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|  Office of Research Integrity - Human Subjects | | | SOP #: ORI(HS)- 5.10 |
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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: | |
| Approved by: Social Behavioral Chair | *Signature on file | Date: | Revision Date: 01/21/2019 |

SOP 5.10 - Continuing Review and Project Completion

1. Objective

To describe the procedures for conducting continuing review (CR) of previously approved protocols.

2. General Description

The Institutional Review Board (IRB) conducts substantive and meaningful CR at intervals appropriate to the degree of risk and not less than once per year. The research protocol must satisfy the criteria set forth in 45 CFR 46.111 for the IRB to approve continuation of the study. Continuing review of research previously determined to be exempt follows a different process; see SOP 5.04 for additional information.

The IRB may use expedited review procedures for CR only under the following circumstances:

- The study was initially eligible and continues to be eligible for expedited review procedures; OR
- The research is permanently closed to the enrollment of new subjects, all subjects have completed all research-related interventions, and the research remains active only for long-term follow-up of subjects; OR
- Where study personnel have enrolled no subjects and no additional risks have been identified either at UNLV or at any study site if the research involves a multi-site study; OR
- The only remaining research activities are limited to data analysis (no interaction/contact with subjects); OR
- The research involves the study of drugs and/or medical devices AND either does not require an Investigational New Drug (IND) (21 CFR Part 312) and/or an Investigational Device Exemption (IDE) (21 CFR Part 812) and/or the device is approved for marketing and being used in accordance with the approved labeling. The IRB must also have determined and documented at a convened meeting that the research is no greater than minimal risk and no additional risks have been identified.

In accordance with federal requirements, the IRB approval period for studies reviewed by the convened IRB can extend no longer than one year after the start of the most recent approval period. The PI may not continue research after expiration of IRB approval; continuation of an expired study constitutes a violation of federal requirements specified in 45 CFR 46.103(a). If the IRB approval expires, the PI must cease all research activities and may not enroll new subjects in the study. However, if the IRB determines that there is an overriding safety concern and/or ethical issue or that it is in the best interests of the individual subjects to continue participating in the research activities,

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the IRB may permit the subjects to continue in the study for the time required to complete the CR process.

3. Roles & Responsibilities

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

The PI must submit continuing review reports for studies as long as the research:

- Remains open to enroll new subjects;
- Remains active for long-term follow-up (even when the research is permanently closed to enrollment and all subjects have completed all research-related interventions); and/or
- Requires analysis of data where data remains individually identifiable.

4. Procedures

CR Requests, Submissions, and Screening

1. Using forms and letters generated by the ORI-HS database, a courtesy notice may be sent by the ORI-HS staff to the PI before the IRB approval period expires (e.g., approximately 4-8 weeks prior to expiration).
2. The PI is ultimately responsible for submitting appropriate CR documentation prior to study expiration. The expiration date is the last date that the protocol is approved. It is advisable to submit the required materials no later than one month prior to expiration. The PI completes the application for CR according to instructions on the form with additional documentation necessary to conduct a substantive review that may include but is not limited to:
 - A completed CR report form (protocol summary and progress report) including, when applicable, the number of subjects enrolled and withdrawn from the study; the reason for withdrawals; summary of unanticipated problems/adverse events involving risks to the subject or others; recent literature update; complaints about the research; modifications to the study; and any new, significant findings;
 - A copy of any currently approved protocol(s) for funded research (which includes any prior IRB approved modifications) and/or research description (summary which addresses all elements of criteria for approval); and if applicable:
 - A cover memo if it contains pertinent information;
 - Attachments (e.g., updates/changes, explanations);
 - Any relevant multi-center trial reports;
 - Researcher’s current risk-potential benefit assessment based on study results;
 - A copy of the consent/assent form for which the investigator is seeking IRB approval; and
 - A revised grant application.
3. Upon receipt of the CR materials, ORI-HS staff screens the submission to determine whether the study is eligible for expedited review and screens the application to ensure compliance with applicable IRB and federal requirements.

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4. If the CR submission includes a new unanticipated problem/adverse event report, ORI-HS staff separates the unanticipated problem/adverse event report from the CR materials and process it under separate cover (See SOP 11.01).
5. ORI-HS staff compares answers in the CR materials with the data in the existing IRB file.
6. ORI-HS staff will contact the appropriate consultants regarding issues for which the IRB does not have the appropriate expertise.
7. The ORI-HS may request additional information or materials from the PI if the CR application is not complete. It is the PI's responsibility to respond in a timely manner before the end of the approval period. ORI-HS staff will attempt to contact the PI and/or research staff for additional information/materials as needed.

Expedited Continuing Review

1. The Chair or designated voting IRB member serves as the expedited reviewer for expedited CR protocols. If the expedited reviewer has a conflict of interest, is unavailable, or does not have the appropriate expertise to review the CR, ORI-HS staff sends the CR to a voting member of the IRB with no known conflict of interest.
2. ORI-HS staff sends the expedited reviewer all documents submitted by the PI for review.
3. All expedited protocols involving children as subjects are reviewed by no less than two expedited reviewers prior to initial approval of the study.
4. All expedited reviewers are responsible for reviewing information in the expedited review packet, applying all criteria for approval as an initial review (i.e., applies 45 CFR 45.111 and informed consent regulatory criteria) and/or may request additional information as necessary to apply criteria. This includes review of informed consent/permission/assent document(s) submitted for re-approval as appropriate.
5. The expedited reviewer is responsible for making the final determination that the protocol meets the criteria for expedited review. If the expedited reviewer determines Full Board review is necessary, he/she documents this determination. Upon receipt of the reviewer's recommendation, ORI-HS staff implements Full Board CR procedures.
6. ORI-HS staff serves as intermediaries between the PI and the IRB expedited reviewer. However, the expedited reviewer may contact the PI directly for clarification. If this occurs, the reviewer documents the issues discussed with the PI.
7. The expedited reviewer documents any determination pertaining to specific findings, as mandated by federal regulations that were not previously addressed by the IRB.
8. The expedited reviewer ensures that the PI provides any significant new findings that might relate to the subject's willingness to continue participation in accordance with regulations.

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9. If the approval might lapse before completion of the CR, the expedited reviewer can make a determination to allow subjects currently participating to continue in accord with procedures described in the section below on lapses of approval.
10. ORI-HS staff lists expedited CRs on the IRB agenda to advise the IRB of the expedited CRs.
11. A decision to re-approve a study and associated documents will be documented in the study file, database, and a formal notification sent to the PI (See SOP 5.11).

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. The consultant will serve in an advisory role only. Any consultant(s) will be asked to provide acknowledgment that the review of study or study related materials are of a private nature, and that confidentiality of any shared information will be maintained.

January 2019 Changes to Continuing Review

Revisions to the continuing review procedure for expedited studies went into effect on January 21, 2019. Continuing Review is no longer required for those studies that are reviewed under the expedited review procedures. Therefore, ORI-HS will now assign a Next Report Date three (3) years from the date of expedited review approval in order to manage and oversee studies that are currently active. As studies come up for continuing review throughout the January 21, 2019 through January 20, 2020 year, these studies will be transitioned to have the three (3) year Next Report Date.

Full Board Continuing Review Procedures

The Biomedical and Social/Behavioral IRB conduct full CR at regularly scheduled convened meetings.

The PI submits relevant information and attachments (see the CR form for a complete list of information and attachments the PI must submit).

1. Approximately 30-60 days prior to the convened meeting, the IRB should receive the continuing review materials and associated documents as submitted by the PI that may include, but are not limited to, revisions previously requested by the IRB made prior to the current meeting, ORI-HS staff recommendations.
2. All IRB members review information in the protocol packet in advance of the meeting in enough depth to be familiar with the protocol, to be prepared to discuss the protocol at the meeting, and to be prepared to determine whether the research meets the regulatory criteria for approval.
3. All IRB members are responsible for evaluating the information communicated to the subject during the consent process. The IRB reviews the informed consent/assent document(s) submitted for re-approval to ensure accuracy and completeness.
4. ORI-HS staff ensures that the complete IRB protocol record is available to all IRB members prior to and, if requested, during the convened meeting.
5. The convened IRB assesses the CR materials using the federal criteria for approval.

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6. When the IRB reviews research that involves subjects vulnerable to coercion or undue influence, ORI-HS staff ensures that representatives or consultants are present for discussions of research involving vulnerable human subjects as may be needed.
7. ORI-HS staff serves as intermediaries between the PI and the IRB. However, the IRB Chair on behalf of the IRB may contact the PI directly for clarification. The PI may also be invited to the convened meeting (in-person, or by phone) to answer any questions posed by the IRB. The PI will not be allowed to be present during voting, or the initial discussion or resolution of concerns. Issues discussed with the PI will be documented in the IRB meeting minutes and/or study file as appropriate.
8. The IRB Chair provides recommendations to the IRB at the convened meeting on issues which they determine do not meet the federal criteria for approval, are controverted, need additional information, or concern compliance with other known applicable policies.
9. If the Chair/Co-Chair is unable to attend the meeting, the meeting is either cancelled, or the Chair/Co-Chair from the other IRB is invited to guest chair.
10. The IRB considers CRs scheduled for full review individually for approval. At the meeting, the IRB reviews the CR report and any issues and their resolution prior to voting. During discussion, the IRB members raise issues that the IRB determines do not meet the federal criteria for approval as specified in 45 CFR 46.111.
11. The IRB ensures that the PI provides any significant new findings that might relate to the subject's willingness to continue participation to the subject in accordance with regulations. The convened IRB makes the final determination on the outcome of the review.
12. The IRB's determinations will be documented in the meeting minutes, study file, and relevant information sent in a formal notification to the PI (See SOP 5.11). The database will be updated with relevant information.

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. Any consultant(s) will be asked to provide acknowledgment that the review of study or study related materials are of a private 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.

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Lapse of Approval

1. If a PI fails to submit a CR request or the IRB has not completed review by the end of the approval period, the PI is notified of study expiration. It is the PI's responsibility to notify the funding agency, sponsor, and or collaborative partners of the expiration of the IRB approval as may be necessary.
2. The PI may ask the IRB for permission to allow subjects currently participating to continue due to an overriding safety concern, ethical issues, or because it is in the best interest of the individual subjects. The IRB makes the final determination, if appropriate. The PI is formally notified of relevant IRB determinations.
3. If a PI submits a CR request or responds to the IRB's request for revisions after expiration, the ORI-HS or IRB may choose to request a written statement that verifies no research activities have occurred since the lapse, (i.e., recruitment or enrollment of new subjects, interaction, intervention, or data collection from currently enrolled subjects, or data analysis), or a written summary of events that occurred in the interim.
4. If the PI submits a CR request after study expiration, it is at the discretion of ORI-HS, the IRB Chair(s), or IRB to either proceed with the CR of the study, or to request a new submission. This will be determined on a case-by-case basis. If applicable, ORI-HS staff will link the new application to the previous protocol.
5. When continuing review and approval of a research study do not occur prior to the end of the approval period, the IRB does not report the expiration as a suspension of approval under Food and Drug Administration or Department of Health and Human Services regulations.

Review Outcomes

1. For expedited CR, the expedited reviewer may make the following determinations: 1) approved; 2) revisions and/or additional information required; 3) review by the full committee required. The expedited reviewer exercises all the authority of the IRB except he/she may not disapprove the CR. Only the convened IRB may disapprove the CR.
2. For full board CR, an IRB member makes a motion, the motion is seconded, and then the IRB members vote for, against, or abstain from one of the following five actions with a majority vote carrying:
 - a.) **APPROVED: IRB approval** - Indicates that the IRB concluded that the research and, if applicable, consent forms meet the federal criteria for approval. The IRB's approval vote verifies that the IRB members agree with the information/materials submitted for continuation of the protocol and/or specific findings described in the CR report by the PI. ORI-HS staff sends the investigator an approval letter accompanied by an informed consent/assent document (if applicable) with the affixed current IRB approval and study expiration dates.
 - b.) **REVISIONS and/or ADDITIONAL INFORMATION:** Indicates that the IRB has approved the protocol pending submission of minor revisions and that the IRB has given the Chair and Co-Chair the authority to approve the minor revisions which do not involve

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substantive issues. ORI-HS staff sends a letter to the PI describing the revisions requested by the IRB.

The PI responds to the IRB's suggested revisions in writing and sends the response to the ORI-HS. ORI-HS staff gives those responses to the IRB member designated at the IRB meeting to review the requested revisions. That IRB member may: forward the responses to the entire IRB for additional review, request additional information, or grant approval if the revisions are consistent with the IRB's requests.

- c.) **TABLED:** Indicates the IRB withholds approval pending submission of major revisions/additional information. ORI-HS staff sends the PI a letter. The letter lists the reasons for tabling and includes a description of the revisions or clarifications requested. For some studies, the IRB may appoint one or more members of the IRB to discuss the reasons with the investigator. ORI-HS staff schedules the PI's response to the requested revisions for review by the full committee. The PI is not required to attend; however, he/she is usually encouraged to be available during the meeting time for questions.
- d.) **DISAPPROVED:** Indicates the IRB disapproves the protocol as written. ORI-HS staff sends the investigator a letter, describing the reasons for disapproving the protocol and the ability to appeal the decision. This outcome usually occurs when the IRB determines that the risk of the procedures outweighs any benefit or if the research does not meet the federal criteria.

Additional motions for action may be made as necessary.

- 3. During the convened meeting, the IRB determines the approval period as appropriate to the degree of risk but not less frequently than once per year. The IRB may set a shorter approval period (for CR to occur more often than annually). When a protocol receives final approval, ORI-HS staff documents the approval period in the approval letter to the investigator. For full CR, ORI-HS staff includes the approval period in the meeting minutes.

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4. For full board CR, the date of the start of the approval period is the date of the convened meeting if approved. When the outcome of the IRB requests revisions (approved pending submission of minor revisions), the ORI-HS staff issues approval after the IRB Chair and/or Co-Chair reviews and approves the revisions. The approval period begins on the date on which the IRB Chair and/or Co-Chair approves the revisions. For expedited CR, the date of the start of the approval period is the date the expedited reviewer approves the study.
5. If the PI has concerns regarding the IRB decision/ recommendations for changes in the study, he/she may submit his/her concerns to the IRB in writing with a justification for appealing the IRB decision. The IRB reviews the request using standard IRB review procedures.

5. References

- 45 CFR 46.103(b)(4)
- 45 CFR 46.108(b)
- 45 CFR 46.109(e)
- 45 CFR 46.110
- 45 CFR 46.111
- 45 CFR 46.115(a)(3)&(7)

UNLV Rules and Procedures for Conducting Human Subject Research, 5.4.1