

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

Section 3.12
Protocol Amendments

Policy

Investigators must submit a complete description of proposed modifications to a project for review. When an amendment is reviewed at the IRB meeting, at least one IRB member leads the discussion regarding the review, and is provided with and reviews the complete protocol. Due to the nature of the e-IRB process, which involves conversion of documents to PDF format for electronic review, all documentation is also made to all other IRB members when the agendas are posted.

Major modifications/amendments are reviewed through the full IRB review process, minor modification requests through the expedited process. Examples of modifications considered to be major in nature include, but are not limited to, escalation in the drug(s) dosage(s), the introduction of an additional drug(s); the addition of a new invasive procedure. Major modifications may impact on the risk/benefit ratio in the study. It is the investigator's responsibility to assess the degree of change in procedures and risks of the study.

The initial determination as to whether a modification is major or minor is the responsibility of the principal investigator, who assesses the degree of change in procedures and risks. However, the acceptance of the determination rests with the IRB. The modification is reviewed by the IRB professional staff and a determination of whether full IRB review is necessary is made.

Minor changes in previously approved research during the period (of 1 year or less) for which approval has been authorized will be done under an expedited review process. The review will be carried out by the IRB Chair, or designee(s). If the Chair or designee believes that the "minor" modification is too substantive to receive this type of review, the application will be referred for full IRB review. A modification is given approval only to the expiration date that was received at the most recent initial or renewal review.

For protocols involving investigational drugs or devices, an amendment or protocol change intended to eliminate an apparent immediate risk or danger to participants may be implemented immediately provided the FDA is subsequently notified by protocol amendment and the reviewing IRB is notified in accordance with 21 CFR 56.104(c). The amendment must undergo full IRB review at the earliest opportunity.

Changes in study sites or investigators or additions must also be reported to the IRB. These requested changes involve sending a cover letter, revised application face page, and may involve revised research plans and consent documents. In the case of a change in the PI, the

cover letter should be signed by the investigator who holds the approval. In addition, a letter signed by the “new” PI should also be provided that indicates the “new” accepts the role of PI and the responsibilities associated with that role.

Process for Conducting Amendment Requests

When reviewing project amendments, the IRB will assess all of the same criteria for approval that were evaluated during initial review. When an amendment is reviewed at the IRB meeting, at least one IRB member is provided with and reviews the complete protocol. The e-IRB process involves conversion of documents to PDFs for electronic review so that all documentation is also made available to all members of the IRB when the meeting agendas are posted. Information is made available to other IRB members who wish to review the project. The PI must submit the following materials to the HRPP office for continuing review:

1. Cover letter outlining the amendment request including summary of changes associated with the amendment and the affect the amendment has on the study including affect to the risk to subjects, risk/benefit ratio, and risk management procedures.
2. Revised application facesheet if there are changes to personnel, facilities or funding
3. Revised Research Plan, if applicable
4. Revised consent/assent forms, if applicable
5. Additional information including updated Master Protocol, Investigator’s Brochure, package insert, recruitment flyers, if applicable.

The amendment request submission 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. Any significant new findings that may relate to the subjects' willingness to continue participation should also be included.

All necessary information relevant to the assessment of the project’s risks and benefits to study participants will be reviewed by the assigned IRB primary reviewer, or Chair or designee in the case of an expedited review.

Based on its review of the above information, the full IRB determines for each approved research protocol whether the amendment is approved, requires modifications to secure approval, is suspended or disapproved (terminated) based on assessment of the amendment risks and benefits. The IRB may also require appropriate changes to the Research Plan and/or informed consent/assent forms 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.

For expedited review, the Chair or designee will determine for each amendment request whether the amendment can be approved or requires modifications to secure approval

based on assessment of the project's risks and benefits. Appropriate changes to the informed consent/assent form content and/or Research Plan may also be requested.

Reports of the amendment request review process will be reported in a timely manner to the investigator, the VA R&D Committee, and institutional officials as required.

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\(a\)\(6\)](#)

[38 CFR 16.109\(e\)](#)

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

[OHRP Guidance: Continuing Review](#)