

## **SOP 6: SUSPENSIONS AND TERMINATIONS OF IRB APPROVAL OF RESEARCH PROTOCOLS**

### **1. Subject of Policy & Procedure**

Federal regulations 45 CFR 46.113 and 21 CFR 56.113 stipulate that the IRB “...shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with serious harm to subjects.” (emphasis added). These regulations further stipulate that “[a]ny suspension or termination. . . shall be reported promptly to the investigator, appropriate institutional officials, and [the sponsoring federal agency, if applicable].” In addition, CCC-UPR’s Federalwide Assurance Registration (FWA) requires that the Office for Human Research Protections (OHRP) receive reports of any suspension or termination of IRB approval of a research protocol.

Protocol Principal Investigators (Protocol PIs) who receive written notification to suspend or terminate a research study involving human participants must cease immediately all research activities for that project, including interactions with human participants, recruitment, analysis of data, publications, and presentations.

This policy sets forth which persons/entities have the authority to enact a suspension or termination of IRB approval; the circumstances under which a suspension or termination is required or may be enacted; and the processes by which a suspension or termination is enacted.

### **2. Scope of Policy & Procedure**

This Policy & Procedure applies to all on-going and future human participant research projects conducted by CCC-UPR faculty, staff, or students or by anyone conducting a research activity supported by CCC-UPR or where CCC-UPR is considered to be engaged in the research.

### **3. Terms and Definitions**

**Suspension** is defined as a temporary halt to all research activities. It occurs when the Chair of the IRB or the convened IRB places a temporary hold on the previously approved research, such that no research activities can be conducted, including recruitment/enrollment of new participants, further research interventions (unless necessary for the safety and well-being of the enrolled participants), follow-up (unless it is in the best interests of the participants and approved by the IRB), analysis of data, publications, and presentations. Suspended research is still subject to Continuing Review. Eventually, a notice of suspension is withdrawn by the IRB or the suspended

protocol becomes subject to termination procedures by the IRB. A Protocol PI may resume research upon withdrawal of a suspension notice.

**Termination** is defined as a permanent halt to all research activities, including recruitment/enrollment of new participants, further research interventions, analysis of data, publications, and presentations. It occurs when the convened IRB votes to withdraw approval or stop all research activities permanently. However, future follow-up may be conducted with the approval of the IRB to monitor the well-being of and any potential risks to participants. Terminated research is no longer subject to Continuing Review. Resumption of a terminated protocol requires the submission of a new protocol application for review and approval by the IRB.

In addition, all parties to whom this policy applies (*e.g.*, faculty, students, staff, IRB members) should consult the [IRB Glossary](#).

#### **4. Attachments**

All parties to whom this policy applies should also consult the CCC-UPR [Federalwide Assurance Registration](#).

#### **5. Regulations Applicable to Suspensions and Terminations of IRB Approval**

**5.1.** 45 CFR 46.113: “An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head.”

**5.2.** 21 CFR 56.113: “An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, and the Food and Drug Administration.”

**5.3.** 45 CFR 46.109; 21 CFR 56.109: IRB Review of Research, mandating IRB review and approval of human participant research.

**5.4.** 45 CFR 46.111; 21 CFR 56.111: Criteria for IRB Approval of Research.

#### **6. Circumstances Meriting Potential Suspension or Termination**

**6.1.** The IRB may suspend or terminate its prior approval of research that: (1) is not being conducted in accordance with IRB policies and procedures, the protocol as previously approved by the IRB, federal regulations, and/or institutional policies governing research and human participant protection (*i.e.*, non-compliance); or (2) is associated with serious unanticipated problems, as defined in [SOP 4: Unanticipated Problems Involving Risk to Human Research Participants or Others](#), Section 6.1: Unanticipated Problems Defined.

Examples of non-compliance with IRB policies and procedures are: (a) conducting research using human participants without IRB review and approval; (b) deviating from the protocol submitted by the Protocol PI and approved by the IRB; (c) continuing to use human participants past the approved expiration date and in the absence of submitting a continuation application to the IRB; (d) failing to follow the IRB-approved consent process; (e) failing to train student researchers in proper procedures; (f) failing to report protocol changes to the IRB; and (g) failing to follow recommendations by the IRB to ensure the safety of research participants.

The IRB may become aware of such a circumstance upon the receipt of a complaint from a participant, researcher, CCC-UPR employee, or member of the public; from the interpretation of information received during a Continuing Review; or from the findings of a random or for-cause audit.

- 6.2. The IRB Chair investigate all occurrences/reports of non-compliance, complaints received from participants, and serious unanticipated problems. Depending on the circumstances, they may elect to investigate the circumstances informally by reading relevant documents and communicating with the affected parties, or IRB may conduct an audit.

## **7. Authority to Suspend or Terminate IRB Approval & Related Authorities**

- 7.1. The convened IRB has the authority to suspend or terminate research activities, taking into consideration protections for current participants' rights and welfare. The IRB Chair also has the authority to suspend research until a convened IRB meeting and to report the suspension to the convened IRB at their next available meeting. The convened IRB must discuss suspensions of all protocols previously approved by the IRB. The Chair, however, does not have the authority to terminate IRB approval unilaterally.
- 7.2. A member of the IRB who is acting as the Expedited Reviewer of an Unanticipated Problem Report Form may request the IRB Chair to suspend a protocol until the convened IRB reviews and acts on the protocol. *See* [SOP 4: Unanticipated Problems Involving Risk to Human Research Participants or Others](#), Section 6.3.3: IRB Review of Unanticipated Problem Report Forms.
- 7.3. The Protocol PI may request a meeting with the IRB Chair regarding any decision to suspend and/or terminate a protocol. In addition, the Protocol PI may be present during the question-and-answer period of the convened IRB's discussion of his or her suspended protocol.
- 7.4. A Protocol PI may decide voluntarily to suspend or terminate some or all research activities that may be under current review or investigation. The Protocol PI should inform IRB of this action, and place the protocol on the agenda for the next available IRB meeting.
- 7.5. Neither the IRB has the authority to take disciplinary action against any individual relating to circumstances meriting suspension or termination of IRB approval. Instead, disciplinary action shall be the responsibility of the institution. The IRB Chair shall report any termination of

research to the appropriate institutional officials and will, if requested, assist in any disciplinary action process.

## **8. Procedures for Suspension or Termination of IRB Approval**

### **8.1. Criteria to Consider for Suspensions or Terminations**

In reviewing information, including complaints, that potentially shows non-compliance or unanticipated problems, the person(s) ordering a suspension or termination of IRB approval should consider:

- (a) Whether the information supports a determination of non-compliance or increased risk;
- (b) Whether the information indicates that a serious unanticipated problem has occurred which warrants further investigation and/or suspension of research in order to protect human participants or others;
- (c) Additional actions to protect the rights and welfare of currently enrolled participants;
- (d) Whether procedures for withdrawal of enrolled participants account for their rights and welfare;
- (e) Whether participants should be informed of the termination or suspension; and
- (f) Whether to require any unanticipated problems or outcomes to be reported to the IRB.

### **8.2. Suspensions by the Chair of the IRB**

**8.2.1.** If a reported occurrence is determined to be a serious adverse event, as defined in [SOP 4: Unanticipated Problems Involving Risk to Human Research Participants or Others](#), Section 6.1.2, the IRB Chair will instruct promptly to issue a suspension notice for the protocol until the convened IRB reviews and acts on the protocol. IRB will place the Unanticipated Problem Report Form (UP Report Form) on the agenda for the next available meeting of the convened IRB for their discussion and resolution.

**8.2.2.** If a reported occurrence is determined to be a serious unanticipated problem, as defined in [SOP 4: Unanticipated Problems Involving Risk to Human Research Participants or Others](#), Section 6.1.2, the IRB Chair will review the UP Report Form and other relevant information, including the Protocol PI's plan to minimize risk for subsequent human participants. If the unanticipated problem is sufficiently serious or if the plan to minimize risk in the future is inadequate, the IRB Chair will instruct to issue a suspension notice to the Protocol PI.

**8.2.3.** As mentioned above in Section 7.2, a member of the IRB who is acting as the Expedited Reviewer of a UP Report Form may request the IRB Chair to suspend a protocol until the convened IRB reviews and acts on the protocol. IRB Chair will issue the suspension notice.

- 8.2.4.** Information or complaints indicating non-compliance or increased risk will be forwarded to the IRB Chair for review. If the Chair determines that the information supports a suspension and/or termination, the Chair will instruct to issue a suspension notice pending further investigation.
- 8.2.5.** The IRB Chair or the convened IRB may suspend the approval of research projects at any time during an inquiry or audit to assure the protection of human participants.
- 8.2.6.** Upon being instructed to issue a suspension notice, IRB will draft and finalize a formal letter to the Protocol PI outlining the reason(s) for the suspension and either proposing a corrective plan to be implemented within a certain timeframe or requesting a corrective plan and a completion timeline from the Protocol PI. The letter will also inform the Protocol PI that further information may be provided after discussion of the suspension by the convened IRB. The convened IRB must discuss suspensions of all protocols previously approved by the IRB.
- 8.2.7.** The IRB Chair may determine, unilaterally or in conjunction with the convened IRB that participants should be notified of the suspension. In this case, the Protocol PI will draft a notification letter to all participants, will mail after it has been approved by the IRB Chair.
- 8.2.8.** Until the Protocol PI receives written notification from the IRB approval has been reinstated following a suspension notice, he or she may not use human participants (including analyzing identifiable data or working with human biological materials) in the suspended study.

### **8.3. Resolution of Suspensions by the Convened IRB**

- 8.3.1.** Whenever the IRB Chair instructs to issue a suspension notice for a protocol, IRB will place the suspension as a discussion item on the agenda for the next available convened meeting of the IRB and provide the IRB with all relevant information, including the protocol, any UP/SAE Report Form, and any investigation results. The Chair and members of IRB will discuss the situation and recommend a plan of action. The Protocol PI may be invited or may request to attend part of the meeting to answer questions. The particular details of the discussion are documented by IRB in the minutes of the convened meeting.

The IRB will suggest a corrective plan that minimizes risks to participants or effects compliance with all applicable policies and regulations and will establish a time frame for the implementation of the plan.

- 8.3.2.** IRB will monitor the Protocol PI's implementation of the corrective plan based on a pre-determined action plan. If the plan is implemented within the requisite timeframe, the convened IRB or the IRB Chair may withdraw the suspension notice and research may resume. If, however, the suspension has not been resolved by the Protocol PI after the

expiration of the timeframe, the IRB Chair may place the suspension on the agenda of the next available meeting of the convened IRB in order to proceed with termination of IRB approval.

**8.3.3.** At any time before, during, or after the issuance of a suspension notice, the IRB Chair may instruct to conduct an audit. The results of the audit will be provided to the IRB Chair, the members of the IRB, and if appropriate, the Institutional Official. These audit results will inform the convened IRB's decision regarding termination of the research.

#### **8.4. Terminations by the Convened IRB**

**8.4.1. Criteria for Termination:** The convened IRB may vote to terminate IRB approval of a research protocol when:

- (a) the IRB determines at any time that termination is in the best interests of the safety and welfare of the research participants; and/or
- (b) a corrective plan approved by the IRB has not been implemented in a complete and satisfactory manner

**8.4.2. Written Notifications:** If the convened IRB votes to terminate a research protocol, IRB will notify, in writing, the following five parties:

- (a) Protocol PI
- (b) Institutional Official
- (c) Department Chair, Center Director of the Protocol PI
- (d) CCC-UPR's Office of Sponsored Programs, when applicable
- (e) Sponsoring federal agency, when applicable
- (f) OHRP, when applicable

These reports will be made in accordance with [SOP 7: Reporting of Unanticipated Problems, Noncompliance, Suspensions and Terminations to Regulatory Agencies and Sponsors](#).

The Protocol PI will also draft a written notification of a termination, in accordance with [SOP 9: Informed Consent Options, Processes and Documentation](#). PI will mail the notification letter after it has been approved by the IRB Chair.

**8.4.3. Audits:** At any time before, during, or after the issuance of a termination notice, the IRB Chair or the convened IRB may instruct to conduct an audit. The results of the audit will be provided to the IRB Chair, the members of the IRB, and if appropriate, the Institutional Official. The audit results will be used, in part, to inform future educational and training initiatives by IRB to ensure compliance by researchers.

**8.4.4. Withdrawal of Participants:** Within a set number of days specified by the convened IRB following a vote of termination by the convened IRB, the Protocol PI must submit to IRB

a detailed plan for safe withdrawal of participants from the research. In developing the plan, the Protocol PI may consult the IRB Chair or other members. IRB will place this plan on the agenda for the next available meeting of the convened IRB. All IRB members should be prepared to discuss the withdrawal plan. The withdrawal plan will be finalized by the Protocol PI to account for any procedures advised by the IRB. IRB will monitor the Protocol PI's completion of withdrawal procedures.

**8.4.5. Follow-Up of Participants:** The IRB may determine that follow-up of research participants by the Protocol PI or another researcher would promote their safety. As with the withdrawal of participants, the Protocol PI must submit and the IRB must approve a plan detailing follow-up procedures. In developing the plan, the Protocol PI may consult the IRB Chair or other IRB members. IRB will place this plan on the agenda for the next available meeting of the convened IRB. All IRB members should be prepared to discuss the follow-up plan. The follow-up plan will be finalized by the Protocol PI to account for any procedures advised by the IRB. PI will notify the participants of the follow-up period and procedures in their notice of termination. Any outcomes, including unanticipated problems, identified during the follow-up period, should be reported to the IRB Chair and handled as appropriate. *See [SOP 4: Unanticipated Problems Involving Risk to Human Research Participants or Others](#).* Federal authorities should be notified, if necessary, in accordance with [SOP 4](#) and [SOP 7: Reporting of Unanticipated Problems, Noncompliance, Suspensions and Terminations to Regulatory Agencies and Sponsors](#).

**8.4.6. Resuming Terminated Research Protocol:** If a Protocol PI wishes to resume a research protocol that has been terminated, he or she must submit an entirely new protocol application for IRB review and approval.

## **8.5. Termination of Research Activities Conducted before IRB Review and Approval**

Upon the first awareness by the Protocol PI, the IRB, or the Director of the Division of Research and Education support that the Protocol PI has conducted research activities that did not receive prior approval by the IRB, the Protocol PI must cease (or be instructed to cease) all such activities permanently. When a Protocol PI has engaged in research activities without prior IRB review and approval, the following actions are required:

**8.5.1.** The Protocol PI must submit an Unanticipated Problem Report Form for IRB review, in accordance with [SOP 4: Unanticipated Problems Involving Risk to Human Research Participants or Others](#). The report must give a detailed accounting of the research activities, including when they occurred.

**8.5.2.** IRB will conduct an audit of the research activities, at the request of the IRB Chair, the convened IRB, or the Executive Director.

**8.5.3.** All data collected during these activities must be turned over to IRB, including hard copies and information from computer hard drives or other electronic media such as CDs,

DVDs, and audio and video tapes. IRB will retain only one copy of all data to be kept in a sequestered, secured file. The rest of the data will be destroyed by shredding or other appropriate methods. The Protocol PI must submit to IRB a written statement certifying that all data has been turned over, the date of the turnover, and the method of removing all electronically-stored data.

**8.5.4.** The Protocol PI's certification of data turnover must also include a statement that the Protocol PI will never use the data for any future research or publications or presentations.

## **8.6. Documentation of Suspensions and Terminations**

All documents relating to suspension and terminations of a research protocol will be maintained by IRB for a period of not less than **5 years**.

These documents include but are not limited to: notices of suspension and termination; correspondence with the Protocol PI; UP/SAE Report Forms; withdrawal and follow-up plans; and data destruction certifications.