P&P: RR 409 Version No:1.2 Effective Date: 11/20/2013	SUSPENSION OR TERMINATION OF HUMAN SUBJECTS RESEARCH	Supercedes: CPHS Policies and Procedures 11/28/2000

1. POLICY

The IRB shall have authority to suspend or terminate approved human subjects research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. In addition, the IRB has the authority to suspend or terminate any human subjects research activity that that has not been reviewed and approved or determined exempt by the IRB (see RR410 – Noncompliance). Any suspension or termination of approval shall include a statement of the reasons for the IRB's action. Suspensions or terminations shall be reported in writing promptly to all appropriate parties as listed under the Responsibilities section of this policy. Although only the procedures for the IRB suspending or terminating a protocol are discussed in this document, the IO also has the authority to not approve research approved by the IRB and to suspend or terminate research protocols for institutional reasons.

Specific Policies

1.1 Definitions

1.1.1 *Suspension*. All project activities must cease until any pending issues can be resolved satisfactorily. Suspended studies are still approved, but in a 'hold' status until the pending issues can be resolved.

1.1.2 *Termination*. The study is no longer approved. All project activities must cease immediately, including data analysis and any resulting data or analysis is null and void. A study may be terminated by the IRB or by the sponsor for administrative, regulatory or other reasons (such as initial study results). Regardless of the reason, terminated studies are not considered completed.

1.1.3 *Closure*. This is an administrative status whereby a previously approved protocol's expiration date has passed and an investigator has not submitted a renewal, or the investigator has submitted a study closure request. The IRB assumes that no human subject research activities are ongoing and, for administrative record keeping, the study record is closed.

1.2 Reasons for Suspension/Termination

The IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with federal and state regulations, University of California Office of the President or UC Berkeley policy, or IRB requirements, or research that has been associated with unexpected serious harm to subjects (45 CFR 46.113). A research project may be suspended or terminated for a variety of reasons, including *but not limited to*:

A. Serious adverse event(s) and unanticipated problem(s)

B. Detrimental change in the risk-benefit ratio of the study

C. Conduct of research activities without prior IRB approval

D. Failure to obtain appropriate consent

E. Failure of investigators to complete required training

F. Other noncompliance issues

1.3 Authorities

1.3.1 The IRB is authorized to suspend or terminate research protocols.

1.3.2 The IRB Chair (or his/her designee - e.g. Vice Chair) is authorized to suspend research protocols in emergency situations (i.e., when the rights, safety, or welfare of subjects are in immediate jeopardy).

1.4 Suspension and Termination Process and Notification

1.4.1 When potential cause for further investigation is demonstrated, an inquiry into the specific circumstances giving rise to concern with a specific protocol will be conducted. The initial inquiry and investigation procedures are described in RR 410 – Noncompliance or as described in RR 408 – Unanticipated Problems and Adverse Event Reporting depending on the nature of the initiating incident. If a protocol is determined to be in noncompliance or a detrimental change in the risk/benefit occurs, further action will be taken by the IRB.

1.4.2 In most cases, the IRB will review the circumstances of the case and make a determination of suspension or need for termination. Other IRB members may be consulted as needed in the decision making process leading up to bringing the issue to the full committee.

1.4.3 In emergency situations, the IRB Chair in consultation with an IRB Vice Chair, the Director of OPHS or IRB Manager or IRB Administrator will make a determination of the need to suspend or terminate a study immediately.

1.4.4 The IRB Chair (or his or her designee) will write a letter that includes the following:

A. a description of the event
B. the determination of the IRB (i.e., suspension, termination)
C. justification for the determination
D. requirements of the investigator (e.g., cease all data collection)

The letter will be forwarded to the Investigator, Investigator's Faculty Advisor (if applicable), Investigator's Department Head, IO, OPHS Director, any Sponsor(s), and applicable federal agencies (e.g., FDA, OHRP). A copy of the form is filed with the protocol's IRB file.

1.4.5 The Lead Investigator is responsible for notifying (in a timely manner) all co-investigators, key personnel, and other research staff associated with the

protocol as well as any subcontract grantees if the protocol has been suspended or terminated.

1.5 Participant Involvement in Suspended or Terminated Protocols

1.5.1 When a protocol is suspended or terminated, the Investigator must stop all activity on the protocol, including subject recruitment and enrollment, procedures, and analysis and/or publication of existing data.

1.5.2 When the suspension or termination of a research protocol involves the withdrawal of current participants from the research, the Investigator will be required to:

A. inform enrolled participants that the study has been suspended or terminated; and,

B. develop procedures for withdrawal that protect the rights, safety, and welfare of participants, and describe those procedures to participants.

1.5.3 In certain circumstances, project activities may continue if stopping study procedures/treatment will adversely affect the welfare of a subject. If the suspension or termination of a research protocol does involve the withdrawal of current participants from the research, the Investigator will be required to:

A. notify the OPHS immediately of the need to continue any procedures/treatment;

B. inform enrolled participants that the study has been suspended or terminated; and,

C. report any serious adverse events or unanticipated problems involving risks to participants to the IRB.

1.6 Reinstatement of Suspended or Terminated Protocols

1.6.1 *Suspended Studies.* To reinstate a project that has been suspended, the investigator must resolve satisfactorily any pending issues as required by the IRB. After one year of suspension or the expiration date of the study (whichever comes first), if adequate progress has not been made on the pending issues then the IRB will administratively close the study protocol.

To reinstate a project that has been suspended the investigator must contact the OPHS in writing within 30 days of the suspension. The investigator must address the following in a letter:

A. Reason for requesting the study be reinstated.

B. Short summary of the purpose of the study and intended objectives/outcomes. This may be incorporated into the protocol narrative noting any changes, revisions or clarifications.

C. Description of how the study has changed, if any, since initial approval using the appropriate Amendment form and procedure for identifying changes in the protocol narrative.

D. Summary of status of the study, including:

(1) how many subjects were enrolled;

(2) at what point in the treatment/procedures were the subjects at the time of suspension;

(3) any adverse events or amendments since last continuing review, including a description of each;

(4) any additional relevant information.

E. Documented plan to ensure that reason for suspension will not happen again and that the study will be in compliance with all applicable laws and regulations

F. Anticipated enrollment, if the study is reactivated

G. In the case that IRB-approval of a protocol is reinstated, the IRB may require that subjects who were previously enrolled be re-consented.

1.6.2 *Terminated Studies.* Terminated studies may be reinstated or reactivated with appropriate modifications to address the reason(s) the study was terminated. Investigators will need to submit a completely new application if they wish to resume a terminated study.

2. SCOPE

These policies and procedures apply to all human subjects research conducted by investigators affiliated with UC Berkeley, regardless of whether the protocol was ever submitted, reviewed, or approved by the IRB or determined to be exempt.

3. RESPONSIBILITY

IRB Chair is responsible for authorizing protocol suspensions and bringing terminations to the IRB. He or she is also responsible for making suspension or termination determinations in emergency situations.

OPHS Director and/or any OPHS staff member is responsible for receiving reports of noncompliance, unanticipated problems involving risks to subjects and/or serious adverse events, or other information relative to Section 1.2 above and reporting it to the OPHS Director and IRB Chair.

IRB Chair and OPHS Director are responsible for ensuring that protocol suspensions and terminations are reported to appropriate individuals (e.g. Institutional Official) and organizations (e.g. department or agency heads, OHRP, sponsor) in a timely manner (e.g. initial verbal reports -as needed - followed by written notification).

The Principal Investigator (PI) is responsible for ensuring prompt reporting of protocol suspensions and terminations to the FDA for studies involving FDA-regulated drugs, devices, and biologics. The PI must also inform CPHS/OPHS of any suspensions or terminations that are determined outside of UCB's IRB.

OPHS Director or his/her designee is responsible for overseeing the process by which protocols that have not been updated, reviewed and approved with proper continuing review paperwork are identified and administratively closed.

4. PROCESS OVERVIEW

Suspensions or Terminations for Cause

When the IRB receives reports of circumstances which may affect the rights, safety, or welfare of human research participants, or reports of research not being conducted in accordance with federal or state regulations, University policy, or IRB stipulations, the IRB will make a determination as to whether the protocol should be suspended or terminated. Under normal circumstances and when the severity of the event in terms of risks to subjects is low (e.g., failure of the LI to complete required training), the determination will be made at the next regularly-scheduled IRB meeting. The IRB Chair may convene an ad hoc committee to meet prior to the next convened IRB meeting to review the case and make a determination of suspension or termination (or no action) if he or she feels it is warranted. In addition, the incident may be referred to the full IRB for discussion and resolution. If the severity of the event is deemed to be high (e.g., noncompliance that puts the rights, safety, or welfare of participants at immediate and/or increased risk), the IRB Chair will review the case and can make an interim determination of suspension. In this later case, the full IRB will review the circumstances of the case and make a determination to continue the suspension, terminate the protocol, or reinstate active approval.

If a study is suspended or terminated, the IRB Chair (or his or her designee) will notify the Investigator in writing of the suspension or termination. The Investigator must cease all project activities effective from the date of the first notice of the suspension or termination.

Administrative Study Closure

Protocols for which an investigator has requested study closure will be administratively closed by OPHS staff. Protocols that have expired and for which no continuing review application has been received by OPHS will automatically be closed 6 months after the expiration date. All human subjects research must have ceased effective the day of expiration or the day of the study closure, whichever comes first.

5. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.113, 45 CFR 46.109(e)
21 CFR 56.113