

II2F PR4 Suspension, Termination and Expiration of Approval for Human Research

Overview

The University of Nevada, Reno (the University) Institutional Review Board (IRB) has the authority to suspend or terminate approval of all or part of the research that is not being conducted in accordance with the IRB's requirements or University policy, or that has been associated with, or has the potential to be associated with unexpected risk to subjects. Likewise, the sponsor, other appointed University oversight committees and the principal investigator have the authority to suspend research activities whenever they believe it is necessary to do so in order to protect the safety or welfare of research participants or the integrity of the research. This procedure explains the steps necessary for the orderly suspension or termination of a research protocol.

Note: Additional regulatory requirements for suspensions and terminations for VA and Department of Defense (DoD) research are noted separately, at the end of this document.

II2F1 Suspensions or Terminations by the IRB

Formal Suspension

The IRB or IRB Chair may suspend a protocol when it is believed to be in the best interest of participants to stop some or all protocol related activities temporarily. Studies may be suspended during an investigation of noncompliance or following a protocol deviation, adverse event or unanticipated problem involving risks to participants or others. Suspended protocols are still considered to be active studies and require continuing review by the IRB.

Formal Termination

A fully convened IRB may terminate a protocol when it is believed to be in the best interest of participants to stop protocol related activities permanently. Studies may be terminated following an investigation of noncompliance, protocol deviation, adverse event or unanticipated problem involving risks to participants or others.

Expiration

Any research protocol that has not been reviewed before the expiration date by the end of its approval period is automatically considered expired and all research activity must cease. Investigators will receive a notice from the IRB stating that authorization to conduct the research expired and that all research-related activities must stop unless it would be in the best interest of research subjects to continue the intervention. The notification describes when it may be in the best interest of research and instructs

investigators to contact the IRB immediately should this be the case. Interventions or interactions with current subjects may only continue if the IRB finds an over-riding safety concern or ethical issue which makes continuation of the research activity to be in the best interest of the currently enrolled subjects. In no case may new subjects be enrolled prior to re-approval of the project by the IRB.

For investigators who wish to continue the research after IRB approval has expired, the notification includes instructions for resubmitting the protocol for IRB review and approval. See section I12F7 Reapproval of Expired Protocols for details.

I12F2 Suspensions or Terminations by the Investigator, Sponsor or Other Oversight Body

Sponsors, investigators and other oversight bodies have the authority to suspend their own research study at any time they believe it is necessary to protect the safety and welfare of research participants or the integrity of the study. Studies may be voluntarily suspended after review or monitoring of study data, upon recommendation from Data and Safety Monitoring Boards or Committees, prior to or during an investigation of noncompliance or protocol deviation, adverse or unanticipated problem involving risks to research participants or others.

When a principal investigator, sponsor or other oversight body determines that it is in the best interest of the participants to suspend or terminate a protocol, the principal investigator must notify the IRB of the decision within five days of the principal investigator deciding to or learning of the suspension or termination. The principal investigator must provide the IRB with the reasons why the study is being suspended or terminated. If only some of the study activities will be suspended (such as suspension of enrollment) then the principal investigator must include a description of what activities will continue and why it is appropriate to do so. The IRB will review the notification and determine if additional protection of research subjects, corrective actions, or investigation is required. The IRB will notify the principal investigator in writing of whether or not the IRB concurs or if additional actions are required.

I12F3 Obligations to Participants During Suspension or Following Termination

If the protocol is terminated or the suspension will require that current participants be withdrawn from some or all research related activities, then the principal investigator must submit to the IRB proposed procedures for withdrawal of currently enrolled participants that considers their rights and welfare. The withdrawal plan must also include a proposed script or letter to notify all currently enrolled participants who are affected by the suspension or termination. The IRB will review the proposed withdrawal plan and script or letter and make recommendations to amend plan or approve the plan.

Following a determination that a protocol must be suspended or terminated, several steps must be taken to ensure the protection of research participants. When procedures for withdrawal of enrolled subjects are necessary to protect their rights and welfare, the IRB may choose to

1. transfer subjects to another investigator,
2. transfer subjects to standard clinical care, or
3. to the degree necessary to protect their rights and welfare, allow subjects to continue in the research under the current principal investigator until the suspension is lifted or until all subjects have been safely withdrawn.

If follow-up of subjects for safety reasons is permitted or required by the IRB, the IRB will require that the subjects should be so informed and that any adverse events or outcomes that occur during the follow-up period be reported to the IRB and the sponsor.

If the suspension is partial (i.e., some of the research procedures will continue), the principal investigator must submit to the IRB proposed procedures for adequate oversight of all aspects of the research that will continue.

During the suspension period or after the termination of the research project, the principal investigator must report any events to the IRB or sponsor that would have required reporting had the former participants continued to be enrolled in the research.

In all instances of suspension or termination, if warranted by the circumstances of the suspension or termination, the IRB may mandate oversight or transfer responsibility to another investigator to ensure implementation of the suspension or termination procedures.

II2F4 Research Activities During Suspension

In the event a research project or protocol is suspended, all research activities must cease unless the project involves therapeutic treatment or intervention and interrupting that treatment, in the opinion of the treating physician and with the approval of the IRB, would be detrimental to the research participants. Only in this case may the principal investigator continue to apply treatment. In all other cases, no protocol related activities may continue unless explicitly authorized by the IRB. This prohibition includes no further enrollment of new subjects; no administration of the research drug, device, therapy or all three; and no use of data (including data analysis) in which a subject identifier is attached.

A principal investigator may request to re-open a suspended research project by submitting a protocol amendment in which the study design, implementation or investigation have been appropriately revised; when the IRB determines that the corrective action proposed by the principal investigator is sufficient or when the IRB determines that the investigators have satisfactorily complied with the corrective action requested by the IRB.

II2F5 Reporting Suspensions or Terminations

When study approval is suspended or terminated by the IRB, in addition to stopping all research activities, the IRB will notify, or will request that the principal investigator or another qualified,

appointed representative to notify any subjects currently participating that the study has been suspended or terminated.

All suspensions and terminations will be reported to the appropriate individuals and agencies as follows: the IRB will notify the principal investigator, faculty advisor for student-initiated research, department chair and the Institutional Official within five working days of the termination; within 30 days of the termination and where applicable, the IRB will notify the University Office of Sponsored Projects; federal agencies such as DHHS OHRP, FDA and VA; the funding agency; and the HRPP administrator and IRB chairs of other institutions engaged in the research.

I12F6 Noncompliance with Continuing Review Requirements

If the IRB notes a pattern of noncompliance with the requirements for continuing review, the IRB should determine whether such a pattern represents serious or continuing noncompliance that needs to be reported to appropriate institutional officials, the HHS agency that supported the research, and OHRP (45 CFR 46.103(b)(5)). Examples of serious or continuing noncompliance may include repeated or deliberate failure of an investigator to submit the continuing review request or the requested revisions in a timely fashion or the IRB itself is frequently not meeting continuing review dates.

I12F7 Re-approval of Expired Protocols

The IRB will review a request for re-approval of an expired protocol if the continuing review application was submitted to the IRB administrative office prior to the expiration date and is in the process of review as determined by IRB support staff. The process of review begins after continuing review materials have been assessed as complete and adequate by IRB staff and either assigned to an expedited reviewer or placed on a full board agenda. Investigators who wish to resume research wherein the expiration date has passed, must submit the following prior to the issue of a certification of approval to resume the research:

1. statement verifying that no subjects were enrolled after IRB approval expired;
2. information about whether any research participants were maintained on a therapeutic intervention after the expiration of IRB approval including the number of subjects maintained and explanation about why it was necessary to maintain the therapy for those subjects; and
3. statement that no other research activities took place after expiration date of IRB approval.

The IRB will review all such submissions under expedited procedures or at convened IRB meetings as appropriate for the proposed research.

I12F7a Email Notice of Expiration While in the Process of Continuing Review

IRB support staff will send the following email to notify investigators if a continuing review application was submitted to the IRB administrative office prior to the expiration date but IRB approval will expire before IRB review can be completed:

Protocol Number:

Protocol Title:

Expiration Date:

The protocol referenced above will expire before IRB review can be completed. It will be necessary for you to cease enrollment and study procedures following expiration of approval until the protocol has been reapproved by the IRB. Please inform all research personnel to cease all research related activities.

Before a certification of approval can be issued to resume the research activities, you must provide a written statement to our office that addresses the following:

1. Whether or not subjects were enrolled after the IRB approval expired;
2. Information about whether any research participants were maintained on a therapeutic intervention after the expiration of IRB approval including the number of subjects maintained and explanation about why it was necessary to maintain the therapy for those subjects (the IRB administrative offices must be contacted by the expiration date if research participants will be maintained on a therapeutic intervention); and
3. Whether or not any other research activities took place after expiration of the IRB approval

Please contact me if you have problems or questions.

I12F8 Definitions, Procedures and Timeframes for VA Research

The following definitions, procedures and timeframes apply when reviewing VA research:

Relevant Definitions for VA Research

Administrative Hold

- An administrative hold is a voluntary interruption of research enrollments and ongoing research activities by an appropriate VA facility official, investigator, or Sponsor (including the ORD when ORD is the sponsor).
- The term “administrative hold” does not apply to interruptions of VA research related to concerns regarding the safety, rights, or welfare of human research subjects, research investigators, research staff, or others.

- An administrative hold must not be used to avoid reporting deficiencies or circumstances that otherwise require reporting by federal agencies.
- Administrative holds are not used when IRB approval has expired.

Suspension or Termination of IRB Approval of Research

- Suspension refers to a temporary interruption in the enrollment of new subjects, activities involving previously enrolled subjects, or other research activities.
- Termination refers to a permanent halt in the enrollment of new subjects, activities involving previously enrolled subjects, or other research activities.
- The terms “suspension” and “termination” apply to interruptions related to concerns regarding the safety, rights, or welfare of human subjects, investigators, research staff, or others.
- Suspensions and terminations do not include
 - Interruptions in research resulting solely from the expiration of a protocol approval period or
 - Administrative holds or other actions initiated voluntarily by a VA facility official, investigator, or sponsor for reasons other than those described in preceding items.

Procedures and Timeframes for Reporting Terminations or Suspensions of VA Research

Any termination or suspension of *research* (e.g., by the IRB or other research review committee, or by the IRB chair or OHRP Director, or the Associate Chief of Staff for Research or other VA facility official) related to concerns about the safety, rights, or welfare of human research subjects, research staff, or others must be reported in writing within five business days after the termination or suspension occurs to the following:

- Medical Center Director,
- Associate Chief of Staff for Research,
- Research and Development Committee,
- IRB, and
- Other relevant research review committees.

Suspensions and terminations of IRB approval must be reported to the following entities:

- Office of Research and Development, if VA-funded;
- Regional Office of Research Oversight;

- Privacy Office, when the report involves unauthorized use, loss, or disclosure of individually identifiable patient information; and
- Information Security Officer, when the report involves violations of information security requirements.

II2F9 Reporting Requirements for Department of Defense-supported Research

For DoD-supported research, any suspension or termination of DoD-supported research must be promptly reported to the DoD human research protection officer.