University of Kentucky Office of Research Integrity and Institutional Review Board Standard Operating Procedures			
SOP #2-5 Revision #8	**TITLE: Modification, Deviations, and Exceptions - IRB Review of Changes**		**Page 1 of 7**
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: 03-29-13

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;
- 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.

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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 Administrative Assistant (AA), ORI Professional Associate (PA), 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 using the Modification Request Form or the equivalent paperwork prior to the implementation of any change.

2. To submit the request, the PI completes the Modification Request Form according to the instructions on the form and submits the form to the ORI.

Screening of Submissions

1. The ORI staff member receiving an MR forwards the request to the appropriate AA, as determined by the protocol's IRB number. The AA then screens the MR form.

2. If the request is incomplete, the AA either returns the MR to the PI or requests additional information from the PI. The AA forwards the MR to the IRB reviewer once the MR is complete. ORI staff document who served as primary reviewer on the assigned line of the applicable reviewer form (i.e., Modification Reviewer Signature Page).

3. If the AA is unclear about what the MR entails, he/she discusses it with the appropriate PA.

4. If the modification references an instrument, apparatus, reagent, machine, implement or device, the AA discusses the modification with the PA to determine if the modification involves use of a medical device under FDA jurisdiction (collecting safety or efficacy data). If so, the PI includes FDA language in the informed consent and HIPAA documents and submits the device form and/or applicable information for the IRBs review and regulatory determinations.

5. 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, the AA discusses the modification with the PA to determine if the modification is under FDA jurisdiction (use beyond the course of medical practice). If so, the PI includes FDA language in the informed consent and HIPAA documents and submits the drug form and/or applicable information for the IRBs review and regulatory determinations.

6. If the modification adds vulnerable populations or requires documentation of specific regulatory findings, the AA sends the appropriate IRB forms to the reviewer with the MR. For example, if the PI adds children as subjects, the AA includes Form W in the MR and sends the UK IRB Policy on Children in Research document to the IRB reviewer.

7. Depending on the requested change, the AA may also secure additional review (i.e., prisoner representative). The IRB is responsible for applying the applicable regulatory requirements.

8. If the MR requires consent/assent form changes, the AA screens to ensure ORI's toll-free number appears on the form(s). PA staff may direct the AA to screen the consent/assent form(s) to reflect any recent changes in the IRB template. The AA alerts the IRB reviewer if the consent/assent form(s) are inconsistent with the template. The IRB has final authority for requiring consent/assent changes.

9. If the MR includes additions to study personnel, the AA screens to ensure that all new SP have completed required human subject protections training. If not, the AA informs the PI that he/she may not add the untrained SP until they have completed required training. The AA 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. In that case, the AA forwards the MR to the IRB after SP training is complete.

10. The AA screens for HIPAA concerns. If appropriate, the AA forwards the MR to the Research Privacy Specialist who reviews in accord with HIPAA in Research SOP.

11. If the protocol is currently undergoing Continuation Review (CR), the AA gives the MR to the appropriate PA. If appropriate, the PA incorporates the MR into the CR. If it is not appropriate, the PA returns the MR to the AA. The AA then processes the MR independent of the CR.

12. If the PI submits the modification with a CR application, the PA processes the modification as part of the CR (i.e., amendments) as outlined in the Continuation Review SOP.

Determining Mechanism of Review (i.e., Expedited vs. Full Review)

1. If the sponsor or the PI specifically requests full review procedures, the AA places the MR on an agenda for full review following procedures outlined in the Initial Full Review SOP.

2. If PI/sponsor does not request a full review, the AA sends the Modification Request Form with attachments and the Modification Reviewer Signature Page to the IRB Chair or, if he/she is not available, to a voting member of the IRB.

3. If the modification involves changes in consent/assent forms, the AA forwards the highlighted version of the forms to the IRB Chair or IRB member. The clean, unmarked copies of the consent/assent forms remain in the ORI.

4. The IRB Chair or IRB member documents his/her determination regarding whether the IRB can review the request using expedited or full review procedures on the Modification Reviewer Signature Page. 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.

Expedited/Full Review Procedures

1. The IRB Chair or an experienced IRB member designated by the IRB Chair 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. The listing of the item on an agenda for the convened IRB serves to advise the IRB of the expedited review.

2. The IRB Chair or designated IRB member documents on the Modification Reviewer Signature Page his/her determinations regarding:

    - Eligibility for expedited review;
    - Whether the research meets the criteria for IRB approval (criteria for approval checklist is part of the Signature Page);
    - Whether proposed changes to the informed consent/assent process continue to meet requirements as set forth in 45 CFR 46.116 and 117, and 21 CFR 50.25; and
    - Whether the proposed modification affects any research categories of the currently approved protocol.

3. The IRB Chair or designated IRB member returns the Modification Request Form and Modification Reviewer Signature Page to the ORI. The ORI staff member who receives the returned materials routes them to the appropriate AA.

4. If the IRB Chair or designated IRB member recommends full review, the AA places the MR on an agenda following procedures outlined in the Initial Full Review SOP.

5. For an MR undergoing full review, the AA invites (e.g., phone call or e-mail) the PI to attend if the IRB requires that he/she attend the meeting. The full IRB reviews the MR following procedures outlined in the Initial Full Review SOP and applying the federal criteria for approval as applicable to the request.

6. For an MR undergoing full review, the IRB Chair or designated IRB member serves as the primary reviewer.

    - Approximately 5-10 days prior to the convened meeting, the AA sends the IRB Chair or designated IRB member the Modification Request Form, a Modification Reviewer Signature Page, and the protocol materials affected by the proposed modification (e.g., revised consent/assent or revised investigator brochure). The AA makes the complete IRB protocol file available to the reviewer and takes the file to the convened meeting.
    - 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.

- 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, the AA provides his/her written comments or recommendations to the IRB at the convened meeting.

- Approximately 5-10 days prior to the meeting, the AA sends the IRB members scheduled to attend the meeting the Modification Request Form and the protocol materials affected by the proposed modification in sufficient detail to enable a determination as to whether the modified research continues to fulfill the criteria for approval.

Review Outcome(s)

1. For expedited review, the outcomes of review are the same as the options outlined in the Initial Expedited Review SOP. The ORI staff notifies the PI in writing of the IRB's decision following procedures outlined in the Initial Expedited Review SOP.

2. For full review, the outcomes of review are the same as the options outlined in the Initial Full Review SOP. The ORI staff notifies the PI in writing of the IRB's decision following procedures outlined in the Initial Full Review SOP.

3. If the IRB Chair or designated IRB member approves an MR via email without having received an MR form, the AA notifies the PI following the Initial Review SOP. In addition, the AA sends the Modification Reviewer Signature Page along with a printout of the approval message to the IRB Chair or designated IRB member who then completes and signs the form and returns it to the ORI. The ORI staff member who receives the returned materials routes them to the appropriate AA. The AA adds the email and completed/signed Modification Reviewer Signature Page to the protocol file.

4. If the IRB approves the modification, the end date of the approval period remains the same as that assigned at initial or continuation review.

5. If an MR is part of a CR, ORI staff who prepare the correspondence incorporate written notification of IRB approval or disapproval of the MR into the IRB CR approval/disapproval letter.

6. If the PI has concerns regarding the IRB’s decision, the PI may submit his/her concerns to the IRB in a written document that includes a justification for changing the IRB’s decision.

7. For inclusion in the IRB files, the AA staples and files as one action the Modification Request Form, Modification Reviewer Signature Page and supporting documents, including as appropriate a clean copy of the stamped consent/assent forms.

REFERENCES

21 CFR 56.110(b)(2)
38 CFR 16.110(b)(2)
45 CFR 46.110(b)(2)
38 CFR 16.111
45 CFR 46.111
21 CFR 56.111
21 CFR 312
21 CFR 812