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. Research participants or others are encouraged by the institution to report to the IRB Office any complaints or allegations of noncompliance.

The following procedures describe how complaints, concerns and allegations of non-compliance are handled by the IRB. In cases where serious non-compliance or continuing non-compliance has occurred, the 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 unproven assertion of non-compliance.

Non-compliance: is the failure to follow federal, state, or local regulations governing human subject research, institutional policies related to human subject research, or the requirements or determinations of the IRB.

Continuing non-compliance: A pattern of non-compliance which

- continues after initial discovery or IRB approval of corrective action plan or
- suggests that non-compliance will continue if there is no intervention, or
- increases the risk of serious non-compliance, or
- if continued, could significantly increase risks to, or jeopardize the safety, welfare, and/or rights of subjects or others, or
- if continued, could decrease potential benefits (the scientific integrity of the research).

Serious non-compliance: Non-compliance that creates an increase in risks to subjects, adversely affects the rights, welfare and safety of the research subjects or adversely affects the scientific integrity of the study. Willful violation of policies and/or federal regulations may also constitute serious non-compliance.

Examples of non-compliance

- Failure to follow any of the regulations and policies described in the HRPP policy
- Failure to follow the determinations of the IRB
- Research being conducted without prior IRB approval

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

10.3 Initial Assessment

The HRPP Director will promptly handle (or delegate staff to handle) and, if necessary, investigate all complaints, concerns, reports and allegations of noncompliance 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/designee.

Initial assessment of the validity of a report will be made by the HRPP Director in consultation with the IRB chair/designee, Director of Legal and Regulatory Compliance or appropriate official within the institution as needed. If the report has no basis in fact or cannot be adequately investigated given the information received, the IRB staff will acknowledge receipt in IRBManager and no further action will be taken.

The initial assessment may include, but is not limited to, a review of the approved consent document and/or protocol, speaking with study staff, or a review of financial records associated with the study.

The initial assessment will include a determination by the IRB chair/designee of whether the complaint warrants immediate suspension of the research project. If a suspension is warranted, the procedures in section, Study Suspension, Termination and Investigator Hold from Policy 3 will be followed.

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

If the report meets the definition of an unanticipated problem, it will be handled according to Policy 8- Unanticipated Problems Involving Risks to Subjects or Others.

If the report meets the definition of a deviation, it will be handled according to Policy 9 – Protocol Deviations.

If the report meets the definition of scientific misconduct, it will be handled according to PBRC policy 285.00 – Misconduct in Research.

Generally within ten (10) working days of the initial assessment, the IRB chair/designee shall generate a letter to acknowledge that the report 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. Principal investigators are required to report results of audits or inspections conducted by sponsors, other external entities such as the Food and Drug Administration (FDA), or internal oversight committees, which indicate noncompliance. 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 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

Reports of non-compliance can include but are not limited to, protocol deviations, unanticipated events involving risks to subjects or others, complaints from participants or others regarding treatment by research staff, reimbursement issues, issues of data integrity, or any other compliance concerns. When a report of non-compliance is made by someone other than the principal investigator, effort will be taken to maintain confidentiality. The name of the reporter will not be disclosed to the individuals involved in the complaint, unless disclosure is required to reconcile the situation.

IRB staff may receive an allegation of non-compliance by any means including, but not limited to:

- voluntary notification by the principal investigator or research staff, through IRBManager or direct communication with the IRB staff,
- information given by other staff of the institution,
- information given by other members of the research staff,
- monitoring reports provided by the study sponsor,
- reports of non-compliance by research subjects via the telephone number listed on all approved informed consent documents, or
- anonymous reports

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/designee may suspend the research as described in the section, Study Suspension, Termination and Investigator Hold with subsequent review by the IRB in Policy 3.

The HRPP Director with the assistance of the IRB chair/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 the definition of serious non-compliance or continuing non-compliance, the determination is reported in writing to the investigator and to the reporting party if applicable. 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 HRPP Director, 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 to 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 approved IRB protocol; and
- The last approved consent document.

At this stage, the IRB may:

- Find that there is no issue of Non-Compliance,

- 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/designee and/or sub-committee, or
- Request additional information.

10.4.3 Sub-Committee Procedures

The HRPP Director, the IRB chair or designee may 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 continuing 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 recommended actions are described in 10.4.6 – Final Review.

10.4.4 Referral to Others

At any point during the initial fact gathering process or later, the HRPP Director with consultation from the IRB chair or designee, determines that the facts raise issues apart from or in addition to noncompliance with applicable federal, state, and local laws and regulations or the requirements or determinations of the IRB, the HRPP Director shall notify or refer the matter or relevant aspects of the matter to others within the institution for review or other remedial or correction action.

10.4.5 Temporary Suspension (Hold) or Termination of Research

10.4.5.1 Voluntary Hold Placed on Research by the Investigator

The Principal Investigator (PI) may voluntarily place the research on hold in whole or in part while the investigation into reports of noncompliance is being conducted. Such temporary holds are not subject to the reporting requirements in 45 CFR 46.103(b) (5) and 21 CFR 56.108(b) (2).

10.4.5.2 Temporary Suspension or Termination of Research by the IRB

At any point during the initial fact gathering process or later, the IRB chair or designee may temporarily suspend in whole or in part or terminate the research.

Such suspensions or terminations will be reported in accordance with Pennington Biomedical Research Center policy. (see section on Suspension or Termination in Policy 3)

10.4.6 Final Review

Final review determinations and/or the results from the subcommittee will be reviewed at a convened IRB meeting. When there is 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. Request verification that participant selection is appropriate and observation of the actual informed consent
3. Request 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. Request that the investigator 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 be given to past participants
13. Suspend the study
14. Terminate the study
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 in Policy 11 - Reporting to Regulatory Agencies and Institutional Officials.

10.4.7 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.

10.5 Audits

Audit reports will be generated for each audit investigation and will be distributed to the principal investigator. For routine audits, the HRPP Director or designee will conduct an initial review of the audit report. If the audit report contains no findings related to serious or continuing non-compliance, the audit report can be accepted as written on behalf of the IRB. A copy of the audit report may be placed on the next agenda for IRB members to review for informational purposes.

The HRPP Director may work with the principal investigator, if requested, to implement any recommendations that were included in the audit report. Failure by the principal investigator to communicate to the IRB Office regarding implementation of recommendations may lead to a “for cause” audit or could be reported to the IRB as continuing non-compliance.

All audit reports that result from “for cause” audits, regardless of the findings, and any audit reports that either the HRPP Director or the IRB chair/designee (or both) determine to include findings of serious or continuing non-compliance will be placed on the next IRB agenda for review at a convened meeting of the IRB. Audit reports will be available for review by all IRB members.

Following the IRB’s review of the audit report and any additional determinations that they have made, the principal investigator will be notified (via IRB Manager) of the outcome of the review. If the IRB offers a plan of correction, the specific changes to be implemented will be communicated, as well as a time frame for implementing the changes. If the IRB has determined that the project is to be suspended or terminated, this information will be communicated to the principal investigator and handled

according to the IRB review process in Policy 3 and Reporting to Regulatory Agencies and Institutional Officials in Policy 11.