

Policy Number: 51:

Title: Hold, Suspension, and Termination of IRB Approval

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Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) that all currently approved research is subject to modification or change in approval status, as deemed necessary by the UCI IRB. The IRB has the authority to suspend or terminate research for not being conducted in accordance with State and Federal laws/regulations, and/or IRB requirements, policies and procedures; or if it has been associated with unexpected serious harm to subjects. The Investigator also has the option to place the research on administrative hold, while investigating a matter of potential noncompliance or to determine if additional risks are posed to human subjects.

I. Investigator-Imposed Administrative Hold

- A. The Investigator has the option to place some or all research activities on administrative hold pending review by the IRB Chair or the convened IRB and/or until additional information can be provided to the Chair or the IRB to determine if a change in the risk-benefit profile has occurred, if a change in the rights or welfare of the participants has occurred or if potential areas of non-compliance exist in a currently approved study. The Investigator can place an administrative hold on the research if:
 - 1. A complaint is received by the UCI IRB;
 - 2. An allegation of non-compliance is reported to the IRB;
 - 3. A discovery by the Investigator of potential additional risks to subjects; or
 - 4. A potential change in the rights or welfare of the subjects.
- B. The Investigator exercising the option for administrative hold, must submit an unanticipated problem (UP) report, a new information report (NIR), or a modification application (MOD) to the IRB. The Investigator could place specific activities on hold. For example:
 - 1. Hold on recruitment;
 - 2. Hold on screening/enrollment;
 - 3. Hold on interactions/interventions with subjects; and/or
 - 4. Hold on collection or analysis of private identifiable information about participants.
- C. The Investigator must address the effect of the administrative hold on the rights and welfare of the current subjects.
- D. The investigator must promptly notify the IRB in writing of the intention to remove the administrative hold prior to implementing the action.
- E. At any point, the IRB Chair or the IRB can suspend the research and report the suspension in accordance with the UCI HRP Policy on Reporting.
- F. Should the IRB impose a suspension, the IRB suspension will be reported (See HRP Policy 53).
- G. The IRB Chair or his/her designee, or the IRB Committee may make recommendations for additional education and/or compliance interventions for the Investigator and research personnel.

II. FDA, Sponsor, or DSMB-Imposed Holds or Suspensions

- A. Notification of a hold or a suspension by the FDA, a sponsor, or a DSMB unrelated to risk to human subjects (e.g., data analysis) is submitted to the IRB for review and approval as a modification request to previously approved research. Such modifications may be considered minor and may be reviewed by the expedited procedure at subcommittee (See HRP Policy 17). The IRB will review the modification to consider if the hold or suspension relates to possible non-compliance.
- B. Notification of a hold or a suspension by the FDA, a sponsor, or a DSMB possibly related to risk to human subjects is submitted to the IRB via the UP or NIR reporting process for review by the full Committee for evaluation as a potential unanticipated problems involving risk to participants or others (See HRP Policy 19). Unanticipated Problems determined by the IRB will be reported as per Policy 53. The IRB will review the report to consider if the hold or suspension relates to possible non-compliance.
- C. The IRB may impose their own suspension of the study, based on their findings. Should the IRB impose a suspension, the IRB suspension will be reported as per Policy 53.

III. IRB-Imposed Suspensions

- A. The IRB Chair or his/her designee, or the full IRB Committee may suspend IRB approval under the following circumstances:
 - 1. Inappropriate involvement of human subjects in research;
 - 2. Inhibition of the rights or welfare of participants;
 - 3. Serious or continuing noncompliance with Federal regulations or IRB policies; or
 - 4. New information regarding increased risk to human participants, etc.
- B. The IRB must consider the effect of the suspension on the rights and welfare of the current participants.
- C. When the IRB Chair suspends a study and the issue is reviewed at the next convened meeting of the IRB.
- D. The IRB reports in writing, all suspensions due to cause, promptly to the Lead Researcher. The letter includes:
 - 1. A statement of the reasons for the IRB's action;
 - 2. A requirement that the Investigator submit to the IRB a proposed script or letter notifying all currently enrolled participants that are affected by the suspension. The IRB Committee reviews the proposed script or letter. If follow-up of subjects for safety reasons is permitted/ required by the IRB, participants should be so informed. The IRB may directly contact participants to fulfill this notification; and
 - 3. A requirement that the Investigator report any events to the IRB or sponsor that would have required reporting had the former participants continued to be enrolled in the research. The IRB may mandate oversight or transfer responsibility to another Investigator to ensure implementation of these procedures.
- E. Investigators receiving repetitive suspensions may necessitate institutional actions for serious and continuing non-compliance (See HRP Policy 52).
- F. All suspensions imposed by the IRB will be reported according to HRP Policy 53.

IV. IRB-Imposed Terminations

- A. The IRB Committee reviews a study for Termination at a convened IRB meeting.
- B. Only the IRB Committee may terminate IRB approval when it is not being conducted in accordance with the IRB's requirements or the Federal regulations or has been associated with unexpected serious harm to participants (See HRP Policy 19)
- C. The IRB must consider the effect of the termination on the rights and welfare of the current participants.
- D. The IRB reports in writing, all Terminations promptly to the Investigator. The letter includes:

1. A statement of the reasons for the IRB's action;
 2. A requirement that the researcher submit to the IRB for review proposed procedures for withdrawal of currently enrolled subjects that considers their rights and welfare. Procedures for withdrawal of enrolled participants may include:
 - a) The IRB may mandate oversight or transfer responsibility to another Investigator to assure implementation of these procedures; or
 - b) Arrangements for medical care outside of a research study;
 3. A requirement that the Investigator submit to the IRB a proposed script or letter notifying all currently enrolled participants that are affected by the termination;
 - a) The IRB reviews the Investigator's proposed script or letter.
 - b) If follow-up of subjects for safety reasons is permitted/required by the IRB, participants should be so informed.
 - c) The IRB may directly contact participants to fulfill this notification; and
 4. A requirement that the Investigator report any events to the IRB or sponsor that would have required reporting had the former participants continued to be enrolled in the research.
 - a) The IRB may mandate oversight or transfer responsibility to another Researcher to ensure implementation of these procedures.
- E. The Investigator is offered an opportunity to respond to the Committee's determinations. The IRB Committee may ask the Investigator to attend the convened meeting to discuss the termination and provide clarification of the issues.
- F. Investigators receiving repetitive Terminations may necessitate additional institutional sanctions for serious and continuing non-compliance (See HRP Policy 52)
- G. All terminations imposed by the IRB are promptly reported according to HRP Reporting Policy (See HRP Policy 53)

V. **Study Expiration**

- A. If an Investigator fails to provide continuing review information to the IRB or the IRB has not reviewed and approved a research study by the specified continuing review expiration date, the study expires. Enrollment of new participants cannot occur after the expiration date and all research activities must stop.
- B. The IRB notifies the Investigator in writing of protocol expiration. The letter indicates that on or after the expiration date:
 1. Enrollment of new participants must stop;
 2. All research activities must stop; and
 3. Any continuation of research activity is a violation of Federal regulations.
 4. The letter also indicates that the Investigator must immediately submit to the IRB, a list of research participants for whom cessation of the research would cause harm.
- C. Research studies not reviewed and approved within thirty (30) days of the notification of Expiration are administratively closed by the IRB. Reinstatement of the research generally requires submission of a new IRB Application.

References:

45 CFR 46.103(b)(5)(ii)
 45 CFR 46.113
 42 CFR 50 Subpart A
 21 CFR 56.113
 21 CFR 56.108(b)(3)

OHRP Guidance Document, "Guidance on Continuing Review" dated July 11, 2002

HRP Policy 53, "Reporting to the Appropriate Institutional Officials, and the Department or Agency Head(s)"

Procedure Number: 51.A

Title: Procedure for Administrative Hold, Suspension, and Termination of IRB Approval

Procedure:

This procedure outlines the circumstances and methods in which a study's approval status may be changed and subsequently reinstated.

I. Lead Researcher (LR) Responsibilities

A. Investigator-Imposed Administrative Hold

1. LR notifies the IRB in writing (via UP, NIR, or MOD) of study activities or recruitment and enrollment activities placed on administrative hold.
2. The LR responds promptly to any requests for additional information from the IRB Committee. In addition, the LR cooperates with the IRB in complying with all recommended education and/or compliance interventions designated by the IRB Committee.
3. The LR contacts the sponsor for any information that he/she cannot provide to the IRB addressing the possible change in risk-potential benefit profile.
4. During the time in which a study is on administrative hold, unanticipated problems and serious or continuing noncompliance continue to be reported to the IRB.
5. The LR promptly notifies the IRB in writing of the intent to remove the administrative hold prior to implementing.

B. FDA, Sponsor, or DSMB-Imposed Hold or Suspension Unrelated to Potential Risk

1. The notice of hold or suspension or its subsequent removal is forwarded to the IRB as a modification request as soon as possible after the LR first learns of the notice of suspension or its removal.
2. Research activities cease as specified in the hold or suspension notice until the study is re-opened and the IRB acknowledges the notification by approving the modification.
3. Unanticipated and serious or continuing noncompliance are still reported to the IRB.

C. FDA, Sponsor, or DSMB-Imposed Hold or Suspension for Potential Risk

1. LRs forward any correspondence indicating a hold or suspension imposed for potential risk, to the IRB via the UP or NIR reporting process as soon as possible, but no later than 5 working days after the LR first learns of the notice of hold or suspension, for full Committee review and approval.
2. Research activities cease as specified in the hold or suspension notice until the study is re-opened by the entity and the full IRB Committee has reviewed and approved a modification request to reinstate the study. Also, the IRB may determine additional criteria for suspension or for re-opening the study.
3. Unanticipated problems and serious or continuing noncompliance are still reported to the IRB.

D. IRB-Imposed Suspensions

1. Research activities cease, as specified in the suspension criteria, until the LR is notified that the full IRB Committee has granted approval of the study to resume. It is within the authority of the IRB to terminate the study.
2. The LR cooperates with the IRB in complying with all corrective actions as designated by the IRB Committee.
3. The LR notifies the sponsor of the UC Irvine IRB imposed suspension/reinstatement.
4. The LR is responsible for notifying all affected participants of the suspension, as required by the IRB.

5. The LR submits the script or letter to the IRB for approval prior to notification to participants.
 6. Unanticipated problems and serious or continuing noncompliance are still reported to the IRB.
- E. IRB-Imposed Terminations
1. The LR ceases all study related activities and notifies the sponsor of the termination of UC Irvine IRB approval.
 2. The LR is responsible for notifying all affected participants of the termination, as required by the IRB.
 3. The LR submits the script or letter to the IRB for approval prior to notification to participants.
 4. Unanticipated problems and serious or continuing noncompliance are still reported to the IRB.
- F. Study Expiration
1. The LR completes all continuing review requirements promptly.
 2. Research activities cease until the IRB has determined continuing review requirements are met and approval is granted.
 3. Enrollment of new participants and interaction of already enrolled participants cannot occur after the expiration of IRB approval.
 4. The LR may provide justification in writing to the IRB Committee for continuing treatment of participants to avoid additional risk or if the drug is available outside the research study.
 5. Unanticipated problems and serious or continuing noncompliance are still reported to the IRB.

II. IRB Committee Responsibilities

- A. Investigator-Imposed Administrative Hold
1. Once the information requested from the LR has been received and reviewed by the IRB Chair or his/her designee, or the IRB Committee, one of the following determinations occur:
 - a) The IRB Chair or his/her designee can determine that the incident does not require convened IRB review or
 - b) The IRB Chair refers the study to the convened IRB for review and further determination.
 2. The IRB Chair or the IRB Committee may require education and/or directed audits be conducted by the IRB Education and Quality Improvement (EQUIP) Team.
 3. The IRB Chair or the IRB can suspend the research and report the suspension in accordance with the UCI HRP policy on reporting (See HRP Policy 53).
 4. The IRB Chairperson or his/her designee may consult, as needed, with the IRB Working Group (a group made up of other IRB Chairs and Vice Chairs, and some HRP staff) regarding the particular project and/or the LR.
- B. FDA, Sponsor, or DSMB-Imposed Hold or Suspension Unrelated to Potential Risk
1. Notification of a hold or suspension and the reinstatement of research for issues unrelated to risks are reviewed as a modification request by expedited procedures and approved by the IRB Chairperson or his/her designee.
- C. FDA, Sponsor, or DSMB-Imposed Hold or Suspension for Potential Risk
1. Notification of a hold or suspension possibly related to risk is received via the UP or NIR reporting process is reviewed by the IRB Chair or his/her designee, or the IRB Committee, one of the following determinations occur:
 - a) The IRB Chair or his/her designee can determine that the incident does not require convened IRB review or

- b) The IRB Chair refers the study to the convened IRB for review and further determination.
 - 2. The IRB Chair or the full IRB Committee may suspend the research. However, the IRB Committee may impose additional restrictions upon research conducted under its jurisdiction.
 - 3. Re-instatement of the research by the FDA, Sponsor, or DSMB is submitted to the IRB as a modification request and approved by the IRB Committee.
 - 4. The IRB notifies the LR in writing of its determinations.
- D. IRB-Imposed Suspensions
 - 1. IRB Chair or his/her designee, or the IRB Committee may suspend at study.
 - 2. The IRB may review a study for Suspension at a full IRB Committee meeting. Examples of these types of circumstances include:
 - a) Failure to comply with prior conditions imposed in writing by the IRB under a Suspension;
 - b) Repeated or deliberate failure to obtain or document informed consent from human participants;
 - c) Repeated or deliberate failure to comply with conditions placed on the study by the University, IRB, Sponsor, or FDA;
 - d) Repeated or deliberate failure to obtain prior review and approval of new protocols and on-going human subjects research by the IRB;
 - e) Repeated or deliberate failure to maintain accurate study records or submit required unanticipated problems involving subjects or others to the IRB;
 - f) Repeated or deliberate falsification or concealment of study records, e.g., by substituting in study records the results of biological samples from participants who met the inclusion criteria for samples of participants who did not meet the inclusion criteria, or by fabricating participants.
 - 3. Prior to presentation at full Committee, the IRB Chair or his/her designee is encouraged to present the details at the IRB Working Group for an open discussion and dialogue to assist the Committee Chairperson in organizing and prioritizing a presentation of the facts for consideration and vote at the next IRB Committee meeting. This promotes consistency and compliance across all IRB Committees.
 - 4. In addition, the Committee may request an ad hoc review from an independent source with expertise in the type of research being conducted or in the specific area of concern.
 - 5. The options for suspension are:
 - a) Suspension of the research; or
 - b) Suspension to recruitment;
 - c) Suspension to screening/enrollment;
 - d) Suspension to interaction/intervention;
 - e) Suspension to analyses with private, identifiable data; and/or
 - f) Suspension to follow-up.
 - 6. The IRB notifies the LR in writing of its decision to suspend the study for cause and provides a rationale for its actions. This letter includes an opportunity for the LR to respond to the Committee's determinations. The IRB Committee may ask the LR to attend the meeting to discuss the suspension and provide clarification of the issues.
 - 7. The Committee may request the development of an education plan and/or the completion of a directed audit by the IRB EQUIP Team.
 - 8. Suspensions for cause are reinstated for approval after corrective actions are completed to the IRB Committee's satisfaction. The Committee may approve the study with or without additional restrictions (e.g., mandating a data and safety monitoring committee to oversee the research at designated intervals, increase in the

frequency of IRB Committee review, observation of the consent process, etc.)

E. IRB-Imposed Terminations

1. The IRB reviews a study for Termination at a full IRB Committee meeting.
2. Only the IRB Committee can terminate research.
3. Prior to presentation at full Committee, the IRB Chairperson or his/her designee is encouraged to present the details at the IRB Working Group for an open discussion and dialogue to assist the Committee Chairperson in organizing and prioritizing a presentation of the facts for consideration and vote at the next IRB Committee meeting. This promotes consistency and compliance across all IRB Committees.
4. In addition, the Committee may request an ad hoc review from an independent source with expertise in the type of research being conducted or in the specific area of concern.
5. The IRB notifies the LR in writing of the decision to terminate the study for cause and provide a rationale for its actions. This letter includes an opportunity for the LR to respond to the Committee's determinations. The IRB Committee may ask the LR to attend the meeting to discuss the termination and provide clarification of the issues.

F. Reporting of IRB-Imposed Suspensions or Terminations

1. All IRB-Imposed Suspensions or Terminations for Cause are promptly reported per HRP Policy 53.
2. The institution may determine that suspensions or terminations associated with a particular study or an LR are repetitive and warrant action for issues of serious and continuing non-compliance.

G. Expiration of Approval

1. The IRB notifies the LR in writing of the pending Expiration.
2. Expired studies may be granted approval after the continuing review requirements are completed and approved at the appropriate level of review for which the study currently qualifies.
3. The IRB Chair or designated Committee Member may review the submitted justification for continuing treatment of participants to avoid additional risk or if the drug is available outside the research study.

III. **Human Research Protections Staff Responsibilities**

A. Investigator-Imposed Administrative Hold

1. The HRP staff (or EQUIP team) notifies the Executive Director of Research Protections or designee within 1 working day of any Investigator requests for Administrative Hold.
2. The HRP staff (or EQUIP team) assists the Committee in obtaining any additional information needed for the Chairperson or his/her designee to determine if a change in the risk-potential benefit profile has occurred.
3. The EQUIP Team completes directed audits and/or develops an education plan as deemed appropriate by the IRB Committee. The EQUIP Team is available as a resource to the LR.
4. The HRP staff (or EQUIP team) updates the HPS database accordingly with the current status of the research.

B. FDA, Sponsor, or DSMB-Imposed Hold or Suspension Unrelated to Potential Risk

1. The HRP staff processes the modification request for notification of a hold or a suspension unrelated to risk for administrative acknowledgement. This may occur via expedited review.
2. The HRP staff update the HPS database accordingly with the current status of the research.

3. In the case that the FDA, sponsor, or DSMB has halted enrollment of new subjects, HRP Staff will remove the IRB approved recruitment materials and consent documents from the IRB Document Depot.
- C. FDA, Sponsor, or DSMB-Imposed Hold or Suspension for Potential Risk
1. The HRP staff (or EQUIP team) processes the UP or NIR report for notification of a hold or suspension due to possible risk for full Committee review.
 2. The HRP staff (or EQUIP team) notifies the LR in writing of the IRB Committee's determinations.
 3. The HRP staff (or EQUIP team) assists the Committee in obtaining any additional information needed for the Chairperson or his/her designee to determine if a change in the risk-benefit profile has occurred.
 4. The HRP staff (or EQUIP team) processes the modification request to report reinstatement of the research by the sponsor for full Committee review.
 5. The HRP staff (or EQUIP team) updates the HPS database accordingly with the current status of the research.
 6. In the case that the FDA, sponsor, or DSMB has halted enrollment of new subjects, HRP Staff (or EQUIP team) will remove the IRB approved recruitment materials and consent documents from the IRB Document Depot.
- D. IRB-Imposed Suspensions
1. The HRP Staff (or EQUIP team) notifies the LR in writing of IRB determinations.
 2. The HRP Staff (or EQUIP team) assists the Committee in obtaining information from the LR. The HRP Staff and the EQUIP Team keeps each other apprised of all corrective actions to be taken by the LR and their status.
 3. The EQUIP Team completes a directed audit and/or develops an education plan as deemed appropriate by the IRB Committee. The team is available as a resource to the LR.
 4. The HRP Staff (or EQUIP team) notifies Executive Director of Research Protections or designee within 1 working day of any Suspensions.
 5. The HRP Staff (or EQUIP team) updates the HPS database accordingly with the current status of the research.
 6. The Executive Director of Research Protections or designees promptly reports the suspension for cause per HRP Policy 53
 7. In the case that the IRB has halted enrollment of new subjects, HRP Staff (or EQUIP team) will remove the IRB approved recruitment materials and consent documents from the IRB Document Depot.
- E. IRB-Imposed Terminations for Cause
1. The HRP Staff (or EQUIP team) notifies the LR in writing of IRB determinations. The letter requires a signature of the Chairperson or his/her designee.
 2. The HRP Staff (or EQUIP team) promptly notifies the Executive Director of Research Protections or designee within 1 working day of any Terminations.
 3. The HRP Staff (or EQUIP team) updates the HPS database accordingly with the current status of the research.
 4. The Executive Director of Research Protections or designees promptly reports the termination for cause are per HRP Policy 53
 5. HRP Staff (or EQUIP team) will remove the IRB approved protocol narrative, recruitment materials, and consent documents from the IRB Document Depot.
- F. Expiration of Approval
1. The HRP Staff assists the Committee in obtaining the additional information required to conduct continuing review of the research.
 2. The HRP staff assists the Committee in obtaining a closing report from the LR.