

**HRPP STANDARD OPERATING PROCEDURE/POLICY APPROVAL &  
IMPLEMENTATION**

**OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS**

**SOP Number: 11**

**SOP Title: SUSPENSIONS AND TERMINATIONS OF IRB APPROVAL AND  
ADMINISTRATIVE HOLDS**

**Distribution: Scientific Directors; Clinical Directors; Clinical Investigators, IRB  
Chairs, IRB Administrators, Protocol Navigators**

**Revision Approval:**

  
\_\_\_\_\_  
**Deputy Director for Intramural  
Research**

9/4/15  
**Date**

**Revision Implementation date:** \_\_\_\_\_

9/4/2015

**Materials Superseded: SOP 11 (rev. 2), dated 10-1-2013**

**SOP 11 – SUSPENSIONS AND TERMINATIONS OF IRB APPROVAL AND ADMINISTRATIVE HOLDS**

**TABLE OF CONTENTS**

**11.1 PURPOSE.....1**  
**11.2 POLICY .....1**  
**11.3 DEFINITIONS.....1**  
**11.4 ENTITIES AUTHORIZED TO REQUEST SUSPENSION OR TERMINATION OF IRB APPROVAL .....1**  
**11.5 REQUIRED IRB ACTIONS RELATED TO SUSPENSION OR TERMINATION.....2**  
**11.6 IRB NOTIFICATION OF SUSPENSION, OR TERMINATION .....3**  
**11.7 REQUIRED PI ACTIONS FOLLOWING SUSPENSION OR TERMINATION.4**  
**11.8 RESUMPTION OF RESEARCH ACTIVITIES AFTER A SUSPENSION .....5**  
**11.9 REQUEST FOR IRB RECONSIDERATION OF A TERMINATED STUDY.....5**  
**11.10 REPORTING SUSPENSIONS AND TERMINATIONS TO NIH INSTITUTIONAL OFFICIALS AND REGULATORY AGENCIES .....6**  
**11.11 ADMINISTRATIVE HOLD .....6**  
**11.12 RESUMPTION OF RESEARCH ACTIVITIES AFTER AN ADMINISTRATIVE HOLD .....8**  
**REFERENCES .....8**

## **SOP 11 – SUSPENSIONS AND TERMINATIONS OF IRB APPROVAL AND ADMINISTRATIVE HOLDS**

### **11.1 PURPOSE**

This SOP describes the procedures and responsibilities of NIH PIs, NIH IRBs and other NIH officials when an IRB suspends or terminates a protocol or when another authorized NIH entity or official, not the IRB, places an administrative hold on a research study. Study closures initiated by the PI are described in SOP 11A - Closure of an IRB-approved Protocol.

### **11.2 POLICY**

An IRB may suspend or terminate a study if research is not being conducted in accordance with Federal regulatory requirements, IRB requirements, NIH policies, or if the study has been associated with unanticipated problems or serious harm to subjects. (See 45 CFR 46.113 and 21 CFR 56.113, if applicable.) Certain other NIH individuals and entities have authority to place an administrative hold on a protocol or close a protocol (see SOP 11A – Closure of an IRB-approved Protocol).

### **11.3 DEFINITIONS**

- A. **Suspension** of IRB approval of a research study is a temporary directive by an NIH IRB (see **11.4** below) to stop some or all previously IRB-approved research activities conducted under an IRB-approved research protocol. Suspended protocols remain administratively open and require continuing review.
- B. **Termination** of IRB approval is a directive of a convened NIH IRB to permanently stop all activities in a previously NIH IRB-approved research protocol. Terminated studies are considered closed and no longer require continuing review.
- C. **Administrative Hold** is a temporary stop, initiated by a Principal Investigator, or other authorized NIH official or entity other than an IRB, to stop some or all previously IRB-approved research activities conducted under an IRB-approved research protocol.

### **11.4 ENTITIES AUTHORIZED TO REQUEST SUSPENSION OR TERMINATION OF IRB APPROVAL**

- A. Suspension: The following parties may request suspension of an IRB approved research study:

1. The IRB Chair or Vice Chair, if delegated by the Chair.
2. Any IRB member or members at the convened IRB meeting.
3. The Institutional Official (IO) currently the Deputy Director of Intramural Research (DDIR) or designee.
4. Other senior NIH officials, such as the Institute Director/Clinical Director or Director, Clinical Center.

The IRB has the final authority for making determinations for actions characterized as suspensions, including whether and/or how an approved research study will be suspended.

- B. Termination: The following parties may request termination of an IRB approved research study:

1. The IRB Chair or Vice Chair, if delegated by the Chair.
2. Any IRB member or members at the convened IRB meeting.
3. The Institutional Official (IO, the Deputy Director of Intramural Research (DDIR)) or designee.
4. Other senior NIH officials, such as the Institute Director/Clinical Director or Director, Clinical Center.

The IRB has the final authority for making determinations for actions characterized as terminations, including whether and/or how an approved research study will be terminated.

- C. Data from terminated protocols may be used for research purposes only after the proposed new research receives prospective approval by an NIH IRB or, when appropriate, OHSRP/IC designee (see SOP 5 – NIH Research Activities with Human Data/Specimens).

## 11.5 REQUIRED IRB ACTIONS RELATED TO SUSPENSION OR TERMINATION

- A. Urgent situations: The IRB Chair/designee may suspend a protocol in an urgent situation if, in his/her judgment, immediate action is required to protect subjects. See Revised SOP 16 - Reporting Requirements for Unanticipated Problems, Adverse Events and Protocol Deviations).

However, the full IRB must convene and vote regarding action to terminate a protocol.

- B. Upon the IRB's determination to suspend or terminate all or some parts of a of a research study, the IRB will promptly notify the PI in writing of:
  - 1. The IRB's decision, including a statement of the reasons for the suspension/termination. The investigator will be given an opportunity to respond in writing.
  - 2. Work with the PI to develop a plan to protect the rights, safety and welfare of enrolled subjects, if any.
  - 3. Review, and take action on as needed, the PI's termination/suspension plan (including as described in 11.6.A.4, below). The IRB will notify the PI and the CC, Office of Protocol Services (OPS), in writing, of what activities, if any, are authorized to continue and conditions for such continuation.
- C. The IRB may require that subjects be informed of the suspension/termination. Written communication to the subjects requires prospective IRB approval.
- D. Prospective IRB approval must be obtained if the researchers wish to re-contact former subjects after study termination to provide the subjects with additional study-related information.

## 11.6 IRB NOTIFICATION OF SUSPENSION, OR TERMINATION

- A. Upon suspension or termination by the IRB, the IRB will notify the PI, IC leadership (Clinical Director), OPS and OHSRP. The Director of the Clinical Center will be notified by the IRB of any suspensions or terminations occurring on protocols implemented in the Clinical Center. The IRB will stipulate that for terminations, the PI will submit a Clinical Study Closure Application consistent with SOP 11 A – Closure of an IRB-approved protocol and, as applicable, provide responses to items noted in section 11.7. The IRB notification will include the following information:
  - 1. The reasons for the suspension or termination.
  - 2. The effective date of the suspension or termination.
  - 3. Delineation of the effect of the suspension or termination on study activities such as enrollment, recruitment, interventions, interactions and data analysis.

4. PI responsibilities (**section 11.7** below) with regard to the suspension or termination.

### **11.7 REQUIRED PI ACTIONS FOLLOWING SUSPENSION OR TERMINATION**

- A. When informed of a suspension or termination, the PI is responsible for:
  1. Complying with the suspension/termination and notifying all other study investigators and sites, if any.
  2. If designated by the IRB, the PI is responsible for notifying the non-Clinical Center institutions and departments involved as well as the sponsor, as applicable, of the suspension/termination.
  3. If the PI believes that subject(s) may be harmed by the suspension/termination of research activities, he/she must submit a written request to the IRB that includes:
    - a. A rationale or justification for the continuation of specific research activities related to preventing subject harm.
    - b. Delineation of the procedures needed to prevent harm to currently enrolled subjects.
    - c. The number and type of subjects for whom research activities will need to continue.
    - d. Proposed duration of research activities needed to prevent harm to enrolled subjects.

Note: Based on the protocol and information from the PI, the IRB Chair, or designee, or the full IRB may determine that specific research activities may continue for affected subjects and may place conditions on the continuation. The IRB will provide written documentation to the investigator about which study activities may continue for affected subjects and any conditions for continuation.

4. Submitting a suspension/termination plan for IRB review and approval, including:
  - a. Procedures to notify currently-enrolled subjects of the suspension or termination of the study and the implications for their participation, health and welfare.

Note: Communications with subjects regarding suspensions/terminations require IRB approval.

- b. Procedures for withdrawal of enrolled subjects that take into consideration their rights and welfare.
- c. Procedures to ensure that subjects are informed of any study-related procedures permitted or required by the IRB.
- d. Ensuring that adverse events and unanticipated problems involving risks to subjects or others continue to be reported to the IRB and other regulatory bodies during continuation of any permitted activities.
- e. Completing continuing reviews in a timely manner for suspended studies.
- f. Notifying the NIH IRB if a multi-site study is suspended or terminated by the lead site.

#### **11.8 RESUMPTION OF RESEARCH ACTIVITIES AFTER A SUSPENSION**

- A. An NIH IRB can approve resumption of suspended research activities if the issues that led to the suspension have been resolved. If a PI wishes to request removal of the suspension, the PI must submit a written memorandum with the following information:
  1. Justification for resumption.
  2. Identification of the issues leading to the suspension and explanation of how they have been resolved.
  3. A description of any changes needed to the protocol or consent document(s) in response to the issues related to the suspension.
- B. A formal amendment (request for modification) must be separately submitted for IRB approval before any changes can be implemented (see SOP 10 – Amendments to IRB-approved Research).

#### **11.9 REQUEST FOR IRB RECONSIDERATION OF A TERMINATED STUDY**

- A. When a PI disagrees with the IRB's decision, it is expected that the disagreements can be resolved amicably. An IRB or PI may, through a

request to the OHSRP, elicit the input of the Institutional Official (IO) for assistance in resolving the matter.

- B. The IO may organize, or delegate OHSRP to organize, a meeting to help facilitate resolution of concerns.
- C. While the IO may provide recommendations to the IRB to help resolve the matter, final determinations rest with the IRB.
- D. Because the Institutional Official (the DDIR) is responsible for policies and procedures followed by the NIH HRPP, including its IRBs, he may review IRB decisions to ensure that the IRB's decision-making processes were appropriate (for example, it followed NIH HRPP SOPs, etc.). If the DDIR has concerns about these IRB processes and procedures, he may request IRB reconsideration of the issue/decision. However, if an IRB terminates research, the DDIR cannot permit the research to move forward/implement the research.

#### **11.10 REPORTING SUSPENSIONS AND TERMINATIONS TO NIH INSTITUTIONAL OFFICIALS AND REGULATORY AGENCIES**

- A. The NIH IRB will notify, as soon as possible, the Institutional Official (the DDIR) through the OHSRP, as well as IC leadership (the Clinical Director and OPS) of any suspensions or terminations of studies. The Director of the Clinical Center will be notified by the IRB of any suspensions or terminations occurring on protocols implemented in the Clinical Center (CC). The IRB, or its designee, will ensure that officials at non-CC study locations are informed about suspensions and terminations, as appropriate, after such a determination is made by an NIH IRB.
- B. The OHSRP and the IRB will comply with the reporting requirements of the appropriate regulatory agency and take appropriate actions per SOP 24 – OHSRP Reporting to the Office for Human Research Protections (OHRP) and Food and Drug Administration (FDA) Regarding Unanticipated Problems, Serious or Continuing Non-compliance or Terminations or Suspensions.

#### **11.11 ADMINISTRATIVE HOLD**

An investigator may institute an administrative hold on a study when he/she wishes temporarily to stop, or as a preliminary step before permanently stopping, some or all approved research activities. An administrative hold may be in response to a directive from a sponsor, or FDA or other authorized review body. Senior NIH officials, such as the Institute Director/Clinical Director or Director, Clinical Center,

may request an administrative hold for NIH institutional reasons, e.g., loss of funding, departure of the PI from NIH.

Administrative holds are not suspensions or terminations, and are not an IRB directive requiring notification to OHRP, but the IRB needs to be notified of administrative holds to ensure that the rights and welfare of subjects are protected. Studies on administrative hold require continuing review by the IRB prior to the expiration date. The procedures for initiating and implementing an administrative hold are:

- A. The Principal Investigator must notify the IRB in writing within five days of the action that he/she is voluntarily initiating an administrative hold on the study.
- B. The administrative hold notification **is submitted as an amendment and** must include a description of the research activities that will be put on hold.
- C. A justification for the administrative hold and any supporting documentation that include the proposed actions to protect and notify currently enrolled subjects.

Upon receipt of written **hold** notification, an administrative hold notice is treated as an amendment to the previously approved **research using the protocol review standards for amendments**. (See SOP 7 – Requirements for the Ethical and Regulatory Review of Research by NIH Institutional Review Boards (IRBs)). **The amendment may receive expedited review, if applicable. The** IRB staff includes the request on the IRB meeting agenda for review.

- D. The IRB Chair or the convened IRB reviews the hold actions and determines whether any additional procedures need to be followed to protect the rights, safety and welfare of currently enrolled subjects.
- E. The IRB Chair or the convened IRB notifies the PI of any additional procedures that need to be followed to protect the rights, safety and welfare of currently enrolled subjects.
- F. The IRB will notify the IC and, where applicable, the CC, Office of Protocol Services (OPS), in writing, of what activities, if any, are authorized to continue and conditions for such continuation. **The IRB should indicate if the current consent form should remain posted or not.**
- G. **When the entire protocol is placed on administrative hold, the accrual status changes to “Clinical Hold/Recruitment or enrollment suspended” in OPS. On clinicaltrials.gov the status will appear as suspended, which**

indicates that participant recruitment and enrollment has halted but potentially will resume.

### **11.12 RESUMPTION OF RESEARCH ACTIVITIES AFTER AN ADMINISTRATIVE HOLD**

- A. The PI should notify the IRB when the administrative hold is lifted and provide an explanation of how issues leading to the hold have been resolved.
- B. A formal amendment (request for modification) must be submitted separately for IRB approval before any changes to the protocol and/or consent form can be implemented (see SOP 10 – Amendments to IRB-approved Research).

### **REFERENCES**

- A. HHS Human Subject Protection Regulations 45 CFR 46:  
<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>
- B. Institutional Review Boards, 21 CFR 56:  
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=56>
- C. OHRP: Investigator Responsibilities – FAQs:  
<http://answers.hhs.gov/ohrp/categories/1567>
- D. Withdrawal of Subjects from Research: Data Retention and Other Related Issues: OHRP Guidance (2010):  
<http://www.hhs.gov/ohrp/policy/subjectwithdrawal.html>
- E. Guidelines for the Conduct of Research in the Intramural Research Program at NIH:  
[https://oir.nih.gov/sites/default/files/uploads/sourcebook/documents/ethical\\_conduct/guidelines-conduct\\_research-6\\_11\\_07.pdf](https://oir.nih.gov/sites/default/files/uploads/sourcebook/documents/ethical_conduct/guidelines-conduct_research-6_11_07.pdf)
- F. NIH Manual Chapter 1743: Keeping and Destroying Records:  
<http://oma1.od.nih.gov/manualchapters/management/1743/>