Public Health Division
Protocol Deviation and Noncompliance

Investigators are responsible for conducting human subject's research in accordance with all applicable federal and state regulations, as well as the specific requirements of the Public Health Institutional Review Board (PH IRB). Once PH IRB approval has been obtained for a research protocol and its supporting documents (consent form, authorization form, data collection tools, etc.), changes may not be made unless prospective review and approval by the PH IRB is granted. Meaning, the research team must request approval for any proposed changes to the PH IRB approved documents by submitting a Project Revision/Amendment Form (PRAF) and applicable documents in "tracked changes" form. The only exception to this rule involves emergency action by an investigator to protect subjects from apparent immediate hazards.

Definitions:
Protocol Deviation: Any alteration or modification in the conduct of the research that has NOT been approved by the PH IRB prior to its initiation or implementation.

- Minor deviation: Does not have a significant impact on the research participants' rights, safety or welfare; the integrity of the data; nor does it substantially alter the expected risks to subjects as determined by the PH IRB.
- Major deviation: May impact the participants' rights, safety or welfare; the integrity of the data; or may substantially alter the expected risks to subjects as determined by the PH IRB.

Noncompliance: Failure to comply with federal regulations or the requirements or determinations of the PH IRB.

- Continuing non-compliance: Repeated instances of noncompliance by the investigator.
- Serious non-compliance: Instances that pose an increased risk to the safety, rights and welfare of research participants including when investigators either avoid or ignore PH IRB policies and fail to comply with PH IRB requirements/determinations and/or federal regulations.

Reporting Requirements:
Formal reports using the PH IRB Protocol Deviation/Non-compliance Report Form must be made by the Principal Investigator to the PH IRB within the following timeframes:

- Minor deviations must be reported to the PH IRB within ten working days of their occurrence or within ten working days of the Principal Investigator becoming aware of their occurrence.
- Major deviations must be reported to the PH IRB within five working days of their occurrence or within five working days of the Principal Investigator becoming aware of their occurrence.
- Non-compliance must be reported as soon as the Principal Investigator becomes aware, however, it is important to note that non-compliance will typically be recognized by the PH IRB itself and thus a report will be requested by the IRB for submission to account for the continuous non-compliance.
- If any of the above involve significant harm or risk of significant harm to a subject, the Principal Investigator must make a report to the PH IRB within 24 hours of discovery.

It is the responsibility of the Principal Investigator to determine whether a deviation is minor or major in nature and to ensure proper reporting to the PH IRB. However, the PH IRB Administrator will review and analyze the report to ensure the description of the occurrence aligns with the context

of the report. All submitted reports should be routed by the Principal Investigator to their study sponsor as outlined in the sponsor's protocol.

PH IRB Review of Submitted Reports:
Upon receipt of the report, the PH IRB Administrator will conduct an extensive preliminary review and assessment to ensure the description of the occurrence aligns with the context of the report, including what the Principal Investigator has distinguished it as. Revisions may be requested. Once vetted for accuracy and completeness, the report will be forwarded to the PH IRB Chair and/or Vice Chair along with a detailed summary, a recommendation for next steps, and a draft determination memo. Either the Chair, Vice-Chair, or a designated PH IRB Board member of their choosing will then provide a formal review, comparing what occurred to the PH IRB approved protocol. At that time, the Principal Investigator may be asked to respond to further questions. Any minor modifications to the protocol or supplemental study documentation that result due to the event, may be reviewed and approved in accordance with expedited procedures by the reviewer. If any resulting modifications are more-than minor in nature however, they must be brought forward to the Full Board. E-mail review and approval will be permissible due to the quick turnaround required for such situations. Additionally, if the PH IRB Administrator is not present to provide the pre-review, that step may be bypassed.

Notification of Review and Determination:
A decision regarding the seriousness of the deviation or non-compliance will be made, including what corrective action, if any, to take. Once approved, a copy of the final determination memo will be sent to the P.I. explaining the details of the PH IRB review and expected next steps, whether or not proposed changes have been approved or if further changes are needed, who else, if anyone will be notified, and in some cases whether or not there will be an increase in reporting requirements, or if the study is suspended or terminated. If a suspension or termination of PH IRB approval occurs, a report must be made to OHRP via the Office for Human Research Protections' Incident Report Form. The report and its conclusions, including the formal PH IRB determination memo, will either be presented at the next scheduled PH IRB Full Board meeting or shared with the Full Board promptly via e-mail. If at that time, additional actions are requested, the research team will be notified.

In the case of minor deviations, if next steps or additional corrective actions are identified in the memo or by the Full Board, investigators will have 30 calendar days to respond. Non-response will constitute non-compliance, and subject recruitment may be suspended, or the project may be terminated. In the case of major deviations, if next steps or additional corrective actions are identified in the memo or by the Full Board, investigators will have 15 calendar days to respond. Again, non-response will constitute non-compliance, and the subject recruitment may be suspended, or the project may be terminated. It is important to note that major deviations and serious or continuing non-compliance may lead to immediate protocol suspension or termination by the PH IRB, but only after consultation with, and agreement by, the Full Board.

Additional Reporting:
Any serious or continuing non-compliance will be reported by the PH IRB to the Office for Human Research Protections (OHRP) and the sponsoring federal department or agency head. The reporting requirements in 45 CFR 46 do not specify a time frame, except to say it must be done in a "prompt" manner. In some instances, it may be appropriate for the PH IRB to submit an initial report to OHRP, indicating that a follow-up or final report will follow by a specific date, or when a final determination has been made.

- Office for Human Research Protections' Incident Report Form

Applicable Regulations
45 CFR 46.108 and 46.113
21 CFR 56.108 and 56.113