

I. PURPOSE

The purpose of this SOP is to identify the standards and responsibilities for handling reports of noncompliance related to research involving human subjects, and the actions taken when the IRB makes a finding of serious or continuing noncompliance.

Note: If at any time during an investigation there are concerns regarding scientific misconduct, such concerns will be referred to the Chief Scientific Officer. Allegations of research misconduct are potentially related but a separate issue that is covered by the Hospital's Research Misconduct Policy.

II. POLICY STATEMENT

It is the policy of the IRB and the Children's Hospital of Philadelphia Research Institute that all allegations of noncompliance in human subjects research must be reported promptly, and each report will be investigated and determinations made about these allegations.

III. SCOPE

This policy applies to all members of the research staff, non-traditional research personnel, members of the medical staff, employees of the Hospital, IRB members and any entity that is controlled by or under common control with the Hospital.

IV. DEFINITIONS

Allegation of Noncompliance: An assertion of noncompliance that has yet to be proved or supported by evidence. See also Noncompliance.

Continuing Noncompliance: A pattern of noncompliance with repeated failure to adhere to the federal research regulations or CHOP policies that may affect the rights or welfare of participants. The pattern of noncompliance is assessed by the number of incidents occurring during the course of implementation of a protocol, or across multiple protocols, conducted at CHOP, and whether the same noncompliant action was repeated or many different noncompliant events occurred, especially after a remediation procedure such as training has been provided to the researcher or research staff.

Finding of Noncompliance: Noncompliance that is proven or supported by substantial evidence.

Noncompliance: A violation of any federal, state, or local regulation that governs human research; any hospital policy on human research; any deviation from the protocol approved by the IRB or stipulations imposed by the IRB as a condition of approval.

Serious Noncompliance: Noncompliance that may affect subject safety, increase risks to subjects, affect the integrity of the data, violate the rights and welfare of subjects, or affect the subject's willingness to participate in research.

V. PRINCIPLE

Federal regulations 45 CFR 46.108(a)(4) , 45 CFR 46.115(a)(6) and 21 CFR 56.108(b) require that institutions have written procedures for ensuring prompt reporting to the Institutional Review Board (IRB), appropriate institutional officials, and the department or agency head of any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with federal regulations or the requirements or determinations of the IRB; and any suspension or termination of IRB approval.

VI. PROCEDURES

A. Responsibility for Reporting Allegations of Noncompliance

All employees and agents of the Children's Hospital of Philadelphia and Institutions relying on the CHOP IRB share the responsibility for reporting incidences of noncompliance with the regulations or the requirements or determinations of the IRB. Allegations of noncompliance in human subjects research may come from many sources including, but not limited to, the following:

- Investigators or investigational team members
- Department/Division chiefs
- Study monitors, auditors, or sponsors
- Research participants or family members
- Individuals not directly involved in research
- Members of the IRB Office
- Any member of the CHOP staff

B. Methods for Reporting Allegations of Noncompliance

Reports of allegations of non-compliance may be made to any of the following individuals:

- Chair, Committees for the Protection of Human Subjects (CPHS chair)
- Vice Chair, Committees for the Protection of Human Subjects
- Chief Compliance Officer, Research

- Vice President, Research Compliance & Regulatory Affairs
- Safe to Say at 1-866-246-7456 or www.mycompliancereport.com
- IRB Staff

C. Documentation of Reports of Noncompliance

All reports of allegations of noncompliance must be documented by its recipient and forwarded to the CPHS Chair (or designee). The report must contain sufficient information to perform an investigation of the allegations.

Note: Allegations of noncompliance against the CPHS Chair will be forwarded to the VP, Research Compliance & Regulatory Affairs.

D. Identity Protection

The identity of the individual making an allegation of noncompliance will be protected to the extent possible when this individual makes a report in good faith. This protection holds even if the concerns or allegations are found, upon investigation, to be without merit.

E. Initial Review of Allegations of Noncompliance

The CPHS Chair (or designee) is responsible for the initial review of allegations of noncompliance. The CPHS Chair/designee informs the Principal Investigator (PI) of the allegation and the initial review and gathers additional facts (e.g., from an audit of the study records), when necessary, to better ascertain the nature and scope of the allegation of noncompliance.

The PI must provide the following materials to the CPHS Chair or designee:

- A report about the investigator's research activities under examination and the associated protocol deviation submission, if one was filed;
- Current versions of applicable study documents that are not available within the eIRB system (e.g., protocol, consent form(s) investigator's brochure, recruitment materials, data collection forms, etc.) and previous versions of these documents, if necessary; and
- Any other materials relevant to the potential noncompliance including but not limited to correspondence with the sponsor, other investigators, subjects, regulatory agencies or third parties, monitoring reports, safety reports, or subject-specific information.

The CPHS Chair or designee makes the initial determination of whether review by the convened IRB is required and if there is support for a finding of noncompliance.

1. When the facts do NOT support a finding of noncompliance:

When the CPHS Chair/designee determines that the facts do not support a finding of noncompliance as defined in this Policy, the report of noncompliance will be dismissed and no further action will be taken. The written report of findings and determinations of the Chair/designee will be sent to the PI and, when relevant, the affected investigator(s).

2. When the facts support a finding of noncompliance that is NOT serious or continuing:

When the CPHS Chair/designee determines that the facts support a finding of noncompliance that is not serious or continuing as defined in this Policy, the CPHS Chair or designee will either allow the research to continue with no further action required or require one or more of the following actions before the research can continue:

- (a) Require modifications in the research and/or consent form;
- (b) Require that subjects who are still participating in the research be re-consented or notified in writing of the noncompliance;
- (c) Require that subjects whose participation has ended be notified in writing of the noncompliance;
- (d) Modify the continuing review schedule;
- (e) Require review of the study activity by the Office of Research Compliance;
- (f) Require training; and/or
- (g) Any other action that is deemed appropriate to the noncompliance.

The written report of findings and determinations of the CPHS Chair or designee and corrective action, if any, will be sent to the PI and when relevant, the affected investigator(s).

Modifications submitted by the investigator in response to the report will be reviewed by the IRB according to **SOP 403**.


3. When the CPHS Chair or designee determines that there is possible serious or continuing noncompliance as defined in this Policy, the matter will be referred to the convened IRB for review. The IRB's determination will be provided to the PI.

F. Suspension of the Research

1. The PI may voluntarily place the research on hold in whole or in part while the investigation of noncompliance is being conducted. Such temporary holds are not subject to the reporting requirements in 45 CFR 46.108(a)(4) and 21 CFR 56.108(b)(2) (**SOP 410**).
2. At any point during the investigation the CPHS Chair or designee, or the IRB may temporarily suspend in whole or in part or terminate the research. Such suspensions or terminations (by the CPHS Chair or designee or IRB) must be reported to the appropriate regulatory bodies in accordance with the Policy on Reporting to Regulatory Agencies & Sponsors Regarding Human Subjects Research (**SOP 410**).

G. Consideration by the IRB

1. The convened IRB will review the report of noncompliance, the associated study documents that were submitted to the CPHS Chair or designee (listed under Section E of this policy), including any relevant audit reports, and the CPHS Chair or designee's preliminary report of findings and determination of serious or continuing noncompliance. The IRB may consider new or additional information.
2. The IRB may make one of the following determinations listed below as a result of its review:
 - (a) Acknowledge the report and allow the research to continue with no additional action required;
 - (b) Defer action pending additional information;
 - (c) Require modifications in the research (e.g., protocol, consent form);
 - (d) Require that subjects who are still participating in the research be re-consented or notified of the noncompliance;
 - (e) Require that subjects whose participation has ended be notified of the noncompliance;
 - (f) Modify the continuing review schedule;
 - (g) Suspend, in whole or in part, the research;
 - (h) Terminate IRB approval of the research;
 - (i) Require training for the PI or the PI and study team;
 - (j) Require periodic audits by the Office of Research Compliance; and/or

 Children's Hospital of Philadelphia RESEARCH INSTITUTE	<i>Committee for the Protection of Human Subjects (IRB)</i>	Published Date: 12/15/2022 Revised Date: 12/13/2022
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- (k) Any other action the IRB deems appropriate to the noncompliance
- 3. The IRB’s findings and actions will be communicated in writing to the PI.

H. Reports of Findings of Serious or Continuing Noncompliance

Within fifteen (15) days of final review by the IRB, the Institutional Official (or designee) is responsible for submitting a formal report of the serious or continuing noncompliance. The formal report will be drafted and distributed as described in **SOP 907**.

VII. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.108(a)(4) and 46.113	21 CFR 56.108(b), 120 and 121
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VIII. REFERENCES TO OTHER APPLICABLE SOPS

CHOP Research Misconduct Policy	IRB SOP 410: Suspensions and Terminations of IRB Approval
IRB SOP 907: Reporting to Regulatory Agencies & Sponsors Regarding Human Subjects Research	

IX. RESPONSIBILITIES

Title	Responsibility
Employee/Agent of CHOP	Responsible for reporting allegations of noncompliance
Recipient of Allegation Report	Responsible for documenting any reports of allegation of noncompliance and forwarding to the Chair, CPHS or designee <i>Note:</i> Allegations of noncompliance against the CPHS Chair will be forwarded to the VP, Research Compliance & Regulatory Affairs.
CPHS Chair	The Chair or designee, performs an initial review of the allegation of noncompliance. When facts support a finding of serious or continuing noncompliance, refers matter to the IRB.

IRB	Makes a determination of whether or not the events constitute noncompliance. Reports serious or continuing noncompliance to the Institutional Official;
Institutional Official (IO)	The IO or designee reports serious or continuing noncompliance internally and externally as appropriate.

X. REVISIONS:

- 10-03-2006: Initial approval date
- 07-08-2010: Revised to include the materials that must be provided to the CPHS Chair/designee and the Executive IRB Committee in order for the Chair/designee and/or Committee to make determinations regarding noncompliance.
- 11-16-2012: Revised to reflect “unchecking the box” on CHOP’s Federal Wide Assurance and the restructuring of the IRB committees.
- 06-02-2016: Revised to reference IRB SOP 907 for reporting requirements and to clarify continuing noncompliance may be across multiple studies.
- 09-25-2018 Revised to update definitions and other minor edits.
- 12-13-2022 Minor administrative edits.

XI. APPROVAL:

Approval Indicator: Approved by Amy Schwarzhoff and Barbara Engel on 12/13/22
Amy Schwarzhoff, Director, Human Subjects Research and Barbara Engel, Chair, CPHS