Policy: Noncompliance and Allegations of Noncompliance Regarding the Conduct of Human Subjects Research (last updated June 17, 2011)

General Overview

This policy describes the Office of the Human Research Protection Program (OHRPP) policies, Principal Investigator responsibilities and the OHRPP and the Vice Chancellor for Research responsibilities and procedures for addressing reports of allegations of suspected or actual noncompliance with federal regulations, state laws, University policies, and/or IRB requirements with respect to human subject research.

The OHRPP through the Quality Improvement Unit (QIU) with the cooperation of the Principal Investigator and/or his or her designees, as appropriate, will strive to formulate a corrective action plan to present to the IRB for review and final approval. The IRB may make additional recommendations or additions to the plan. The IRB may also direct the QIU to investigate any allegations or reports of noncompliance with the expectation that the QIU will assist the Investigator in developing an appropriate corrective action plan to be returned to the IRB for review.

If the allegation of noncompliance cannot be resolved as described above or an appropriate corrective action plan that is acceptable to the IRB cannot be developed, the IRB has the authority to impose corrective actions and recommend sanctions to the Vice Chancellor for Research.

Policy

All researchers conducting human subjects research are expected to comply with the provisions of the IRB-approved study as well as all related federal regulations, University policies and state and local laws. If a researcher becomes aware of any noncompliance with respect to a specific study, then a post-approval report must be made to the IRB, preferably through the Principal Investigator, to the IRB. If any allegations of noncompliance are made to the UCLA OHRPP, then those allegations must be investigated and it must be determined whether the allegation has a basis in fact or not. The procedures for this investigation and the outcome of the investigation are described below.

The Institution, which includes the IRB, is expected to comply with the University of California and UCLA the policies and procedures as well as all federal regulations and state laws related to the protection of the safety, rights and welfare of human subjects in

research. If any allegations of noncompliance are made to the OHRPP or to the Vice Chancellor for Research, then those allegations must be investigated and it must be determined whether the allegation has a basis in fact or not. The procedures for this investigation and the outcome of the investigations are described below.

UCLA personnel, including investigators, research team, faculty, staff, administration or students are responsible for reporting to the OHRPP suspected or actual noncompliance with the provisions of an IRB-approved study as well as with any applicable human research regulations, University policies and state and local laws when conducting human subjects research. Reports of noncompliance may come in the form of a complaint or from the result of an audit.

Research participants, participants' family members, and others external to the University, including regulatory agencies may also report suspected noncompliance to the OHRPP, IRB or to the Vice Chancellor for Research. These reports may be in the form of complaints and may also be made anonymously.

Reports of research misconduct or Whistleblower reports are subject to different rules and will be referred to the UCLA Office of Research Policy and Compliance or the UCLA Administrative Policies and Compliance Office if received by the OHRPP, the IRB or Vice Chancellor for Research.

Definitions

Allegation of Noncompliance: An unproven assertion of noncompliance.

Continuing Noncompliance: Repeated instances of noncompliance by the same investigator or the Institution. Repetition may be of the same instance or repetition of different instances. For investigators, this repetition may be in the same or in different protocols by a single investigator. Such repetition if unaddressed may affect the protection of human research subjects. For the Institution, repetition may be of the same or different policies and/or procedures and/or regulations and/or laws.

Investigator Noncompliance: Failure to comply with federal regulations, state laws, UC, UCLA, or OHRPP policies related to the protection of human subjects, and/or the requirements or determinations of the IRB, or provisions of the approved research study.

IRB or other Institutional Noncompliance: Failure to comply with federal regulations, state laws, UC, UCLA, or OHRPP policies related to the protection of the safety, rights and welfare of human subjects in research.

Research Misconduct: Fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. It does not include honest error or differences of opinion. For additional information, see the UCLA Research Policy and Compliance website regarding Research Integrity and Misconduct.

Serious Noncompliance: Instances that pose an actual or potential increased risk to the safety, rights and welfare of human research subjects, when:

- Investigators fail to comply with federal regulations, state laws, UC, UCLA or OHRPP policies related to the protection of human subjects, and/or the requirements or determinations of the IRB; or
- There is a systemic failure of the Institution to follow or implement practices described in the University's policies and/or federal regulations or state laws related to the protection of human subjects in research.

Whistleblowing: A report of improper activities, including any activity by UC or a UC employee that violates any state or federal law or regulation (e.g., corruption, malfeasance, bribery, theft or misuse of government property, fraud, coercion or conversion); or involves economic waste, gross misconduct, gross incompetence or gross inefficiency; or poses a significant threat to the health or safety of employees or the public. UCLA wants suspected improper activities reported and will protect the person reporting these activities from retaliation for whistleblowing. For additional information, please click here.

Principal Investigator Responsibilities

Investigators are required to self report to the IRB any instances of noncompliance that involves potential risk to subjects or others, or involves failure to comply with federal regulations, state laws, University policies, and/or IRB requirements, determinations or provisions of the approved research study. See OHRPP Guidance and Procedure: IRB Reporting Procedures for Unanticipated Problems, Noncompliance, Suspension, or Termination.

Investigators are encouraged to seek the assistance of the OHRPP Quality Improvement Unit (QIU) in order to develop a corrective action plan to accompany any reports of noncompliance submitted to the IRB.

Investigators are required to respond promptly to any inquiries, correspondence or directives from either the Quality Improvement Unit or the IRB with respect to any allegations of or actual noncompliance. They are also expected to cooperate with any requests for information or any investigations.

Quality Improvement Unit Procedures

Upon request by a researcher, the Quality Improvement Unit (QIU) staff of the OHRPP, with input from the IRB Chair as appropriate, will work with the research team to develop a corrective action plan to present to the IRB for review and approval. This corrective action plan will outline what steps the investigator has taken or will take to resolve the noncompliance and to prevent such noncompliance in the future.

Upon receipt of an allegation of suspected noncompliance, the QIU staff of the OHRPP will be responsible for conducting an initial inquiry into the allegation. The QIU staff may call upon the expertise of an IRB Chair or member or outside consultant when conducting this inquiry.

- The inquiry is administrative fact-finding and may be informal or may involve an extensive review of the study records, interviews with associated researchers or administrators, interviews with the complainant, and may include correspondence to the principal investigator or to the an appropriate person within the Institution, to obtain additional information.
- Correspondence to the Principal Investigator or the appropriate person within the Institution will provide the investigator or the Institution with an opportunity to respond to the allegations of suspected noncompliance.
- When possible or appropriate, the QIU will in cooperation with the Principal Investigator develop an initial corrective action plan to accompany any reports noted below.

Upon completion of the initial inquiry into the allegation, the QIU staff will prepare a written report describing the allegation and the outcome of the inquiry, a recommended corrective action plan when appropriate, and forward that report and plan to the IRB Chair or Vice Chair for initial review, and/or to the Vice Chancellor for Research if the allegation of noncompliance involves the IRB or another component of the Institution. If during the course of the

investigation it appears that the activities in question may also involve research misconduct or whistle blowing, the allegation will be directed to the appropriate office(s) at UCLA.

IRB Procedures

Noncompliance that is self-reported to the IRB by the principal investigator will first be screened by the QIU to make sure that sufficient information is included for IRB review and that an appropriate corrective action plan is included as needed. The report will then be processed and reviewed according to OHRPP Guidance and Procedure: IRB Reporting Procedures for Unanticipated Problems, Noncompliance, Suspension, or Termination. If upon initial review by the IRB Chair/Vice Chair it is determined that there is no serious or continuing noncompliance, the report will be acknowledged and accepted. If upon initial review by the IRB Chair/Vice Chair it is determined that the noncompliance is serious and/or continuing, then the applicable procedures in this policy will also apply. If it is determined that the activity involves research misconduct, the information will be referred to the appropriate UCLA office, as previously described in Policy.

Initial IRB Review of Allegations of Noncompliance

The IRB Chair or Vice Chair will make an initial determination as to whether the allegation of noncompliance:

- ***Has possible basis in fact, but is not serious and not continuing noncompliance.***
    - Full Committee review shall proceed as described below.
    - The IRB Chair or Vice Chair may request additional information from the Principal Investigator or from the QIP prior to review by a convened IRB meeting in order to facilitate the review process.
- ***Has possible basis in fact, and is serious and/or continuing noncompliance.***
    - Full Committee review shall proceed as described below.
    - The IRB Chair or Vice Chair may request additional information from the Principal Investigator or from the QIU prior to review by a convened IRB meeting in order to facilitate the review process.
- ***Has no basis in fact***.
    - No further review is required.
    - The outcome and determination made will be documented in correspondence and forwarded to the Principal Investigator or to the appropriate person within the Institution within ten working days of the IRB Chair/Vice Chair's determination.
    - The OHRPP staff will oversee and coordinate with the IRB Chair/Vice Chair all written correspondence from the IRB.
- ***Has a possible basis in fact and is of such a nature that the safety, rights and welfare of subjects are at immediate risk or hazard.***

  In this case the IRB Chair/Vice Chair will contact the PI in order to establish an interim measure to be taken to protect subjects until such a time that the Full Committee can review the study. An example of such a measure is to suspend all new subject enrollment.

Review by a convened IRB meeting (Full Committee Review)

The review of noncompliance by a convened IRB meeting will occur as follows:

- The reported noncompliance or allegation of suspected noncompliance and appropriate review materials will be distributed to the primary reviewer(s) and all IRB Committee members approximately one week prior to the meeting, time permitting.

- Appropriate review materials may include but are not limited to the following: the written report prepared by the QIU, inquiry correspondence (to and from investigator or to the appropriate person at the institution), study protocol, IRB application, current approval notice, current approved informed consent document, Investigator's Drug/Device Brochure (if applicable), and other pertinent documents. Other IRB records are also available as needed.

- The IRB may request additional information from the Principal Investigator, the appropriate person in the Institution, or from the QIU regarding the reported noncompliance or allegation of suspected noncompliance in order to facilitate a thorough review before a final determination is made.

- The Full Committee may determine that a subcommittee composed of selected IRB members and IRB staff is necessary to investigate the allegation further and prepare a written report and recommendations to present to the Full Committee for final determination. In the case of an allegation of or actual Institutional noncompliance, the Full Committee may ask the Vice Chancellor for Research to appoint a subcommittee to investigate the allegation and prepare a written report and recommendations to present to the Full Committee.

- The IRB will make one of the following determinations:

  For allegations of noncompliance:

  - There is no basis in fact.
  - There is a basis in fact, but the noncompliance is neither serious nor continuing.
  - There is a basis in fact and the noncompliance is serious and/or continuing.
  - There is basis in fact and the noncompliance constitutes an unanticipated problem.

  For reported noncompliance:

  - The noncompliance is neither serious nor continuing.
  - The noncompliance is serious and/or continuing.
  - The noncompliance constitutes an unanticipated problem.

- The IRB will consider which of the following actions is required. This consideration may include but is not limited to the following:

  - Require no further action;
  - Accept and approve the Principal Investigator's or the Institution's proposed corrective action plan or changes;
  - Require that the Principal Investigator modify the protocol to minimize risk;
  - Require the interval at which continuing review is conducted to be modified to less than one year as appropriate to the degree of risk;
  - Require that the Principal Investigator modify the recruitment or consent documents;

- Require that currently enrolled subjects be reconsented with the additional relevant information provided;
- Require notification of previously enrolled subjects of new information;
- Require notification of currently enrolled subjects of new information, as such information may relate to a subject's willingness to continue participation in the
- research;
- Require observation of the research or the consent process;
- Require submission of status reports on a defined set schedule to the IRB;
- Require additional education and training for the investigators and support staff;
- Require additional monitoring of the research or the Institution;
- Impose sanctions to achieve compliance or prevent recurrence of noncompliance
- Refer the Principal Investigator or all of the researchers to another University entity (i.e., Institutional Official, Campus Counsel, Risk Management);
- Suspend any or all components of the research (i.e., new enrollment, treatment, follow-up and data analysis) until a corrective action plan can be developed and implemented or until additional review can occur;
- Terminate the research;
- Require a directed for-cause investigation by QIU;
- Require an outside consultant or consultants to conduct a for-cause investigation of the Institution.
- Require an outside consultant or consultants to help develop and implement a corrective action plan for the Institution.
- Refer the matter to the appropriate UCLA office(s) that handle(s) research misconduct and/or whistleblowing activities.

The outcome of the IRB meeting will be documented in the correspondence to the principal investigator or the appropriate persons in the Institution, and/or the IRB meeting minutes. Written correspondence from the IRB will be forwarded to the Principal Investigator, and/or the appropriate persons within the Institution within ten working days of the final IRB determination.

IRB Reporting Requirements

Unanticipated problems involving risks to subjects or others; any serious and/or continuing noncompliance; any suspension or termination of IRB approval are reportable to the appropriate federal department or agency head(s) and Institutional Official according to *OHRPP Guidance and Procedure: IRB Reporting Procedures for Post Approval Reporting, Noncompliance, Suspension, or Termination*.

Any IRB and/or Vice Chancellor for Research determination of serious and/or continuing noncompliance with respect to the IRB or the Institution and the outcome of the IRB or Vice Chancellor's actions are also reportable to the appropriate federal department or agency head(s) and appropriate institutional officials according to *OHRPP Guidance and Procedure: IRB Reporting Procedures for Post Approval Reporting, Noncompliance, Suspension, or Termination*.

References and Regulations

- DHHS
  - 45 CFR 46.103(b)(5)(i)
  - OHRP Guidance on Reporting to Incidents to OHRP (May 27, 2005)

- FDA
  - 21 CFR 56.108(b)(2)
  - FDA Suspension or Termination of IRB Approval (September 3, 2009)
- UCLA
  - UCLA Annual Whistleblower Notice, published annually on the UCLA website
  - UCLA Policy 620.1: Reporting Whistleblower Complaints, August 1, 2002
  - UCLA Policy 993: Responding to Allegations of Research Misconduct, October 27, 2010