10.0 Complaints and Non-compliance

10.1 Policy

As part of its commitment to protecting the rights and welfare of human subjects in research, Pennington Biomedical Research Center reviews all complaints and allegations of non-compliance and takes any necessary action to ensure the ethical conduct of research.

All investigators and other study personnel involved in human subject's research are required to comply with all laws and regulations governing their research activities, as well as with requirements and determinations of the IRB.

The following procedures describe how complaints and allegations of non-compliance are handled by the IRB. In cases where serious non-compliance or continuing non-compliance has occurred, the IRB may exercise its authority to monitor, suspend, or terminate the research.

Regulations & Guidance: DHHS 45 CFR §46.103(b)(5)(i); 45 CFR §46.116(b)(5); FDA 21 CFR §50.25(b)(5); 21 CFR §56.108(b)(2); OHRP Guidance on Reporting Incidents to OHRP.

10.2 Definitions

Allegation of non-compliance: is defined as an unproved assertion of non-compliance.

Continuing non-compliance: is defined as a pattern of non-compliance that, in the judgment of the convened IRB, suggests a likelihood that instances of non-compliance will continue without intervention. Continuing non-compliance also includes failure to respond to a request to resolve an episode of non-compliance.

Finding of non-compliance: is an allegation of non-compliance that is proven true or a report of non-compliance that is clearly true. (e.g., a finding on an audit of an unsigned consent document, or an admission of an investigator that the protocol was willfully not followed would represent reports of non-compliance that would require no further action to determine their truth and would therefore represent findings of non-compliance.)

Non-compliance: is a failure to comply with any of the regulations and policies described in this document and failure to follow the determinations of the IRB. Non-compliance may be minor or sporadic or it may be serious or continuing.

Non-serious or minor noncompliance: Noncompliance that does not increase risk to research participants, compromise participants' rights or welfare, or affect the integrity of the research/data or the human research protection program. Examples of minor noncompliance may include, but are not limited to the following: lapses in continuing IRB approval, failure to obtain exempt determination before exempt research involving human subjects is conducted, minor changes in or deviations from an approved protocol, or administrative errors.

Serious non-compliance: is the failure to follow any of the regulations and policies described in these SOPs or failure to follow the determinations of the IRB and which, in the judgment of the convened IRB, increases risks to participants, decreases potential benefits, or compromises the integrity of the Human Research Protections Plan. Research being conducted without prior IRB approval is considered serious non-compliance.

Regulations and Guidance: OHRP Guidance on Reporting Incidents to OHRP.

10.3 Complaints

TheHRPP Director will promptly handle (or delegate staff to handle), and, if necessary, investigate all complaints, concerns, and appeals received by the IRB. This includes complaints, concerns, and appeals from investigators, research participants and others.

All complaints, written or verbal (including telephone complaints), and regardless of point of origin and funding source are recorded by IRB staff and forwarded to the IRB Chair.

Upon receipt of the complaint, the IRB Chair will make a preliminary assessment whether the complaint warrants immediate suspension of the research project. If a suspension is warranted, the procedures in section 3.11 - Study Suspension, Termination and Investigator Hold will be followed.

If the complaint meets the definition of Non-Compliance, it will be considered an allegation of non-compliance according to section 10.4 – Non-Compliance.

If the complaint meets the definition of an unanticipated problem, it will be handled according to section 8.1- Unanticipated Problems Involving Risks to Subjects or Others.

Within 10 business days of receipt of the complaint, the IRB Chair shall generate a letter to acknowledge that the complaint has been received and is being investigated to the party that reported the incident, if a follow-up contact name is provided.

10.4 Non-Compliance

Investigators and their study staff are required to report instances of possible non-compliance. The investigator is responsible for reporting any possible non-compliance by study personnel to the IRB. Common reports to the IRB that are serious or continuing are typically protocol deviations/violations. However, any individual or employee may report observed or apparent instances of non-compliance to the IRB. In such cases, the reporting party is responsible for making these reports in good faith, maintaining confidentiality and cooperating with any IRB and/or institutional review of these reports. Pennington Biomedical will take reasonable steps to protect persons who file reports in good faith from retaliatory actions based on such filing, in accordance with federal, state and local law.

If an individual, whether investigator, study staff or other, is uncertain whether there is cause to report non-compliance, he or she may contact the IRB Chair (or designee) or IRB Staff directly to discuss the situation informally.

Reports of non-compliance must be submitted to the IRB office within 10 working days of discovery of this non-compliance. The report must include a complete description of the non-compliance and the personnel involved.

Regulations & Guidance: FDA 21 CFR §56.108(b).

10.4.1 Review of Allegations of Non-Compliance

All allegations of non-compliance will be reviewed by the IRB Staff for completeness. The IHRPP Director will assign a primary reviewer, who will review:

1. All documents relevant to the allegation
2. The last approval letter from the IRB
3. The last approved IRB application and protocol;
4. The last approved consent document
5. The grant, if applicable; and
6. Any other pertinent information (e.g., questionnaires, DSMB reports, etc.).

The primary reviewer will review the allegation within 10 working days and make a recommendation following the review as to the truthfulness of the allegation (unless additional time is granted to conduct the review by the IRB Chair or HRPP Director).

When a recommendation of non-compliance is made because the incident was within the limits of an approved protocol for the research involved, the determination is reported by the IRB in writing to the investigator following the review and, if applicable, the reporting party.

If in the judgment of the reviewer, any allegation or findings of non-compliance is considered true, the non-compliance will be processed according to section 10.4.2 – Review of Findings of Non-Compliance.

If in the judgment of the IRB, any allegation or findings of non-compliance warrants suspension of the research before completion of any review or investigation to ensure protection of the rights and welfare of participants, the IRB Chair (or designee) may suspend the research as described in section 3.11- Study Suspension, Termination and Investigator Hold with subsequent review by the IRB.

The HRPP Director, IRB Chair (or designee) may determine that additional expertise or assistance is required to make these determinations and may form a sub-committee to assist with the review and fact gathering process. See 10.4.3 – Subcommittee Procedures.

10.4.2 Review of Findings of Non-Compliance

10.4.2.1 Non-compliance is Not Serious or Continuing

When the IRB determines that non-compliance occurred, but the non-compliance does not meet definition of serious non-compliance or continuing non-compliance, the determination is reported in writing to the investigator and if applicable the reporting party. The investigator will develop a corrective action plan to prevent future non-compliance, which will be reviewed by the IRB to confirm it's adequate. The report of non-compliance and corrective action is reported to the IRB and reflected in the IRB minutes. If however, the investigator refuses to cooperate with the corrective action plan, the matter is referred to a convened meeting of the IRB with notification to the Institutional Official.

10.4.2.2 Serious Non-Compliance or Continuing Non-Compliance

When the IRB Chair (or designee) determines that non-compliance has occurred and that the non-compliance meets the definition of serious non-compliance or continuing non-compliance, the report of non-compliance is referred for review by the IRB at the next convened available meeting. However, the HRPP Director with the support of the IRB Chair (or designee) may use discretion and call an emergency IRB meeting should the circumstances warrant such an urgent meeting or determine the non-compliance needs further review by the sub-committee.

Examples of serious non-compliance may include the following, but are not limited to: falsifying IRB documents; conducting human subject's research

without IRB approval; deviating from the IRB approved protocol or consent process; modifying the protocol or consent process without prior IRB approval.

All findings of serious or continuing non-compliance referred to the IRB will be reviewed at a convened meeting. All IRB members will receive:

- All documents relevant to the allegation,
- The last approval letter from the IRB.
- The last approved IRB protocol; and
- The last approved consent document.

At this stage, the IRB may:

- Find that there is non-compliance that is neither serious non-compliance nor continuing non-compliance and an adequate corrective action plan is in place
- Find that there is serious or continuing non-compliance and approve any recommended determinations proposed by the IRB Chair and/or sub-committee
- Request additional information.

10.4.3 Sub-Committee Procedures

The HRPP Director can appoint a subcommittee consisting of IRB members, and non-members if appropriate, to ensure fairness and expertise. The subcommittee is given a charge by the IRB, which can include any or all of the following:

1. Review of protocol(s) in question;
2. Review of sponsor audit report of the investigator, if appropriate;
3. Review of any relevant documentation, including consent documents, case report forms, subject's investigational and/or medical files etc., as they relate to the investigator's execution of her/his study involving human subjects;
4. Interview of appropriate personnel if necessary;
5. Preparation of either a written or oral report of the findings, which is presented to the convened IRB at its next meeting;
6. Recommend actions if appropriate.

The sub-committee will substantiate the findings of serious or non-serious non-compliance in writing to the convened IRB for review. The HRPP Director (or designee) is responsible for assuring that minutes of the meeting are generated and kept to help support any determinations or findings made by the sub-committee.

The report will include any recommended actions. These recommened actions are described in 10.4.4 – Final Review.

10.4.4 Final Review

The convened IRB and/or the results from the subcommittee will be reviewed at a convened IRB meeting. When a finding of non-compliance, the IRB's possible actions could include, but are not limited to:

1. Request a correction action plan from the investigator
2. Verification that participant selection is appropriate and observation of the actual informed consent
3. An increase in data and safety monitoring of the research activity
4. Request a directed audit of targeted areas of concern
5. Request a status report after each participant receives intervention
6. Modify the continuing review cycle
7. Request additional investigator and staff education
8. Notify current subjects, if the information about the non-compliance might affect their willingness to continue participation
9. Require modification of the protocol
10. Require modification of the information disclosed during the consent process
11. Require current participants to re-consent to participation
12. Require additional information given to past participants
13. Suspend the study (see below)
14. Terminate the study (see below)
15. Defer to the Research Integrity Officer and the Institutional Official

In cases where the IRB determines that the event of non-compliance also meets the definition of unanticipated problem, the policy and procedure for review of such events will also be followed.

The investigator is informed of the IRB determination and the basis for the determination in writing and is given a chance to respond. If the IRB determines that the non-compliance was serious or continuing, the results of the final review will be reported as described below in section 11.0 - Reporting to Regulatory Agencies and Institutional Officials.

10.4.5 Reinstatement of a Suspended Study

The corrective action(s) and stipulations necessary for the IRB to consider reinstatement of the research must be decided by the convened IRB. The approval will be described in written correspondence to the Principal Investigator.