

	Modification to an Approved Protocol			
	P & P	VERSION DATE	REPLACES P & P	PREVIOUS VERSION DATE
	3.03	02.11.2020	3.03	11.22.2019

I. INTRODUCTION

IRB review is an ongoing process. Federal regulations require that IRBs have written procedures for ensuring prompt reporting to the IRB of any modifications to approved research and for ensuring that such changes are not implemented without prior IRB approval, except when necessary to eliminate apparent immediate hazards to subjects. Implementation of any changes to a protocol without IRB approval will be considered to be non-compliance with the policy herein.

A. Modifications Requiring IRB Review and Approval

Examples of modifications that must be submitted for review include, but are not limited to, changes in:

- Study Personnel
- Subject population and enrollment numbers
- Duration of study
- Recruitment methods
- Consent/assent form
- Investigator Brochure or device information
- Study design, methods, procedures, or randomization
- Adding or dropping an arm of the study
- Questionnaires, surveys, interview scripts, advertising
- Source of funding
- Data and Safety Monitoring plan
- Location where research will be conducted
- Any change that effects a criterion for approval of research

B. Changes Necessary to Eliminate Apparent Immediate Hazards to the Subject

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 report the changes to the IRB within 30 days as a modification request. The IRB will review the changes and make a determination as to whether the changes are consistent with the subject's continued welfare.

C. Modifications to Exempt Research

In contrast to studies initially approved by the expedited procedure or at a convened full Board meeting, some modifications to exempt research do not require IRB approval prior to implementation. Minor (non-substantive) modifications to exempt studies do not require review and approval unless the modification may change the study's eligibility for exemption. Substantive modifications that have the potential to change the nature of the research and, therefore, the study's eligibility for exemption, require

review and approval prior to implementation of the modification. Examples of non-substantive vs. substantive changes specific to exempt studies are provided below.

Non-substantive Changes to Exempt Research	Substantive Changes to Exempt Research
<ul style="list-style-type: none"> • Editorial changes that clarify but do not alter the existing meaning of a document: <ul style="list-style-type: none"> ○ grammatical correction ○ wordsmithing ○ addition of clarifying questions ○ addition of questions very similar to existing questions ○ deletion of questions • Increasing or decreasing the number of subjects • Insignificant revisions to recruitment materials and methods. <ul style="list-style-type: none"> ○ change to the phone number ○ addition of a newspaper ad when using similar language as in a current flyer 	<ul style="list-style-type: none"> • Change in Principal Investigator (PI) • Change in risk/benefit ratio <ul style="list-style-type: none"> ○ Adding sensitive questions about a subject’s behavior to a survey/interview • Addition of activities that disqualify the research from exemption • Change in study population • Change in federal funding • Change in study purpose or procedures

D. Modifications to Research Approved by an External IRB

The current policy is applicable to research approved by the LSUHSC-NO IRB and not for modification to research in which an external IRB serves as the IRB of record.

II. RESPONSIBILITY

Execution of P&P: Investigator/Principal Investigator (PI), IRB Chair or Designee, IRB Vice-Chair, IRB, Designated Reviewer, IRB Specialist, IRB Staff.

IRB Specialists are regular or alternate members of the IRB; those that have, in the judgment of the Chair, sufficient experience in the review of protocols, may function as Designated Reviewers for modifications evaluated by the expedited procedures.

III. POLICY

A. All changes to currently approved research must be approved by the IRB prior to implementation, except when necessary to eliminate apparent immediate hazards to the human subjects or if the change is a minor modification to an exempt study. This requirement is applicable to the following studies approved by the LSUHSC-NO IRB:

- All full board-approved studies,
- All studies initially approved by the expedited procedure, and

- Exempt studies for which the proposed changes are substantive as defined above.
- B.** Minor changes to applicable research may be reviewed by expedited review procedures. Additionally, changes to protocols previously approved by the expedited review procedures also may be reviewed under the expedited review procedures. Modifications that render a research study ineligible for expedited review under the applicable regulatory categories will be reviewed by the full Board.
- C.** The criteria for approval of changes to previously approved research are the same as those for initial review. The IRB must determine that, in light of the proposed changes, the research continues to satisfy 45 CFR 46.111 and/or 21 CFR 56.111, as applicable.

IV. PROCEDURES

A. Submitting a Modification to the IRB for Review

1. All proposed modifications to approved studies are submitted via the Modification process in the IRBManager electronic system.
2. Investigator provides the IRB with complete descriptions of the modifications, including the rationale(s) for the modifications and the anticipated impact upon current and future subjects.
3. A complete submission include, as attachment(s), a track changes and clean copy of any revised versions of those study documents affected by the modification(s). This could include modifications to the protocol, informed consent, or HIPAA authorizations. Copies of any new study documents must also be attached.
4. The Principal Investigator electronically signs the modification request if he/she is not the individual submitting the request.

B. Initial Review and Level of Review

1. IRB Office Staff reviews submission for accuracy and completeness. As appropriate, IRB Staff request additional information, require revisions, or determine that the submission does not meet the definition of a “modification”.
2. If the proposed modification includes addition of new personnel or a change in PI, IRB Staff verifies completion of education and disclosure requirements. If these requirements have not been met, IRB staff will facilitate assignment of courses, if necessary, and inform the investigator of deficiencies.
3. IRB staff forwards the submission to an IRB Specialist once the application is deemed to be complete (other than any temporary deficiencies in required training), accurate, and ready for IRB review.
4. The IRB Specialist reviews the proposed modification to determine if the change is appropriate for expedited review procedures or if it requires full Board review as prescribed by federal regulations and the policies detailed in the present document.

When necessary, the Specialist consults with the IRB Chair or Vice-Chair in making this decision.

- a) The IRB Specialist makes the determination to use expedited review procedures if the requested changes are **minor** based on the definition below.

*A **minor** change is one that makes no substantial alteration in:*

- *The level of risk to subjects;*
- *The research design and 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.*

Examples of minor modifications include, but are not limited to, addition of a performance site, changes in the number of subjects, modifications to surveys/questionnaires that do not increase risk level.

The IRB Chair has discretion to forward such changes to the full Board for review if appropriate.

- b) The IRB Specialist makes the determination to submit the application for full Board review if the modifications represent more than minor or significant changes.

Examples of significant modifications include addition of new risk information, change to drugs used in the protocol, changes in the study design, or change in PI of a greater-than-minimal-risk study. In general, these changes would potentially affect the risk/benefit ratio as determined at initial review.

5. The IRB Specialist, in consultation with the IRB Chair if necessary, assigns the modification application for review to an IRB member as the Designated Reviewer based on the review level and his/her expertise.

C. Expedited Review Procedure

1. The Reviewer conducts the review using expedited procedures. He/She determines whether the research, in light of the proposed changes, continues to satisfy the applicable criteria for approval. This includes determining whether the proposed changes reflect new information that may relate to a subject's willingness to continue participation, thus warranting re-consent or notification of subjects.
2. The Reviewer may request additional information from the study team during his/her review. All requested information or revisions must be provided through the Modification application form in IRBManager.
3. The Reviewer exercises all the authority of the IRB except the Reviewer cannot disapprove the research.

4. The IRB Chair or Vice-Chair makes the final determination of whether or not the modified research continues to fulfill the criteria for IRB approval, and documents his/her determination in IRBManager. The PI is notified of this determination via a system generated e-mail.
5. Protocols approved by the expedited process are reported to the full Board at a convened meeting. Any Board member may request further consideration of any protocol approved by the expedited process.

D. Full Board Review Procedure

1. The Designated Reviewer evaluates the modification(s) application and associated documents for compliance with the 45 CFR 46.111 criteria for IRB approval of research.
2. IRB Staff make available electronic copies of the modification application and all associated documents to all IRB members at least one week before the scheduled IRB meeting. The Designated Reviewer or any IRB member may request additional information or documents which may be relevant for evaluation of the modification.
3. All IRB members are expected to review all modified documents in sufficient depth to discuss the information at the convened meeting.
4. The Designated Reviewer will enter his/her review comments and recommendation to the online application. The comments and recommendation are made available electronically to all IRB members at least 48 hours prior to the scheduled meeting.

E. IRB Convened Meeting

1. Each study modification is presented by the Designated Reviewer, or in the case of the Reviewer's absence, by the Chair or his/her designee. The Principal Investigator or another study investigator are present if requested by any Board member or if the Chair thinks the investigator needs to be present to clarify issues/concerns.
2. In evaluating the proposed modification, IRB members and staff consider OHRP, FDA and, as relevant, VA regulatory criteria. If the IRB determines that the information presented in the modification application and associated documents would affect a participant's willingness to continue participation, the IRB will request the Principal Investigator contact and re-consent the participants.
3. When the modification is the result of an immediate change initiated without IRB approval in order to eliminate apparent immediate hazards to participants, the IRB will review the facts surrounding the hazard in order to determine that the benefits of such change outweighed the risks inherent in instituting such change without IRB approval and that the change was consistent with ensuring the participants' continued welfare. An example would be the Principal Investigator reading a scholarly scientific article reporting the deleterious effects of a drug dose, which, had not been previously reported.

4. Each modification application will be discussed and voted on individually.
5. The Board may approve, require further modifications to secure approval, defer, or disapprove a modification to a study.
6. A determination of deferral or disapproval warrants substantive revisions to the application. The revised application must be reviewed by the full Board procedure at a future convened meeting.
7. If the Board requests minor changes that do not substantially impact the risk/benefit analysis, the Board may approve the modification contingent on final review and approval by the Chair or the Chair's Designee.
8. Final review and approval of Board-requested changes to study documents also may be deferred to the Chair or Chair's Designee.
9. Approval of a modification to a study does not result in a change to the approval period for the study.
10. If a modification request is not discussed at the convened meeting due to a lack of quorum or other unforeseen circumstances, the request will be discussed at the next convened meeting.

F. IRB Administration Responsibilities Post-Meeting

1. If the modification is approved at the meeting, the IRB Staff forwards the application to the Chair or Vice-Chair for documentation of the Board's decision in the electronic system, which transmits the approval to the Principal Investigator.
2. If applicable, the new version of the informed consent/HIPAA authorization is date stamped with the modification approval date. A new version of the revised informed consent/HIPAA authorization document, with an original IRB approval stamp, is released to the study contact. The previously approved version becomes "obsolete".
3. For modifications in which the Board has approved contingent upon completion of requested minor changes which do not substantially impact the risk/benefit analysis, the IRB Staff will notify the study contact electronically of any required changes. When revisions are received in the electronic system, they will be reviewed and if acceptable, the approval will be released.
4. If modifications are substantive in nature or if the Board defers or disapproves the modification request, the IRB Staff/Chair will notify the study contact in writing outlining the Board's requirements. Any revised application submitted by the investigator will be reviewed by the full Board procedure at a future convened meeting.

V. REFERENCES

- [21 CFR 56.110: Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.](#)

- [21 CFR 56.111: Criteria for IRB approval of research.](#)
- [45 CFR 46.110: Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.](#)
- [45 CFR 46.111: Criteria for IRB approval of research.](#)