

 JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH	Human Research Protection Program Policies & Procedures	
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Title: Non-Compliance and Study Complaints	Date Effective June 8, 2005	Supercedes P&P dated November 18, 2004

BACKGROUND

All members of the JHSPH community who participate in human subjects research, or review such research as CHR members or HRPP staff, are committed by the School's Federal Wide Assurance to comply with the highest standards of ethical and professional conduct and with applicable Federal regulations when conducting such research. They must also comply with applicable State and local laws and regulations, and with HRPP policies and procedures. Principal Investigators have primary responsibility for protecting the rights and wellbeing of research subjects by ensuring that their studies meet these standards. Failure to do so may create avoidable risks for study subjects and/or the University.

Definitions

- A *study complaint* occurs when an individual expresses dissatisfaction with some aspect of the research. A minor complaint is one that does not involve non-compliance. Examples of study complaints that are not necessarily non-compliance would be: (i) the payment to research subjects is not delivered as scheduled, or (ii) a potential subject feels he or she was excluded from a study inappropriately.
- *Non-compliance* is failure to comply with relevant Federal, State or local laws or regulations, HRPP policies and procedures, or determinations of the IRB. This definition applies to investigators, research staff, IRB members and HRPP staff. For investigators, non-compliance includes, but is not limited to, initiating research without CHR approval and conducting research in an unapproved manner. Specific categories of non-compliance are:
 - *Non-compliance that is not serious.* This includes deviations from the approved research plan and unapproved changes to research practices that do not increase risk to subjects. Some examples of non-compliance that may be considered non-serious are:

- revising the advertisement used to recruit subjects without prior CHR approval,
 - failure to notify CHR before an investigator is added to, or removed from, an ongoing study, and
 - minor, non-substantive, changes in wording of a consent form.
- *Non-compliance that is serious.* This is non-compliance which, in the judgment of the Director, ORS, the CHR Co-Chair(s) or the convened CHR, increases risks to participants or adversely affects their rights or wellbeing. Some examples of non-compliance that may be considered serious are:
- initiating human subjects research without prior review and approval by CHR,
 - substantively modifying research plans or procedures without formal CHR approval, unless to eliminate immediate hazards to subjects,
 - failing to provide timely reports of problems related to the research that are both serious and unanticipated,
 - using consent forms not approved and stamped by CHR, and
 - breaching research subject confidentiality or violating their privacy.
- *Continuing non-compliance.* This is a pattern of repeated non-compliance which, in the judgment of the CHR Co-Chair(s) or CHR, suggests that, without intervention, instances of non-compliance will likely continue. The instances of non-compliance may or may not be serious or similar. Continuing non-compliance also includes failure to respond to a request by CHR to resolve an episode of non-compliance.
- *Intentional non-compliance.* This includes fraud or deception by a member or members of the research team or HRPP staff. The intent is usually to mislead study subjects, other investigators, study sponsors or others regarding study procedures or results. All intentional non-compliance is considered to be serious non-compliance.
- An *allegation of non-compliance* is an assertion made by a second party that must be supported by evidence before it is considered to be confirmed. Allegations of non-compliance may come from a variety of sources, including the investigators, collaborating researchers, study staff, research subjects or their families, CHR members and CHR staff. They may also be made anonymously.
 - *Research fraud (or scientific misconduct)* is intentional "fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results." It does not include honest error or honest differences in interpretations or judgments of data. See [PPM7](#).
 - An *administrative hold* occurs when the PI agrees, in response to a request from CHR, to voluntarily stop enrollment or other aspects of the study for a defined period.

- *Suspension of a study* involves suspension of CHR approval for all or part of the study. This is a temporary measure that must be reported to OHRP and to Federal sponsors of the study. It must be resolved by either restoring approval, possibly after required corrective actions, or withdrawal of approval.
- *Withdrawal of approval* is permanent withdrawal of approval by CHR; all research-related procedures must stop.

JHSPH POLICY AND PROCEDURES

This document describes how the HRPP investigates and resolves study complaints, and reports and allegations of non-compliance. It also describes the process for handling suspected research fraud or misconduct.

Reporting Study Complaints and Non-Compliance to the ORS

Minor study complaints that are resolved by the research staff need not be reported to ORS. All other study complaints and all instances of non-compliance shall be reported promptly to ORS.

Resolving Minor Study Complaints

Minor study complaints that are reported to the ORS are usually resolved by the ORS. The Director, ORS or ORS staff will work directly with the complainant(s), research staff and investigators to investigate and resolve the problem. The complaint and how it was resolved will be documented in writing by ORS staff, provided to the Director, ORS for review, and a copy placed in the study file. If the problem cannot be satisfactorily resolved by the ORS staff or the Director, ORS, it will be referred immediately to the appropriate CHR Co-Chair for evaluation and action as described below.

The procedures for investigating and resolving non-compliance and study complaints are described below. A flow diagram describing the process is available ([LINK](#)). Numbers in parentheses following the headings of sections below refer to numbered steps in the flow diagram.

Investigating Alleged Non-compliance (1)

When noncompliance is alleged, further information must be obtained to determine whether the allegation is true. An investigative team will be convened that includes the Director, ORS, the Institutional Official (IO) (or designee), and the Research Regulations Specialist (RRS). The RRS and/or the Director, ORS will compile the relevant background information and present the issue to the IO. The IO (or his or her designee) will then promptly contact the complainant, the respondent and the Principal Investigator, or others, to obtain a greater understanding of the facts surrounding the allegation. If the allegation

concerns serious or continuing non-compliance, the investigation will continue under the advice of JHU Counsel.

Individuals alleging non-compliance may be in sensitive positions relative to colleagues and superiors and must be protected from possible retaliation. All investigations will be confidential and whistleblower protections (**LINK**), as well as researcher integrity, will be respected.

Confirmed non-compliance (2)

A report of non-compliance is considered to be confirmed. It is typically made by the investigators or is based on information included in continuing review applications, requests for study amendments, reports of unanticipated problems, study audits, published reports, or student theses. Alleged non-compliance that is determined to be true is also considered to be confirmed non-compliance.

The relevant CHR will be informed of the non-compliance and of plans for the investigation on a regular basis.

Initial Inquiry: Is the Non-Compliance Serious or Continuing? (3)

When a confirmed report of non-compliance is received, an initial inquiry shall be made promptly to determine whether the non-compliance is serious or continuing. The fact-finding is carried out by the responsible Co-Chair (or designee) or the Director, ORS through confidential correspondence or direct discussion with the Principal Investigator. Other persons may also be interviewed and records may be obtained and reviewed.

Suspend the Study or Place it on Administrative Hold? (4)

If the non-compliance is serious or continuing, the Co-Chair shall determine whether the PI should be asked to voluntarily place all or part of the study on *administrative hold* for a defined period. Alternatively, the Co-Chair may *suspend CHR approval* of all or part of the study and report this action to OHRP, any Federal sponsors and JHSPH officials. When reaching this decision, the Co-Chair may consult with the CHR Executive Committee, the convened CHR, the IO or other officials of JHSPH. Either action is taken to protect subjects from possible continuing increased risk until corrective actions are developed and implemented. Study procedures will not be stopped or placed on hold, however, if doing so would place subjects at increased risk.

Investigation (5)

A single CHR Co-Chair (or designee) will lead the investigation, with assistance from the Director, ORS and ORS staff, and has primary responsibility for all communication with the investigators and with the relevant CHR until the issue is resolved. The decision as to which Co-Chair is responsible is made by the two Co-Chairs of the CHR that normally reviews the affected research.

The investigation should fully describe and document the instance of confirmed non-compliance and gain sufficient information to allow a decision to be made regarding appropriate corrective actions, as follows:

- For minor episodes of non-compliance the Co-Chair may give this task to the Director, ORS. Otherwise, the Co-Chair (or designee) will determine who should assist him or her with the investigation. The investigative team would normally include at least the Director, ORS and a Research Subjects Specialist.
- When the non-compliance is serious or continuing, the team may also include the Research Regulations Specialist. The team will plan and carry out the investigation under direction of the Co-Chair (or designee). The investigation is carried out through confidential correspondence or direct discussion with the PI. Other persons may also be interviewed and records may be obtained and reviewed. The EC, IO or CHR may be consulted at any time during the investigation. Depending on the findings, an audit of the study (or of other studies of the PI), may be carried out. The CHR will receive status reports on the investigation, as appropriate.

Developing Corrective Actions

Non-compliance that is not serious or continuing (6)

If the Director, ORS has led the investigation, the Director will usually be authorized by the responsible Co-Chair to develop corrective actions. If, however, the investigation is led by a Co-Chair (or designee) the corrective actions will be developed and communicated to the PI by the Co-Chair. The EC, IO or CHR may be consulted during this process. The incident and corrective actions will be documented in writing by the person leading the investigation and a copy placed in the study file. Reports of non-compliance that is not serious or continuing, and its resolution, will be provided every three months to the CHRs.

Non-compliance that is serious or continuing (7)

The Co-Chair (or designee) leading the investigation will develop proposed corrective actions in consultation with other members of the investigative team. The EC, IO, CHR or others may be consulted during this process to ensure that the actions are appropriate and take into account past decisions in similar situations, legal and policy requirements, and all requirements per 45 CFR 46.111. A report of the investigation, with recommended corrective actions, will be prepared by the Co-Chair (or designee).

The report will be provided to the CHR with the research plan, consent form(s) and any required supporting documentation in ample time for review prior to its meeting. The convened Committee will review the report and vote on the corrective actions. It may accept or modify the team's recommendation(s), develop different corrective actions, or request more information.

Examples of corrective actions the CHR may vote to take include:

- Withdraw CHR approval for some or all research activities (see below).
- Lift a suspension or ask the PI to lift an administrative hold; this may be contingent upon prior implementation of specified corrective actions.

- Modify the research plan to minimize risk to subjects.
- Modify the consent form.
- Monitor the consent process or other specific research activities.
- Modify the continuing review schedule.
- Notify current participants of protocol violations and obtain written confirmation of their willingness to continue to take part in the research.
- Notify investigators that:
 - a. CHR and JHSPH cannot certify that the research was approved, or was conducted as approved, by CHR; or
 - b. if asked to verify IRB review and approval, they must state that the research was not approved by CHR, or was not conducted as approved by CHR; or
 - c. they must include with any journal submission or other publication a statement that the research was not approved by CHR, or was not conducted as approved by CHR; or
 - d. part or all of the research may not be published and the relevant data must be destroyed.
- Require additional training for investigators or staff in good clinical practice (GCP), the responsible conduct of human subjects research and/or research bio-ethics.
- Disqualify the investigator from serving as PI on CHR-reviewed studies for a defined period.

Other actions are also possible.

If CHR approval is withdrawn and the study is terminated, CHR requires that all enrolled subjects with whom there is ongoing contact be notified. If termination is likely to adversely affect the rights or welfare of these subjects, CHR will require procedures for withdrawal that protect them to the greatest extent possible. If follow-up of subjects for safety or other reasons is permitted or required by CHR, the subjects must be informed that the study is being terminated and any unanticipated problems involving risks to the subjects or others must be reported to CHR (**LINK**).

If the non-compliance involves research that was conducted without prior approval by CHR, approval for the research already done cannot be provided retroactively.

Non-compliance that involves risks to JHSPH or JHU

Non-compliance may create a risk to JHSPH or JHU, such as the possibility of legal action. If this is considered possible or is threatened, the Institutional Official should be immediately informed. The IO shall, then, inform the General Counsel, the Dean or both, so that appropriate steps may be taken to protect the interests of JHSPH and JHU. Such situations are handled on a case-by-case basis.

Documentation and Reporting (8)

Confirmed non-compliance

When the investigation is complete and corrective actions have been decided, the Co-Chair (or designee) will prepare a written report of the investigation, the findings and the required corrective actions.

The report will include the following elements:

- the nature of the event;
- the findings of CHR, ORS or others who took part in the investigation;
- a summary of problems that required corrective action;
- the corrective actions taken by CHR; and
- any plans for further investigation or follow-up actions.

Copies of the report and cover letter will be placed in CHR files and be sent to:

- the Principal investigator,
- the responsible CHR Co-Chair,
- the Chairperson of the Principal Investigator's department (when appropriate),
- the Dean of JHSPH (when appropriate),
- the highest academic official of any collaborating institution(s) (when appropriate),
- JHSPH Legal counsel (when appropriate)
- the Research Regulations Specialist (when appropriate)
- the Chairperson of the local or collaborating IRB (when appropriate),
- the Chairperson of the study DSMB (when appropriate)
- FDA, whenever the study is FDA-regulated, with a cover letter signed by the JHSPH Institutional Official,
- the Associate Dean for Graduate Education and Research (when appropriate)
- the Professional Liability Claims Office and the Office of Legal Counsel, if the report raises issues of legal liability or there is a threat or perceived threat of a lawsuit,
- the study sponsor or the CRO representing the sponsor, if the study is sponsored (when appropriate),
- the JHSPH Office of Research Administration, if the study is sponsored, and
- the WIRB (when appropriate).

Alleged non-compliance

In the case of alleged non-compliance, whether confirmed or not, a report of findings and any actions taken will be provided to the complainant and the respondent, the Research Regulations Specialist, and others listed above, as appropriate.

Reports to OHRP and Federal Sponsors

Reports of serious or continuing non-compliance with Federal regulations, or of suspension or withdrawal of CHR approval, will be made to the Office for Human Research Protections (OHRP). The report will be drafted by the Co-Chair (or designee) for review and approval by the Institutional Official. The approved report will be signed by the CHR Co-Chair. The

cover letter to OHRP will be signed by the Institutional Official.

Reporting to OHRP shall be completed within 30 days after the investigation is complete and corrective actions have been agreed by CHR. If the investigation and decision on corrective actions will require more than 30 days after the non-compliance is first confirmed, the Co-Chair shall prepare a preliminary report that describes the situation, indicates an investigation is in progress, and provides a time frame for a follow-up report.

This will be signed by the Institutional Official and sent to OHRP and any Federal sponsor of the study.

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Reporting of possible research fraud or intentional non-compliance

If, during an investigation of reported or alleged non-compliance, evidence is uncovered of possible research fraud (scientific misconduct; fabrication or falsification of data, or plagiarism), or an allegation of fraud is made, this must be reported immediately to the Associate Dean for Graduate Education and Research, to be handled according to JHSPH Faculty PPM 7 - Fraud in Research. At any stage during an inquiry or investigation of possible research fraud, the CHR Co-Chair may be informed as to the proceedings or the resolution if the Dean deems it necessary to protect the research subjects.

If, during investigation of reported or alleged non-compliance, the investigator is found to be in intentional non-compliance, the matter shall be forwarded immediately to the Associate Dean for Graduate Education and Research, to be handled according to JHSPH Faculty PPM 8 - Procedure for Handling Allegations of Unsatisfactory Performance or Unacceptable Behavior. In this case, the CHR Co-Chair will serve as the complainant and will be involved in the process. This action shall be taken in addition to any measures to protect research subjects from increased and continuing risk. When the preliminary inquiry, and/or investigation is complete, the CHR Co-Chair will be informed as to the resolution.

RESOURCES & REFERENCES

21 CFR 56.113

45 CFR 46.113

OHRP Requirement _____

FDA Requirement _____

AAHRPP Element _____