
Yale University Human Research Protection Program

700 PR.4 Suspension and Termination of Human Research Studies

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Overview

Each Yale Institutional Review Board (IRB) has the authority to suspend or terminate approval of all or part of a research study that is not being conducted in accordance with the IRB's requirements, University policy, or that has been associated with unexpected serious harm to participants (45 CFR §46.113; 21 CFR §56.113). Likewise, the sponsor, federal oversight agencies (e.g., U.S. Food and Drug Administration), other appointed University oversight committees and the local Yale Principal Investigator (PI) have the authority to place all or some of the research activities on hold or to close a research study 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 study by the IRB, as well as the steps necessary for a PI, sponsor, or other oversight body to place a research study on hold (partial or full) or to terminate a research study.

Suspension or Termination by the IRB

Formal Suspension: A fully-convened IRB may suspend part or all of a research study when the IRB determines it to be in the best interest of participants to temporarily stop some or all research-related activities (45 CFR §46.113; 21 CFR §56.113). Studies may be suspended during the investigation and evaluation of an allegation of noncompliance or a human subject safety issue.

In addition, the IRB Chair or designee is authorized to take immediate action to protect the health and safety of research participants. Such action may take the form of: (i) asking the PI to voluntarily impose a partial or full hold on the recruitment and enrollment of participants to facilitate further inquiry by the IRB and/or institutional officials; (ii) asking the PI to voluntarily impose a partial or full hold on a research intervention to facilitate further inquiry by the IRB and/or institutional officials; (iii) suspending recruitment or enrollment; (iv) altering or suspending current interventions or interactions; or (v) suspending the research project entirely.

Any such action of the IRB Chair will be documented in the IRB record immediately. If the IRB Chair imposes a partial or complete suspension, the IRB Chair will immediately report the suspension to the Institutional Official. The IRB Chair shall report to the convened IRB at its next regularly scheduled meeting of any such action taken.

Formal Termination: A fully-convened IRB may terminate the IRB approval of a research study when it is believed to be in the best interest of participants to permanently stop research-related activities (45 CFR §46.113; 21 CFR §56.113).

A fully-convened IRB has the authority to make a determination to suspend or terminate a research study on an urgent basis. For biomedical studies, one of the IRBs meets each week and therefore, such a determination could be made within seven (7) days. The social, behavioral and educational IRB meets monthly. In the event that the determination must be made prior to the next regularly scheduled IRB meeting, a special IRB meeting may be convened, for which one or more members of the IRB may participate by teleconference, videoconference or other electronic means and shall be counted toward meeting quorum. (See 100 PR.1 – Review by Convened Institutional Review Board (IRB)).

Notification: When a fully-convened IRB makes a decision to suspend or terminate approval of any research study for any reason, the IRB will notify the following individuals in writing within five (5) working days: the PI and where applicable, the Faculty Advisor, the Department Chair involved in the research, and the Institutional Signatory Official. Such notification will include the reason for the suspension or termination (45 CFR §46.113; 21 CFR §56.113).

Where applicable, the IRB will also notify within thirty (30) days the Office of Grant and Contract Administration (GCA), the Office of Grant & Contract Financial Administration (GCFA); the Office for Human Research Protections (OHRP); the U.S. Food and Drug Administration (FDA); the funding agency and for other institutions participating in the research, the HRPP Administrator(s) and the IRB Chair(s) of those institutions (45 CFR §46.103(b)(5); 45 CFR §46.113; 21 CFR §56.113).

Request by the Principal Investigator for a Voluntary Hold or Closure

A Principal Investigator (PI) may request that his/her own research study be put on a full or partial (e.g., recruitment only) hold or closed at any time if he/she believes such action is necessary to protect the safety and welfare of research participants or the integrity of the study. Examples of situations in which a PI may decide to put his/her research study on a voluntary hold include the following: as a result of a review or monitoring of study data, upon recommendation from Data and Safety Monitoring Boards or Committees, prior to or during an investigation of an allegation of noncompliance, following adverse events or an unanticipated problem involving risks to subjects or others (UPIRSO).

When a PI determines that it is in the best interest of the participants to close his/her research study prior to completion or to place the study on hold, the PI must notify the IRB of his/her decision within five (5) business days in writing and must provide the IRB with the reasons why the study is being placed on hold or closed. If only some of the study activities will be placed on hold (such as suspension of enrollment) then the PI 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 participants, corrective actions, or investigation is required. The IRB will notify the PI in writing regarding whether or not the IRB concurs or if additional actions are required.

Notice of a Hold or Closure by the Sponsor

A sponsor may decide to close a research study or to put a research study on a full or partial hold at any time it believes such action is necessary to protect the safety and welfare of research participants or the integrity of the study. When a PI receives notification from a sponsor that the research study is being closed or is being put on a full or partial hold, the PI must inform the IRB of the sponsor's decision within five (5) business days and provide the IRB with a copy of the sponsor's notification. If only some of the study activities will be placed on hold (such as suspension of enrollment) then the PI 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 participants, corrective actions, or investigation is required. The IRB will notify the PI in writing regarding whether or not the IRB concurs with the action of the sponsor and if additional actions are required.

Request for a Clinical Hold or Closure by an Oversight Body

An oversight body, such as a Data Safety and Monitoring Board (DSMB), the Yale Cancer Center Data and Safety Monitoring Committee (DSMC), or the FDA, may request that a research study be closed or put on a full or partial hold any time it believes such action is necessary to protect the safety and welfare of research participants or the integrity of the study. (21 CFR §312.42) When a PI receives notification from an oversight body that the research study must be closed or put on a full or partial hold, the PI must inform the IRB within five (5) business days of receipt of such notification and provide the IRB with a copy of the written notification from the oversight body. If only some of the study activities will be placed on hold (such as suspension of enrollment) then the PI 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 participants, corrective actions, or investigation is required. The IRB will notify the PI in writing regarding whether or not the IRB concurs with the action of the oversight body and if additional actions are required.

Obligations to Participants

If a research study will be put on hold (either partial or full), suspended, terminated or closed, several steps must be taken to ensure the protection of research participants as described below:

1. If current participants will be withdrawn from some or all research-related activities, then the PI must submit to the IRB proposed procedures for withdrawal of currently enrolled participants that considers such participants' rights and welfare. The withdrawal plan must include a proposed script or letter to notify all currently enrolled participants (and possibly any previously enrolled participants who are no longer actively participating in the study) who are affected by the hold, suspension or termination. The IRB will review the proposed withdrawal plan and may make recommendations to amend the plan or may approve the plan. If follow-up activities are permitted or required by the IRB, participants should be so informed and the PI should continue to report any events (e.g., serious adverse events or UPIRSOs) to the IRB and sponsor, as required.
2. If some of the research procedures will continue during a hold or suspension, the PI must submit to the IRB proposed procedures for adequate oversight of all aspects of the research that will continue.
3. If circumstances should warrant, the IRB may mandate oversight or transfer responsibility to another investigator to ensure implementation of the above listed requirements.

Activities During Suspension

In the event a research study is suspended, all research activities must cease unless the project involves therapeutic treatment or intervention and interrupting that treatment/intervention, in the opinion of the treating physician and with the approval of the IRB, would be detrimental to the research participant(s). Only in this case may the PI continue to provide such intervention. In all other cases, no study-related activities may continue unless explicitly authorized by the IRB including no further enrollment of new participants, administration of the research drug, device and/or therapy, and use of data (including data analysis) in which a subject identifier is attached.

In addition, research funds supporting the engaged human subject research activities of the study (e.g., recruitment and enrollment activities, data collection or data analysis) may not be expended during a suspension of the study. The PI is responsible for reporting the study suspension to the Office of Grant and Contract Administration (GCA).

Process to Reopen Studies which are Suspended or on Hold

To reopen a research study that has been suspended or put on hold, the PI must submit a request for reapproval, including a submission of the full protocol application with any amendments incorporated therein. The PI also must provide the IRB with a written explanation regarding how the issues that prompted the hold or suspension have been addressed and/or corrected, including the PI's proposed corrective and preventive action (CAPA) plan, if needed. The IRB will review and approve the reopening of the study once it determines that an acceptable CAPA has been implemented by the PI.

Revision History

February 25, 2013, and February 21, 2012