

Continuing Review	
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1. PURPOSE

1.1. Periodic review of non-exempt research is required to reassess the totality of the project and assure that it still meets criteria for approval in *SOP 014 Initial Review*, with particular emphasis on the criterion that risks to subjects are minimized and reasonable in relation to anticipated benefits to the subjects and the knowledge that is expected to result. The IRB conducts continuing review of research at intervals appropriate to the degree of risk.

2. POLICY and PROCEDURE

2.1. Interval of Review for Renewals

Research that is greater than minimal risk

- 2.1.1. For purposes of renewing the IRB approval period, the IRB must conduct a continuing review of research that **presents greater than minimal risk** of harm not less than once per year (45 CFR 46.109 (e)), meaning that the research must be reviewed and approved on or before the one-year expiration date of the previous IRB approval period.
- 2.1.2. If a protocol is reviewed after the protocol's expiration date, all research related to human subjects must cease until the renewal protocol has been reviewed and approved by the IRB, unless waived by the IRB as described under 2.2.
- 2.1.3. For each study, the IRB will conduct a risk assessment to determine the frequency of continuing review that is necessary to ensure the continued protection of the rights and welfare of the human subjects participating in said research study.

Minimal risk research

- 2.1.4. For purposes of renewing the IRB approval period, the IRB will generally not conduct continuing review of minimal risk research protocols, unless as otherwise determined and documented by the IRB and communicated to the investigator.
 - a. Studies determined to be exempt do not expire and continuing review is not required.
 - b. Studies approved after the 2018 Common Rule and are determined to be eligible for expedited review per 45 CFR 46.110 are approved for up to a ten year period and continuing review is not required. If after ten years the research is ongoing, then the researcher may seek approval for another ten year period, which will include a reassessment of risk to subjects.
 - c. Studies approved pre 2018 Common Rule that were determined to be eligible for expedited review per 45 CFR 46.110 are required to have continuing

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review annually, until either the study is closed or the study has transitioned to the 2018 Common Rule.

- 2.1.5. If a minimal risk protocol modification results in reclassification as greater than minimal risk, it becomes subject to continuing review requirements. Continuing review will be required at the time of modification and the interval of review of will meet the criteria as described in 2.1.1.
- 2.1.7. The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of whether the research is federally funded or non-federally funded and reviewed by the convened IRB or by expedited review procedures.

2.2. Lapses in Approval

- 2.2.1. There are no provisions for extending protocol approval periods beyond the protocol's expiration date. When continuing review and approval does not occur on or before the expiration date, the approval expires and the investigator must halt all human subjects research activities, including recruitment, enrollment, data collection and/or analysis unless it has been determined to be in the best interest of the subjects enrolled in the study to continue participating in the research. New subjects cannot be enrolled in a study for which the approval has expired.
- 2.2.2. Continuing participation of already-enrolled subjects in research during the period in which IRB approval has lapsed may be appropriate in extenuating circumstance, when, for example, withholding of the research interventions poses an increased risk to the subjects or when the interventions hold out the prospect of direct benefit to the subjects. The determination of whether it is in the subjects' best interest to continue in the research project may initially be made with the investigator in consultation with the IRB Chair/Designee or Research Integrity Director. If the investigator finds that it is in the best interests for one or more subjects to continue in the research interventions, they must inform the IRB staff and IRB members as soon as possible and request confirmation of the IRB's agreement to this arrangement. The investigator must submit a memo to the IRB stating:
 - a. Why allowing the research to continue would be the best interest of the already enrolled subjects;
 - b. Confirmation that no new subjects will be enrolled in the study during the lapsed approval period;
 - c. Any other pertinent information that the IRB should be made aware of to facilitate review the request.

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2.2.3. If an investigator fails to submit an application for continuing review prior to the protocol's expiration and the protocol approval period expires, the investigator has 180 days from the date of expiration to submit a continuing review application for renewal. The investigator must halt all human subjects' activities during this lapsed period of approval (except in instances as described in 2.2.2 above) and may not resume the research activities until the renewal has been reviewed and approved by the IRB. When submitting the renewal application to the IRB for review, the investigator must include the following information:

- Certification that no human subjects research activities have occurred during the lapse in approval (if human subjects research was conducted during this time see HSC SOPs 020 and 021 - *Data Collection without IRB Approval and Protocol Deviations and Non-Compliance*).
- A progress report of the research including 1) how many subjects have been run, 2) summary of the research to date, 3) any unexpected complications or complications, complaints, and resolutions, 4) modifications (if any), and other pertinent information such as reactions from subjects and publications or presentations resulting from the research.

2.2.4. If more than 180 days has passed, the investigator must submit a new application to the IRB for review. The investigator must halt all human subjects activities after the protocol's expiration and until a new application has been reviewed and approved by the IRB. Investigators should reference the expired protocol in the new application so the IRB is aware the protocol is based off an expired study.

2.3. Criteria for Renewal

Continuing review must be substantive and meaningful. When considering whether or not to approve a renewal of a study, the IRB must minimally determine that the criteria used to grant initial approval (see HSC SOP 014 *Initial Review*) has been satisfied. The IRB will initiate the review with the presumption that the research, as previously approved, satisfied these criteria and focuses on any new information that would alter the IRB's prior determinations. However, the IRB reserves the right to review the whole project in its entirety if needed to ensure that the previously approved criteria still satisfies the initial requirements for which the protocol was approved.

2.4. Continuing Review Process

2.4.1 Continuing review application – The investigator must submit to the IRB a complete continuing review application that includes:

- For greater than minimal risk research, or other studies as determined by the IRB, a renewal with no changes and its progress;

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- An updated protocol, or renewal with changes, if modified;
 - A current informed consent document(s) and any newly proposed or modified consent document(s);
 - A summary of the progress of the renewal application which must include the following information:
 - ✓ A summary of the research to date
 - ✓ The number of subjects enrolled since the last review
 - ✓ A summary of the number and nature of complaints received and how they were resolved or mitigated
 - ✓ Other comments or reactions from the subjects
 - ✓ Any publications or presentations of the research data
 - ✓ A summary of adverse events, complications or unanticipated problems involving risks to the subjects or others and any withdrawal if the subjects
 - ✓ Any additional pertinent information, such as recent scientific literature or information that might affect the risk/benefit ratio for subjects
- 2.4.2 Consent document(s) – The IRB shall review the consent document(s) and ensure that this information is still accurate and complete. Any significant new findings that may relate to the subject’s willingness to continue to participate must be provided to the subject in accordance with regulations set forth at 45 CFR 46.116(c)(5). Review of currently approved or newly proposed consent documents must occur during the continuing review of the research by the IRB, but informed consent materials should be reviewed whenever any new information becomes available that would require a modification of the consent document.
- 2.4.3 Currently approved protocol – A copy of the protocol including any previously approved modifications will be assigned to at least one member of the IRB for continuing review. Any IRB member will have complete access to the protocol file and relevant meeting minutes prior to or during the convened meeting.
- 2.4.4 Amendments – During the course of the study, any changes to a research protocol should be submitted to the IRB staff to set-up for review. Amendments may also be submitted at the time of continuing review. A description of the change(s), regardless when they are submitted, along with all relevant materials must be included in the protocol for IRB review and approval. Changes to a protocol should not be initiated prior to IRB review.
- 2.4.5 Types of Review – A protocol that was originally submitted using expedited review procedures may receive its continuing review using the same review criteria provided the renewal application is no more than minimal the risk to the human subjects and the protocol is still eligible expedited review. A protocol that

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was originally submitted using full board review procedures may receive its continuing review as either full board review if the risk level is more than minimal risk or provided at the convened meeting of the full board review, the IRB determined that the protocol presents no more than minimal risk and may be reviewed by expedited review categories (8) and/or (9).

- 2.4.6 External reviews – In general, the IRB that conducted the initial review of a research protocol will conduct the continuing review. If the need should arise, another IRB may conduct continuing review of the protocol, but only if the IRB members have the appropriate experience and expertise as well as access to all prior relevant IRB records.

2.5. Significant New Findings

The IRB may review reports generated from adverse event reports, current literature, and other sources to ascertain the status of the study and assess whether or not the risk/benefit ratio is still acceptable. The IRB will also determine whether or not the new information needs to be conveyed to the subjects (e.g., if a segment of the population may be bearing an undue burden of research risk).

2.6. Study Completion

Continuing review is required for studies that meet the criteria (e.g., full board) as long as a research study continues to involve human subjects. A study is considered to involve human subjects if any of the following activities are ongoing:

- Research-related interactions or interventions with human subjects;
 - Collection or receipt of identifiable private information or biological specimens;
- and

Once all the above activities as described in the IRB approved protocol are completed, then the research study is considered complete and the investigator is no longer required to obtain continuing review and approval for that specific study.

Continuing review is not required for studies that have progressed to the point that it involves only one or both of the following:

- a. Studies limited to data analysis, including analysis of identifiable private information or identifiable biospecimens, where no new subjects are enrolled and no further interactions or interventions are planned with the human research participants.
 - i. Investigators should consult with the IRB staff to determine whether their research has progressed to the point where it would be eligible for this criterion.
- b. Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

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3. SCOPE

These policies and procedure apply to all non-exempt human subjects' research.

4. RESPONSIBILITY

The investigator is responsible for fulfilling requirements associated with the renewal process in sufficient time for the IRB to carry out its continuing review of the research before the current approval expires.

The IRB staff are responsible for establishing the processes for conducting ongoing review of research protocols.

The IRB Chair/Designee is responsible for preliminary assessments of adverse events and significant new findings.

The IRB is responsible for conducting the continuing review of research protocols.

5. PROCESS OVERVIEW

Continuing Review – Reminders

The expiration date of the approval period is clearly listed on the approval letter for each protocol. It is the investigator's responsibility to keep track of the expiration date and initiate the renewal process in sufficient time for the IRB to conduct the review before current approval expires. However, as a courtesy, ORahs is designed to send investigators automatic email reminders at set intervals prior to the protocol's expiration. If a continuing renewal application is not received and the protocol approval period expires, it is the responsibility of the investigator to stop all research activities including recruitment and enrollment of the subjects until the renewal application has been submitted, reviewed and approved by the IRB.

Continuing Review – Expedited

In general, annual continuing review of research is not required for studies reviewed via expedited procedures, unless otherwise determined by the IRB as documented and communicated to the PI. When a continuing review application that qualifies for expedited review procedures is submitted, the IRB staff will conduct an initial review of the submission. If additional documentation or information is necessary, the responsible staff member initiates correspondence to the investigator, which may include requests for revisions or clarifications, via the protocol application or occasionally via email.

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After the investigator has revised the protocol application or responded to the requested information, the IRB staff member will verify that all items have been addressed and the application can be set-up for expedited review procedures. The application will be reviewed at the next regularly scheduled expedited review meeting. During this meeting, the IRB Chair/Designee and IRB staff member, who also serves as a voting member of the committee, will review the renewal protocol. If there are any clarifications or concerns, the application will be returned to the investigator to address the expedited review comments. If there are no comments, clarifications, or concerns, or once these items have been addressed, the protocol can be approved for continuing approval.

After the renewal application is approved all approved documents, including the protocol, informed consent, parental permission, assent, measures, interview questions, etc., will be made available to the investigator along with the protocol approval letter.

If there are any items that cannot be resolved or if it is determined that the renewal application does not meet the criteria for expedited review procedures, the application must be reviewed by full board review (i.e., convened IRB). Expedited review procedures may not result in withholding approval or disapproving a study.

Continuing Review – Full Board Review

In general, when a continuing review application requiring a full board review is submitted, it is added to the agenda of the next regularly scheduled full board meeting. An IRB staff member will conduct a preliminary review of the application and may prepare comments for the IRB to review at the convened meeting. The IRB staff will inform the committee members that the protocol is available for review and will assign a discussion leader for each protocol set-up for full board review. If a research protocol requires special consideration or expertise, the IRB Chair/Designee, IRB staff, or Research Integrity Director may arrange for a consultant's participation and the necessary documentation will be forwarded to the consultant for comments.

At the convened meeting, the IRB discussion leader presents the study to the committee and responds to the staff member's comments included in the application. The IRB discussion leader may also elaborate on any aspect of the study they deem appropriate to discuss. All IRB members may ask questions and engage in discussion of the protocol review. The IRB may approve the protocol, require modifications to secure approval, disapprove the continuation of the research, or table the protocol for consideration at future convened meeting. The investigator will be notified in writing of the committee review outcome. If modifications are requested, the IRB will designate the IRB staff and/or IRB member to

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review the investigator's response and revisions in order to verify that the conditions for approval have been satisfied.

If the requested revisions are substantive or sufficient detail is missing in the renewal application, the IRB will request re-review at a future convened meeting.

After the renewal application is approved, all approved documents, including the protocol, informed consent, parental permission, assent, measures, interview questions, etc. will be made available to the investigator along with the protocol approval letter.

If the IRB does not re-approve the research, an IRB staff member will notify the investigator in writing identifying the reason for withholding approval.

References:

45 CFR 46 Regulations

Federal Register Volume 63, No 216

UC Berkeley Policies and Procedures

OHRP Guidance on IRB Continuing Review of Research

The Belmont Report