Human Research Protection Program
Policies & Procedures

Serious & Continuing Non-Compliance

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Background
The DHHS and FDA regulations require that institutions develop written policies and procedures for ensuring prompt reporting to the 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.

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.

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

II. Policy

A. All members of the OHSU community engaged in Human Subjects Research are expected to comply with federal regulations pertaining to the research and OHSU IRB requirements and determinations.

B. 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.

C. 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 or appropriate institutional officials.

D. The OHSU Research Integrity Office (ORIO) is responsible for investigating and addressing alleged or suspected non-compliance on the part of OHSU investigators and research staff..

1. For allegations involving the conduct of research, the OHSU IRB is responsible for making the final determination as to whether serious or continuing non-compliance has occurred.
2. 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 has been associated with unanticipated problems involving risks to subjects or others.
3. When unapproved research is discovered, the OHSU IRB will act promptly to halt the research, require appropriate remedial action regarding any breach of

regulatory or institutional human subject protection requirements, and address the investigator's fitness to conduct human subject research.

E. For allegations of non-compliance involving the OHSU IRB, the OHSU Integrity Office is responsible for investigating the allegation and determining whether serious or continuing non-compliance has occurred.

III. Procedure

A. Principal Investigator Responsibilities

1. Report any information (of which they are or reasonably should be aware) related to non-compliance with federal regulations pertaining to the research or OHSU IRB requirements or determinations. Reports shall be made as soon as possible.

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.** The OHSU Integrity Hotline at 1-877-733-8313; or
- **c.** A protocol deviation report in the eIRB, if the incident pertains to a specific IRB-approved protocol.

3. A report of non-compliance may be based on various potential sources of information, including 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 non-compliance;
- **b.** An explanation of how the non-compliance 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 non-compliance is alleged or suspected, further information may be needed to determine whether non-compliance has occurred.

- **a.** An investigative team may be convened by the ORIO if appropriate.
- **b.** 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 report of non-compliance is confirmed, an initial inquiry will be made promptly to determine whether the non-compliance is serious or continuing.

C. OHSU IRB Chair or Designee Responsibilities

1. All incidents of non-compliance reported to the ORIO will be reviewed by the OHSU IRB Chair or designee, and a determination will be rendered to include any action and/or recommendations.

2. The IRB Chair or designee will communicate with the investigator(s) in question to obtain any necessary information and/or develop a corrective action plan.

3. Issues of non-compliance that are neither serious nor continuing will be resolved administratively by the IRB Chair or designee, in consultation with other ORIO staff as needed.
4. The IRB Chair or designee may take one or more of the following actions in addressing alleged or confirmed non-compliance:
   a. Place the research on administrative hold ;
   b. Require that the research be inspected and/or monitored with or without notice to the investigator;
   c. Make a finding of serious or continuing non-compliance; or
   d. Refer the matter for further consideration by the convened IRB.

D. OHSU IRB Responsibilities

1. When IRB Chair or designee refers alleged non-compliance to the convened IRB for further consideration, the board will review the relevant information and determine whether non-compliance has occurred and whether it is serious or continuing. If there is insufficient information to make a determination, the IRB may request additional information from the investigator or others.
2. If necessary, the IRB may use any 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 at the request of the Chief Integrity Officer 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.
3. Official written notice of the suspension or termination will be provided to the principal investigator shortly after informal communication of the same. The PI must be informed of the following:
   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:
      - Current participants are notified that the study has been suspended and/or terminated;
      - Procedures to ensure that withdrawal of enrolled participants considers the rights and welfare of participants;
      - When follow-up of participants for safety reasons is permitted or required by the OHSU IRB, the participants should be so informed; and
      - When follow-up of participants is permitted or required by the OHSU IRB for safety reasons, any unanticipated events or outcomes should be reported to the OHSU IR and the sponsor.

4. Circumstances that may result in suspension or termination of previously approved research include:
   a. When research is not conducted in compliance with OHSU IRB requirements.
   b. When research is associated with unanticipated problems involving risks to subjects or others.

E. Noncompliance by the OHSU IRB or ORIO

1. Persons who know of or reasonably suspect noncompliance by the OHSU IRB or ORIO with federal regulations or OHSU policies should report this information via the OHSU Integrity Hotline at 1-877-733-8313.
2. Allegations of non-compliance by the IRB or ORIO will be investigated by the OHSU Integrity Office.
   a. Any verified serious or continuing noncompliance will be reported to federal and institutional authorities in a manner consistent with federal regulations and the policy on Institutional Reporting Requirements.
   b. A plan to address the non-compliance will be developed and implemented by appropriate authorities.
3. Investigations of non-compliance will be executed in accordance with the OHSU Audit and Advisory Services Internal Audit Manual.

IV. 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 and 45 CFR 46.113**, 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

V. Definitions

Non-compliance is defined as a failure on the part of the PI, a member of the research team, or member of the OHSU IRB or ORIO staff to: adhere to the terms of the OHSU IRB approval and/or abide by applicable laws, regulations, or OHSU policies.

Serious non-compliance is defined as failure to adhere to the terms of the OHSU IRB approval and/or abide by applicable laws, regulations or OHSU policies when that failure increases risk to participants or adversely affects the rights and welfare of the participants. A single instance of non-compliance may be serious. Examples of serious non-compliance may include the following:

- **Falsification of IRB documents**
- **Human subjects research conducted without IRB approval**
- **Deviation from the IRB approved protocol or consent process**
- **Modification of protocol without prior IRB approval**
- **Failure to maintain regulatory documents**
- **Inadequate oversight of research**
- **Conducting a research protocol without oversight of a functional investigator**

Continuing Non-compliance is defined as a pattern of repeated non-compliance actions or omissions that, if unaddressed, may compromise the integrity of the OHSU human research protection program. The pattern may reflect a lack of knowledge on the part of the investigator or a lack of commitment by the investigator and/or research team to human subjects protection.