

 Research Integrity Office	Human Research Protection Program Regulatory Sheet	
Title: Serious and Continuing Non-Compliance	Date Effective 4/21/2008	Supersedes P&P dated: N/A
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BACKGROUND

The DHHS and FDA regulations require that institutions develop written policies and procedures for ensuring prompt reporting to a IRB, appropriate institutional officials and the department or agency head in three situations: (i) unanticipated problems involving risks to subjects or others; (ii) serious or continuing non-compliance; and (iii) suspensions or terminations of previously approved research.

In accordance with 21 CFR 56, the OHSU IRB has the authority to place research activities on hold, as well as to suspend or terminate approval of research that is not being conducted in accordance with the OHSU IRB policies or federal regulations for the protection of human subjects.

SCOPE

This policy covers definition, identification and management of occurrences of serious and continuing non-compliance.

AUTHORITY

Federal regulation 45 CFR 46.103(b)(5)(i) requires that any serious or continuing non-compliance with DHHS human subjects regulations or the determinations of the IRB must be promptly reported to the Office of Human Research Protections.

Under 21 CFR 56.113, an IRB shall have the 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.

21 CFR 56.108(b)(5) requires that the IRB follow written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials and the Food and Drug Administration of any instance of serious or continuing non compliance.

AAHRPP Tip Sheet: Reporting of Unanticipated Problems, Terminations, Suspensions, and Non-compliance. www.aahrpp.org

I. POLICY

- A.** All members of the OHSU community engaged in Human Subjects Research are expected to comply with federal regulations pertaining to research and OHSU IRB requirements and determinations.
- B.** Any member of the OHSU community who is or becomes aware of information related to non-compliance with federal regulations pertaining to research or OHSU IRB requirements or determinations should report that information to the OHSU IRB. Special protections are in place to protect the identity of a whistleblower.
- C.** Any serious or continuing non-compliance with federal regulations affecting human subjects research or the requirements or policies of the OHSU IRB must be promptly reported to the OHSU IRB, appropriate institutional officials, the sponsor, if any, and appropriate federal agencies.

- D. The OHSU IRB is responsible for making the final determination as to whether serious or continuing non-compliance has occurred.
- E. The OHSU Office of Research Integrity (ORIO) is responsible for handling suspicions, allegations or detected non-compliance at OHSU. When non-compliance is alleged, further information will be obtained by the ORIO to determine whether the allegation is true.
- F. The OHSU IRB has the authority to suspend or terminate approval of human subject research that is not being conducted in accordance with the OHSU IRB's requirements or that have been associated with unexpected serious harm to subjects.
- G. When unapproved research is discovered, the OHSU IRB will act promptly to halt the research, assure remedial action regarding any breach of regulatory or institutional human subject protection requirements, and address the investigator's fitness to conduct human subject research.

II. PROCEDURES

A. Principal Investigator Responsibilities

1. Report to the OHSU IRB any information (of which they are or reasonably should be aware) related to non-compliance with federal regulations pertaining to research or OHSU IRB requirements or determinations. Reports will be made as soon as possible, but in no event later than 10 working days.
2. Reports may be made via:
 - a. A phone call, letter or e-mail to ORIO Director, Associate Director, IRB Chair or Co-Chair.
 - b. Via the OHSU Integrity Hotline 1- 877 733-8313
3. A report of non-compliance is typically made by the investigators or may be based on information included in continuing review applications, requests for study amendments, reports of unanticipated problems, study audits, published reports or student theses.
4. The report of non-compliance should include the following information:
 - a. A description of the noncompliance;
 - b. An explanation of how the noncompliance occurred and how it was discovered;
 - c. A description of any problems regarding the rights of subjects, such as recruitment, informed consent processes, etc., or potential or resulting risks to subjects; and
 - d. A proposed action plan to avoid similar reoccurrence in the future.
5. The PI must respond to all requests from the ORIO or the OHSU IRB for further information or clarification regarding concerns or issues under investigation.

B. The OHSU Research Integrity Office Responsibilities

1. When noncompliance is alleged, further information must be obtained to determine whether the allegation is true. An investigative team will be convened by the ORIO.
 - a. Individuals alleging non-compliance may be in sensitive positions relative to colleagues and superiors and must be protected from possible retaliation. Investigations will be confidential and whistleblower protections, as well as researcher integrity, will be respected.
2. When a confirmed report of non-compliance is received, an initial inquiry should be made promptly to determine whether the non-compliance is serious or continuing.
3. The ORIO Director or Designee will notify immediately the IRB Chair(or designee) about the report

C. OHSU IRB Chair or Designee Responsibilities

1. All incidents of non-compliance reported to the OHSU IRB will be reviewed by the OHSU IRB, Chair or her designee, and a determination will be rendered to include any action and/or recommendations.
2. In conjunction with the ORIO Director, administratively resolves issues of non-compliance that are neither serious nor continuing.
3. Takes one of the following actions:
 - a. Determines if the research should be placed on administrative hold prior to presenting allegations to the convened OHSU IRB;
 - b. Determines if the research should be inspected and/or monitored with or without notice to the investigator prior to presenting allegations to the convened IRB;
 - c. Reviews investigator's responses to communication of notice and inquiry;

- d. Makes referral to the compliance subcommittee when preliminary findings suggest possible serious or continuing non-compliance or the non-compliance is not amenable to administrative resolution.
- D. OHSU IRB Leadership Committee Responsibilities**
1. Reviews all referrals for non-compliance;
 2. Receives and reviews the following materials:
 - a. The recorded allegations;
 - b. All information gathered during the inquiry phase of the investigation including responses, monitoring reports, and other materials generated to evaluate the issues;
 - c. Human Subjects Protocol;
 - d. Relevant IRB-approved consent documents;
 - e. Research protocol, Sponsor protocol and Investigator Brochure, as applicable;
 - f. Most recent investigator progress report, if any; and
 - g. Any other relevant materials.
 3. Holds a meeting with the investigator to ascertain preliminary findings;
 4. Issues a written report of findings and recommendations to the OHSU IRB on the matter;
 5. Forwards a copy of the report of preliminary findings to the investigator;
 6. Forwards report of preliminary findings and subcommittee's recommendations to the IRB Chair and the ORIO Director for referral to the convened OHSU IRB for inclusion on the agenda at the next appropriate meeting;
 7. Schedules report for presentation.
- E. OHSU IRB Responsibilities**
1. Receives and reviews the Leadership Committee's written report prior to a meeting in which a compliance referral will be presented; and other documents relevant to determine and resolve the allegation of non-compliance;
 2. Considers the oral presentation of the Leadership Committee's findings at a meeting in which the investigator has the opportunity to attend and provide information;
 3. Considers whether to make a determination of non-compliance following presentation of all the evidence;
 4. Utilizes one of the following three methods for suspending or terminating previously approved research. Each method allows for the group or individual to take swift and immediate action in order to ensure the immediate protection of research participants:
 - a. Administrative suspensions and terminations can be put into effect by the Director of the Office for Human Research Protections, the Director of the Office of Education and Compliance Oversight or the Vice President for Research. The preceding events and the imposed action are reviewed for on-going status at the next convened OHSU IRB meeting.
 - b. Expedited OHSU IRB suspensions and terminations can be put into effect by the IRB Chair or designee. The preceding events and the imposed action are reviewed for on-going status at the next convened OHSU IRB meeting.
 - c. IRB Full Board suspensions and terminations are put into effect by board action within a board meeting, where the board members vote to take this action based on one or both of the circumstances described above.
 5. Official written notice of the suspension or termination must be provided to the principal investigator shortly after informal communication of the same. If a suspension or termination is imposed by Administration, the IRB Chair or designee, or the convened OHSU IRB, the PI must be informed according to the following criteria:
 - a. Effective date of suspension or termination;
 - b. Reason for suspension or termination;
 - c. Corrective actions necessary, request for corrective actions, or instructions for closure of the study, as appropriate;
 - d. Who the notice is copied to; and
 - e. Specific instructions pertaining to currently enrolled research participants, including language to ensure that:
 - f. Current participants are notified that the study has been suspended and/or terminated;

