University of Kentucky Office of Research Integrity and Institutional Review Board Standard Operating Procedures			
Revision #11	**TITLE: Modification - IRB Review of Changes**		**Page 1 of 6**
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: 05-14-2023

OBJECTIVE

To describe the policies and procedures for reviewing a modification 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 and implements protocol changes without prior IRB approval in order to eliminate apparent hazards to the subject(s), the investigator must immediately report the changes to the IRB. The IRB will review the changes and make 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 protocol status, such as suspension, 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.) Change in status includes any suspension or pause in research activities due to test article availability lasting longer than two weeks.

Definition

Modifications are defined as changes that impact the overall protocol.

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

1. The PI is responsible for submitting a modification request (MR) to the ORI prior to the implementation of any change.

2. The PI updates/alters the sections of the IRB application as applicable.

3. An MR must include all approved documents unless the document is being updated as part of the MR. In this case, the PI deletes the currently approved version of the document and attaches the updated document along with a highlighted/tracked changes version of the updated document.

   Please note: Modifications can be requested within a continuation review (CR) submission. A PI cannot submit a separate MR and CR simultaneously.

Screening of Submissions

1. ORI staff screen the MR for completeness and accuracy. ORI staff request additional information from the PI as necessary.

2. If UK is the reviewing IRB for a reliance study, ORI staff contact the Reliance Team to determine if the proposed changes conflict with the reliance agreement/communication plan and/or local context form.

3. ORI staff determine if the modification involves use of a medical device under FDA jurisdiction (i.e., collecting safety or efficacy data), if the requested changes reference an instrument, apparatus, reagent, machine, implement and/or device. If so, ORI staff screen the application to ensure the PI has provided all relevant materials (e.g., device labeling, indications, risk justification), and included FDA language in the informed consent and HIPAA authorization.

4. ORI staff consult applicable sources to determine if the modification involves use of or testing of products under FDA jurisdiction (i.e., use beyond the course of medical practice) if the requested change references a drug, biologic, therapeutic dietary supplement, substance affecting structure or function of the body, and/or product intended to diagnose, cure, mitigate, treat, or prevent disease. If so, ORI staff ensure the PI has provided all relevant materials (e.g., product labeling, investigator brochure) and included FDA language in the informed consent and HIPAA authorization.

5. ORI staff ensure relevant materials are available for IRB review as needed if the modification adds vulnerable populations or requires documentation of specific regulatory findings.

6. ORI staff may also secure additional review (i.e., prisoner representative) depending on the nature of the requested change, if applicable. The IRB reviewer in such cases is responsible for applying the relevant regulatory requirements or ethical principles.

7. ORI staff screen changes to consent/assent forms for apparent issues (e.g., absence of ORI's toll-free number, use of incorrect/unapproved versions). ORI staff alert the IRB reviewer of any omissions or inconsistencies. The IRB has final authority for requiring consent/assent changes.

8. ORI staff screen changes to study personnel (SP) to ensure that all new SP have completed the required human subject protection training. If SP have not completed the required training, ORI staff inform the PI that the request cannot be approved by the IRB until the required training has been completed. ORI staff ask the PI whether they wish to remove the SP in question from the MR. Alternately, the PI may choose to wait for approval until the SP in question complete the training. In that case, ORI staff assigns the MR to the IRB after SP training is complete.

9. ORI staff select the IRB Chair or other IRB member as the primary reviewer.

10. ORI staff screen for compliance with HIPAA regulatory requirements. ORI staff assign the MR to the Research Privacy Specialist (RPS) to review the submission in accordance with the HIPAA in Research SOP when applicable.

Administrative Review Procedures

1. ORI staff may approve an MR submission as an administrative change if the request only involves adding study personnel, without removing or replacing other personnel, or making any other changes to the protocol, since the IRB made the initial determination that the number of staff listed on the study is adequate and the credentials and/or described qualifications are representative of the appropriate expertise needed to conduct the study.

2. For exempt review protocols, ORI staff approve an MR submission as an administrative change if the edit that is clear and straightforward. This includes, for example:
   - adding study personnel, without removing or replacing other personnel, since the IRB made the initial determination that the number of staff listed on the study is adequate and the credentials and/or described qualifications are representative of the appropriate expertise needed to conduct the study;
   - directive requested revisions made in response to the IRB's review;
   - addition of a letter of support from a non-UK research site (if site addition was reviewed by reliance);
   - addition or minor modifications to recruitment materials, advertisements;
   - changes to study duration or schedule, (e.g., extending end date of study, adding an additional semester of the same data collection activities);
   - minor changes to study population in non-therapeutic studies (e.g., raising inclusion criteria from age 20 to 30);
   - small changes to incentives (e.g., $25 instead of $15 gift card); and
   - minor changes to data collection instruments in non-limited review protocols.

   Minor changes are limited to directive revisions such as grammatical edits, new dates, expanding a Likert scale, clarifying an item, or adding questions that would not change the subject matter or overall time commitment. Revisions that are substantive, ambiguous, open-ended, or involve sensitive topics are not minor.

Expedited Review Procedures

1. The IRB Chair or designated IRB member conducts an MR review using expedited procedures if the requested changes are minor. 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 designated IRB member reviews 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 or research activity. The listing of the expedited review 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 to determine whether the modified research continues to fulfill the criteria for IRB approval, and documents their determination on the Modification Reviewer Signature Page.

Full Review Procedures

1. ORI staff place an MR on an agenda for a convened meeting, following procedures outlined in the Initial Full Review SOP, when the MR involves more than just minor changes, an IRB Chair or designated IRB member recommends full review, or the sponsor or PI specifically request full review procedures.

2. ORI staff invite the PI to attend the meeting if the IRB requires that they attend. 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 close the agenda. The MR and the protocol materials affected by the proposed modification become available to the full board for review.

4. The IRB Chair or designated IRB member who serve as the primary reviewer reports recommendations to the IRB at the convened meeting. The IRB Chair or designated IRB member makes recommendations on issues they determine 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, written comments or recommendations are provided to the IRB at the convened meeting.

5. The convened IRB reviews and votes on the MR consistent with procedure outlined in the Initial Full Review SOP. The IRB Chair or designated IRB member documents the IRB determination on the Modification Reviewer Signature Page.

Review Outcome(s)

1. ORI staff notify the PI of the IRB's decision following the procedures in the Initial Full and Initial Expedited Review SOP.

2. The end date of the protocol approval period remains the same as that assigned during initial or continuation review when the IRB approves a modification.

3. If the PI has concerns regarding the IRB decision/recommendations for changes in the study, they may submit their 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
21 CFR 312
21 CFR 812