

 Office of Research Integrity - Human Subjects			SOP #: ORI(HS)- 5.08
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Approved By: ORI Executive Director	*Signature on File	Date:	Date First Effective: 11/12/2013
Approved by: Biomedical Chair	*Signature on File	Date:	
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SOP 5.08 – Modifications, Deviations, and Exceptions

1. Objective

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

2. General Description

Investigators may not initiate any changes in research procedures or consent/assent processes or 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 procedures or forms;
- Recruitment procedures; or
- Premature completion of the 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.

Definitions

Modification - is any change to an IRB-approved study protocol, regardless of the initial level of review (Excluded, Exempt, Expedited, or Full Board).

Deviation - is any departure from the approved protocol for a human subject (subject) once the subject has actually been enrolled in the study. This typically occurs for a single subject.

Exception - is the enrollment of a research subject in a protocol who fails to meet specified protocol inclusion criteria, or falls under specified protocol exclusion criteria.

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Violation - Deviations and/or exceptions to IRB approved protocols must be reviewed and approved prior to their implementation. If either a protocol deviation or protocol exception occurs without prior IRB review and approval, the event is considered a protocol violation. For reporting a protocol violation, the PI must submit a summary report to the IRB for review (See SOP 11.01). Modifications made without prior review and approval may constitute noncompliance with UNLV Policy on Research Involving Human Subjects, or applicable UNLV Rules and Procedures for Conducting Human Subject Research.

3. Roles & Responsibilities

Execution of SOP: Principal Investigators (PI)/Study Personnel (SP), IRB Chair, IRB, Office of Research Integrity – Human Subjects (ORI-HS) Staff

4. Procedures

Submission of Modifications, Deviations, and Exceptions

1. The PI is responsible for submitting a modification request (MR) using the Modification Request Form and acquiring approval prior to the implementation of any change.
2. To submit the request, the PI completes the MR form and submits the form accompanied by all proposed alterations in relevant study documents and/or proposed additional study documents (i.e. protocol proposal form, informed consent form) to the ORI-HS. The MR form should be used whether the requested change is a modification, a deviation, or an exception.

Screening of Submissions

1. The ORI-HS staff member receiving a MR form reviews the submission. The ORI-HS staff member receiving an MR assigns the request to the appropriate administrative reviewer.
2. If the MR is incomplete, the administrative reviewer either returns the MR to the PI or requests additional information from the PI. If the MR is complete, the administrative reviewer forwards the MR and associated documents to the IRB reviewer.
3. Depending on the requested change, the administrative reviewer may also secure additional review (i.e., prisoner representative). The IRB is responsible for applying the applicable regulatory requirements.

Determining Mechanism of Review (Expedited vs. Full Review)

1. The IRB Chair or IRB member documents his/her determination regarding whether the IRB will review the request using expedited or full review procedures. Modification to a study previously determined to be exempt may follow a different process; see SOP 5.04 for additional information. 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.

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Excluded Review Procedures

1. If changes occur to previously Excluded activities, the researcher is responsible for consulting with ORI-HS to ascertain whether additional protocol submissions may be needed.

Exempt Review Procedures

1. Procedures for conducting review of modifications to research previously determined to be exempt are discussed in SOP 5.04.

Expedited/Full Board Review Procedures

1. The IRB Chair/Co-Chair or an experienced IRB member designated by the IRB Chair conducts expedited review of the MR using standard expedited review procedures and criteria. The expedited reviewer exercises all the authority of the IRB, except that the reviewer cannot disapprove the research changes. The listing of the item on an agenda report for the convened IRB serves to advise the IRB of the expedited review.
2. The IRB Chair or designated IRB member will consider:
 - Eligibility for expedited review;
 - Whether the research meets the criteria for IRB approval;
 - Whether proposed changes to the informed consent/assent process(es) continue to meet requirements as set forth in 45 CFR 46.116 and 117, and/or 21 CFR 50.25;
 - Whether there are any significant new findings that arise from the review process and that might relate to participants' willingness to continue participation are provided to participants; and
 - Whether the proposed modification affects the status of the previously determined federal research category.
3. The IRB Chair or designated IRB member sends their review comments to the ORI-HS. The ORI-HS staff member who receives the returned materials routes them to the appropriate administrative reviewer.
4. If the IRB Chair or designated IRB member recommends full review, the administrative reviewer places the MR on an agenda following procedures outlined in the Full Board Review SOP 5.06.
5. The full IRB reviews the MR following procedures outlined in the Full Board Review SOP 5.06 and applying the federal criteria for approval as applicable to the request.
6.] The IRB Chair or IRB may procure, for the purposes of providing expertise or special knowledge surrounding a topic or issue of concern, an outside consultant(s) to advise an IRB review of a protocol or IRB related request. An IRB members' CV or comprehensive IRB roster is used to assess for scientific and scholarly knowledge and expertise; knowledge or expertise involving specific populations; and organizational affiliation of IRB members when deciding if additional expertise/consultant will be needed to review the protocols. The consultant will be approached by the IRB chair/co-chair or ORI-HS staff to assess their willingness to serve as a consultant. The consultant will serve in an advisory role only, is not a voting member of the IRB and will not be counted toward quorum. The consultant will receive relevant study materials. They will then provide their assessment at the meeting or via a written document to be considered at the meeting. Any consultant(s) will be free of conflict of interest and will be asked to provide acknowledgment that the review of study or study related materials are of a private

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nature, and that confidentiality of any shared information will be maintained. If a consultant is not available, the protocol may be postponed pending inclusion of this consultant.

Review Outcomes

1. For expedited review, possible outcomes of review are the same as the options outlined in the Expedited Review SOP 5.05. The ORI-HS staff notifies the PI in writing of the IRB's decision following procedures outlined in the Initial Expedited Review SOP 5.05.
2. For full board review, possible outcomes of review are the same as the options outlined in the Full Board Review SOP 5.06. The ORI-HS staff notifies the PI in writing of the IRB's decision following procedures outlined in the Full Board Review SOP 5.06.
3. If the IRB approves the modification, the end date of the approval period remains the same as that assigned during initial or most recent continuing review.
4. If the PI expresses concerns regarding the IRB's decision about the MR, the PI may submit his/her concerns to the IRB in a written document that includes a justification for appealing the IRB's decision.
5. All IRB findings are documented in the IRBNet system where the UNLV Office of Research Integrity (ORI) Executive Director and Associate Vice President of Research have access and may review as needed. Other UNLV officials may contact the UNLV ORI Executive Director for more information.

5. References

45 CFR 46.110(b)(2)

45 CFR 46.111

45 CFR 46.116

45 CFR 46.117

21 CFR 50.25

UNLV Rules and Procedures for Conducting Human Subject Research, 4.1. 5.4.2

UNLV ORI-HS SOP 5.05, 5.05, 5.06, 11.01