REPORTING PROTOCOL DEVIATIONS AND NONCOMPLIANCES

Key Points

- Reporting protocol deviations is important to protect the welfare of research subjects and to ensure compliance with University and regulatory requirements.
- If there is a deviation from the approved protocol, an initial report should be made to the Director within no more than one week (7 calendar days) of the Principal Investigator learning of the incident. The report can be made via eProtocol on a Protocol Deviation Report, by phone, or by email.
- A Protocol Deviation Report must be submitted via eProtocol within two weeks of learning of the incident. See Quick Guide for instructions.
- After a Deviation Report is submitted, the PI will be contacted if further information or clarifications are needed.
- The PI will be notified of the CPHS determination (whether a noncompliance, and if so, whether it is simple (minor), serious, and/or continuing), as well as any corrective actions that may be required.

A. Scope

Investigators are responsible for ensuring that their research is carried out as approved by CPHS and in accordance with applicable University and regulatory requirements, but there are instances when the research does not follow this plan. Such occurrences can have a negative impact on research participants. Protocol deviations and noncompliances can alter the risk-benefit ratio for participants or may otherwise jeopardize in some way the safety, rights, and welfare of subjects. On the other hand, there are certain times when it is necessary to deviate from the approved research plan or continue aspects of the research during a lapse in approval in order to protect participants.

Regardless of the reason behind them, all protocol deviations and noncompliances must be reported to and reviewed by CPHS. Such reports are considered *possible* noncompliances until a determination has been made by the Committee. This guidance outlines the reporting responsibilities and review process for noncompliances and protocol deviations.

B. Important Definitions/Examples

Noncompliance: Failure to comply with the requirements of an applicable law, regulation, or institutional policy pertaining to the protection of human subjects, and/or with the requirements or determinations of an IRB.
NOTE: It is not noncompliance when there is a need to deviate from the approved protocol or continue aspects of the research after expiration of approval in order to protect the welfare of research participants. However, these occurrences must also be reported to the IRB as protocol deviations. Also, departure from the protocol that is due to a study participant's non-adherence is not considered to be a protocol deviation, but may need to be reported as an unanticipated problem (see Guidelines on Unanticipated Problem and Adverse Event Reporting).

Examples of noncompliance:

- Conducting human subjects research without CPHS approval (or determination of exemption) or conducting human subjects research during a lapse in study approval, unless it is determined that it is in the best interests of already-enrolled subjects to continue participating in the research.

- Any deviation from the approved protocol unless it is necessary to eliminate apparent immediate hazards to the subject, such as:
    - Enrollment of subjects who do not meet the study inclusion criteria.
    - Exceeding the approved sample size for a study.
    - Consenting of subjects without the current approved consent form (for non-exempt research).
    - Use of recruitment materials (for non-exempt research) that differ from those submitted and reviewed by the Committee.
    - Engagement of new study personnel in human subjects research without prior approval.
    - Maintenance and storage of study data in a manner that differs from the plans approved by the Committee.

C. Reporting Responsibilities

Reports of noncompliance may come to CPHS/OPHS from various sources. A subject may submit a complaint, a member of the research team may contact OPHS to report an incident, or a possible noncompliance may be discovered through formal or informal monitoring or auditing. In cases where the report comes from a source other than the PI, the Committee may ask the PI to submit a formal report.

Research staff who become aware of a noncompliance or protocol deviation should notify the PI as soon as possible. However, there are cases when research staff would prefer not to notify the PI. In such cases, reports should be submitted directly to the Director of Research Subject Protection, or the individual may report according to the University of California's whistleblower policy.

D. Reporting Timeframes

Regardless of the source, when a noncompliance or protocol deviation has occurred, an initial report should be made to the Director within no more than one week (7 calendar days) of the Principal Investigator learning of the incident. The report can be made via eProtocol on a Protocol Deviation Report, by phone, or by email. The initial report (if not done in eProtocol) must be followed by a formal report via eProtocol within no more than two weeks (14 calendar days) of the Principal Investigator learning of the incident (see eProtocol Quick Guide "Report a Protocol Deviation/ Noncompliance").

If any changes are needed to the protocol or consent materials (e.g., to reflect permanent changes to the protocol as a result of a deviation), these should be briefly described in the report. These changes must also be submitted as a separate amendment application. CPHS may require additional/different changes as a result of the review.

E. CPHS Review and Actions

When a report of protocol deviation or noncompliance is received, the PI or other parties may be asked to provide additional information in order to investigate the allegations and to ensure the report is complete. When reviewing reports of noncompliance or protocol deviation, CPHS will determine if the event was a noncompliance, and if so, whether it was (1) simple noncompliance, or (2) serious noncompliance and/or continuing noncompliance.

1. **Simple (minor) noncompliances** are the result of an unintentional deviation or omission from a protocol that CPHS has approved or determined to be exempt, or the conduct of research without CPHS/OPHS review that would have qualified for an exemption. These noncompliances do not negatively affect the rights, safety, or welfare of the subjects.

2. **Serious noncompliances** are noncompliances that adversely affects the rights or welfare of

participants. Some examples are: the noncompliance has increased the risk and/or decreased the benefit to individual subjects; the non-exempt research has occurred without appropriate CPHS review and approval; when egregious or intentional noncompliance has occurred; and/or another situation exists which the Committee has determined to be a serious noncompliance.

Continuing noncompliance is a pattern of noncompliance that indicates an inability or unwillingness to comply with the requirements of an applicable law, regulation, or institutional policy pertaining to the protection of human subjects and/or with the requirements or determinations of an IRB.

CPHS will respond to a report of noncompliance relative to its level of severity. In all cases, the determinations and required corrective actions (if any) will be communicated to the investigator in writing, and OPHS staff will follow up with the investigator to ensure and document that the corrective action has been taken. Potential actions may include but are not limited to:

- Establishing a corrective plan.
- Requiring investigator(s) to complete remedial training.
- Requiring subjects to be re-consented.
- Permitting or disallowing the use of data collected during the noncompliance.
- Requiring more frequent CPHS review of the project.
- Limiting the investigator's human subjects research privileges.
- Findings of serious or continuing noncompliance will be reported to the appropriate institutional officials and the federal agency (e.g., the Office for Human Research Protection, FDA, etc.) or funding agency as appropriate. In addition, campus policy includes failure to comply with requirements for the protection of human subjects as research misconduct, and further action may be required per University policy.
- CPHS has the authority to suspend or terminate approval of research that is not being conducted in accordance with CPHS policy and federal regulations or that deviates from the approved protocol. The Committee also has the authority to halt any activity that meets the definition of "human subjects research," even if the activity was not previously submitted for OPHS/CPHS review and approval or determination of exemption.

F. Additional information

CPHS Policies and Procedures (RR 410: Noncompliance)