 of 5

(e.g., device labeling, indications, risk justification), and included FDA language in the informed consent and HIPAA.

4. If the modification references a drug, biologic, therapeutic dietary supplement, substance affecting structure or function of the body, or product intended to diagnose, cure, mitigate, treat, or prevent disease; ORI staff consults applicable sources to determine if the modification involves use of or testing under FDA jurisdiction. If so, ORI staff screens the application to ensure the PI has provided all relevant materials (e.g., product labeling, investigator brochure) and included FDA language in the informed consent and HIPAA.
5. If the modification adds vulnerable populations or requires documentation of specific regulatory findings, ORI staff screens the application to ensure relevant materials are available for the IRBs review.
6. Depending on the requested change, ORI staff may also secure additional review (i.e., prisoner representative). The reviewer is responsible for applying the applicable regulatory requirements.
7. If the MR requires consent/assent form changes, ORI staff screens the documents for apparent issues (e.g., absence of ORI's toll-free number, unapproved versions). ORI staff alerts the IRB reviewer regarding omissions or inconsistencies. The IRB has final authority for requiring consent/assent changes.
8. If the MR includes additions to study personnel, ORI staff screens to ensure that all new SP have completed required human subject protections training. If not, ORI staff informs the PI that he/she may not add the untrained SP until they have completed required training. ORI staff asks the PI whether he/she wishes to remove the SP in question and continue with the MR. Alternately, the PI may choose to wait until the SP in question complete the training.
9. If the MR adds study personnel without removing or replacing personnel, ORI staff may approve as an administrative change as the IRB has made the initial determination that the number of staff is adequate and the credentials and/or described qualifications are representative of the appropriate expertise needed to conduct the study. If the MR includes removal or replacement of personnel, ORI staff assigns the MR to the IRB.
10. ORI staff screens for HIPAA concerns. If appropriate, ORI staff assigns the MR to the Research Privacy Specialist who reviews in accord with HIPAA in Research SOP.
11. ORI staff selects the IRB Chair or IRB member as the primary reviewer.

University of Kentucky Office of Research Integrity and Institutional Review Board Standard Operating Procedures		
Revision #9	TITLE: Modification, Deviations, and Exceptions - IRB Review of Changes	Page 4 of 5

Expedited Review Procedures

1. If the change is minor, the IRB Chair or IRB member conducts the review using expedited procedures. A minor change is one which makes no substantial alteration in:
 - The level of risk to subjects;
 - The research design or methodology;
 - The subject population;
 - Qualifications of the research team;
 - The facilities available to support the safe conduct of the research; or
 - Any other factor that would warrant review of the proposed changes by the convened IRB.
2. The IRB Chair or an experienced IRB member conducts the MR undergoing expedited review, using standard expedited review procedures. The expedited reviewer exercises all the authority of the IRB except the reviewer cannot disapprove the research. Listing of the item on an agenda for the convened IRB serves to advise the IRB of the expedited review.
3. The IRB Chair or designated IRB member is responsible for reviewing the proposed modification, determining whether the modified research continues to fulfill the criteria for IRB approval, and documenting his/her determinations on the Modification Reviewer Signature Page.

Full Review Procedures

1. If the IRB Chair or designated IRB member recommends full review, or if the sponsor or the PI specifically requests full review procedures, ORI staff places the MR on an agenda for full review following procedures outlined in the Initial Full Review SOP.
2. For an MR undergoing full review, ORI staff invites the PI to attend the convened meeting if the IRB so requires. The full IRB reviews the MR following procedures outlined in the Initial Full Review SOP and applies the federal criteria for approval as applicable to the request.
3. Approximately 5-10 days prior to the meeting, ORI staff closes the agenda. The Modification Request and the protocol materials affected by the proposed modification are available to the full board for review and determination as to whether the modified research continues to fulfill the criteria for approval.
4. For an MR undergoing full review, the IRB Chair or designated IRB member serves as the primary reviewer.

University of Kentucky Office of Research Integrity and Institutional Review Board Standard Operating Procedures		
Revision #9	TITLE: Modification, Deviations, and Exceptions - IRB Review of Changes	Page 5 of 5

5. The IRB Chair or designated IRB member reports recommendations to the IRB at a convened meeting. The IRB Chair or designated IRB member makes recommendations on issues he/she determines do not meet the federal criteria for approval, involve controverted issues, or need additional information. If the IRB Chair or designated IRB member is unable to attend the meeting, ORI staff provides his/her written comments or recommendations to the IRB at the convened meeting.
6. The Full IRB Reviews and votes on the MR consistent with procedures outlined in the Initial Full Review SOP.
7. The IRB chair or designated IRB member, documents the IRB determination on the Modification Reviewer Signature Page.

Review Outcome(s)

1. ORI staff notifies the PI in writing of the IRB's decision following procedures outlined in the Initial Full and Initial Expedited Review SOP.
2. If the IRB approves the modification, the end date of the approval period remains the same as that assigned at initial or continuation review.
3. If the PI has concerns regarding the IRB decision/recommendations for changes in the study, he/she may submit his/her concerns via a written appeal that includes justification for changing the IRB decision. The PI sends the request to the ORI. The expedited reviewer, IRB Chair, or convened IRB review the appeal. The appeal determination is final.

REFERENCES

21 CFR 56.110(b)(2)
45 CFR 46.110(b)(2)
45 CFR 46.111
21 CFR 56.111