

University of California, San Diego  
Human Research Protections Program  
Institutional Review Board  
Standard Operating Policies and Procedures

Section 3.11  
Continuing Review

***Policy***

The UCSD HRPP limits all project approvals to an initial approval period of 365 days, and upon continuing review to an additional approval period not to exceed 365 days. After one initial approval and nine continuing review approvals, all projects must be resubmitted in full for Initial Review. This policy has served well over the past decade due to the rapid evolution of scientific methods. Investigators are required to provide the complete continuing review submission not later than 15 days prior to the continuing review deadline but should be provided 30-45 days prior to deadline to ensure no lapse in approval. The continuing review form is used as 1) a request for reapproval of ongoing research where annual (or more frequent) review is required, 2) a final report to be used when research has been completed or terminated, or 3) an interim report (an IRB-required report of study progress that is not required for reapproval). Continuing review actions will be carried out at a convened IRB meeting, except in those cases where expedited review is permitted.

Interim Report

If the IRB determines that a study requires an Interim Report, the investigator may be asked to submit an application for continuing review and reapproval by a specified date, upon enrollment of a specified number of subjects, or upon reaching a specified point in the study. If interim reports are not received as scheduled, the IRB may suspend enrollment until reports are reviewed. The IRB will review the Interim Report, and if appropriate the continuing review form, at a convened meeting, and may require modifications or take other actions within its authority.

Reapprovals

Investigators may not continue to conduct their investigations beyond the continuing review deadline. Studies that have expired before the form has been reviewed will be suspended until the IRB review has been conducted. UCSD HRPP will provide assistance to investigators in the form of deadline reminders and online status information for investigators, and will issue a letter within 30 days of protocol lapse or expiration stating affirmatively that the study no longer has IRB approval and research activities must cease. However, if the investigator is in communication with the IRB at the time of approval expiration, the information regarding conduct of the study is forthcoming, and, in the opinion of the Chair, the subjects participating in such a study would suffer a hardship if medical care were discontinued, appropriate medical care may continue beyond the expiration date for a reasonable amount of time. However, new subjects cannot be enrolled

and the data acquired during the period of lapse of IRB approval may not be used for analysis or publication..

As stated above, when an investigator does not provide continuing review information to the IRB or the IRB has not approved continuation, the IRB must ensure that all activities including recruitment, advertisement, screening, consent, and collection of private identifiable data are stopped. The IRB must notify investigators to submit immediately to the IRB Chair, a list of participants for whom stopping research activities would cause harm, if applicable. Upon IRB Chair approval (and for VA studies, in consultation with the Chief of Staff), the IRB may allow current participants to continue interventions or interactions if the IRB finds an over-riding safety concern or ethical issue involved such that it is in the best interests of individual participants to continue participating.

### Completion Reports

A notice of study completion should be submitted by the Principal Investigator to the UCSD HRPP within 60 days after completion or termination of the study. A study may be considered completed once all interactions with human subjects and all data collection from human subjects, including subject follow up, have been completed. Additional reports information about the status of the study, such as computer printouts, telephone reports, sponsor's completion summary, letter, etc. may be submitted. The Chair or a designated reviewer will review the report.

### Reporting of Adverse Events/IND Safety Reports

Investigators are required to report Adverse Events which are serious (SAEs), or which are unexpected and are associated with the research procedures or investigative product. This applies whether the events occur at local or at outside sites in a multicenter study.

Investigators will also report to the IRB:

1. Other unexpected events related to the safety of subjects.
2. All significant deviations from the protocol, good clinical practice, applicable regulations or institutional policies involving the conduct of the study or subject participation.
3. Summaries of the DSMB findings, if a DSMB is used.
4. Other types of adverse events, as defined by the monitoring plan in the protocol or in FDA regulations or other applicable federal regulations.

The investigator will submit reports of adverse events occurring at the investigators own site on the UCSD Serious Adverse Event Form, or via the online Adverse Event Reporting system available at <http://irb.ucsd.edu>. A separate report must be submitted for each incident. In the report, the principal investigator will indicate the nature of the event, whether, in the investigator's opinion, the adverse event was related to the research activity, why the investigator holds this opinion, and whether changes in the protocol and/or consent form are warranted.

All fatal or immediately life-threatening events must be reported in writing to the IRB as soon as possible, but no later than 10 working days after discovery. The report should

include copies of any reports sent to the study sponsor or FDA. Other types of adverse events must be reported within 10 working days of awareness of the problem.

Reports of adverse events occurring at non-local sites will be submitted with a cover letter or memo containing the reference number of the report(s) and a signed statement by the investigator that he/she has reviewed the events and whether he/she feels that any modifications are required in the protocol or consent. These adverse events must be reported within 10 working days of receipt.

Serious Adverse Events Reports (including IND Safety Reports) from both local and non-local sites will be reviewed by the Chair or designee. The reviewer may recommend to the Chair that the report be accepted or that it undergo full IRB review. If the Chair or designee determines that the risk of the study may have changed, that the consent form may require modification, or that further action may be needed to protect the safety of research subjects (e.g.; unexpected nature or frequency of reported adverse events), the Chair will take immediate actions as needed and the report will be forwarded to the IRB to be discussed at a convened meeting. Based upon this review, the IRB may reconsider its approval of the study, require modifications to the study and/or informed consent form, revise the continuing review timetable, or require notification and/or re-consent of subjects already enrolled in the study.

The IRB must also ensure that reports of unanticipated problems involving risks to human subjects or others, instances of serious or continuing noncompliance, and suspension or termination of IRB approval are reported to FDA, ORO, OHRP, and/or institutional officials according to the requirements of each agency. Usually, this reporting is accomplished through the normal reporting channel, i.e., the investigator to the sponsor to FDA.

#### Process for Conducting Continuing Review

When reviewing a project for reapproval, the IRB will assess all of the same criteria for approval that were evaluated during initial review. The assigned primary IRB reviewer leads the discussion regarding the review. All IRB members have access to the information necessary to enable them to conduct a review in enough depth to be able to discuss the protocol at the meeting including the materials listed below.

The PI must submit the following materials to the HRPP office for continuing review:

1. Continuing Review Facepages and Narrative Summary of Progress to Date: these documents should contain sufficient information to permit determination of the current risk-benefit assessment based on study results. Special attention should be paid to determining whether new information or unanticipated risks were discovered since the previous IRB review. Any significant new findings that may relate to the subjects' willingness to continue participation should also be included. Specifically, the IRB must determine that any significant new findings that arose from the review process and that might relate to participants' willingness to continue participation was provided to participants, if applicable.

2. A copy of the stamped, approved consent and/or assent document(s) currently in use to ensure that the document has current IRB approval and to determine whether the information contained in it is still accurate and complete, including whether new information that may have been obtained during the course of the study needs to be added.
3. A description of approved or proposed amendments, including updated Master Protocols, Investigator's Brochures, package inserts as well as minor changes, (if any) and the IRB action on each amendment.
4. The number of subjects enrolled in the study. If a VA study, the number of subjects by gender must be provided.
5. A description of the research findings to date.
6. A description of adverse event reports from investigators, sponsor safety reports (e.g., IND or IDE Safety Reports).
7. Documentation of protocol violations and/or deviations, or non-compliance with applicable regulations.
8. A description of all reports of injuries to subjects, unanticipated problems, complaints from subjects or others, new scientific findings, or any information that may change the risk/benefit ratio for subjects.
9. A statement from the investigator that all SAEs and unexpected adverse drug experiences have been reported as required.
10. Review of a summary of the Data Safety Monitoring Board (DSMB) meetings (if applicable) or findings based on information collected on AEs and SAEs as required by the approved data and safety-monitoring plan.
11. Any new recruitment documents.
12. In addition to copies of the documents required for continuing review, the IRB may consider the following information, where applicable, for continuing review:
  - a. Recent published medical or scientific studies applicable to the protocol.
  - b. Number, gender, and minority status of subjects enrolled and entered into the study.
  - c. Number of subjects considered to part of a vulnerable population.

All necessary information relevant to the assessment of the project's risks and benefits to study participants will be reviewed by the primary reviewer, the IRB and an analyst assigned to the IRB committee.

Based on its review of the above information the IRB determines for each approved research protocol whether the research is re-approved, requires modifications to secure reapproval, is suspended or disapproved (terminated) based on assessment of the project's risks and benefits. The IRB may also require appropriate changes to the informed consent form content, frequency of continuing review, level of safety monitoring, and may determine whether the project requires verification from sources other than the investigator that no material changes have occurred since previous IRB review. The IRB will vote upon the recommendations made by the reviewers, and will determine the frequency of review.

## *Procedures*

1. IRB Members including Chair will review the information in forms submitted for continuing review, adverse experience reports submitted by the investigator, proposed revisions to the approved research protocol, if any, and any significant new findings which may affect the welfare and safety of the subjects; review the consent form and update it if needed based upon review of previous items; review any other pertinent reports in the study file (e.g.: audit reports, correspondence, complaints, etc.); and vote on a category of action.
2. IRB Administrator or HRPP staff designee will check Interim, Renewal and Completion Reports for completeness; make copies of reports available to IRB members prior to next convened meeting; notify members of continuing review actions by the Chair or designee using expedited review process; notify investigators of reapproval and other report submission deadlines; and maintain documentation of any new significant findings relevant to study subjects and how the information was provided.

***Applicable Regulations***

[21 CFR 50.25\(b\)\(5\)](#)

[21 CFR 56.108\(a\)\(4\)](#)

[21 CFR 56.108\(b\)\(1\)](#)

[21 CFR 56.109 \(f\)](#)

[21 CFR 56.110\(b\)](#)

[21 CFR 812.150\(a\)\(6\)](#)

[45 CFR 46.109\(e\)](#)

[OHRP Guidance: Continuing Review](#)

[FDA Guidance: Continuing Review](#)