Procedure

Subject: Investigating and Managing Any Non-Compliance, Serious, or Continuing Non-Compliance

Procedure:
This procedure outlines the process for assuring the prompt reporting and management of any serious or continuing non-compliance with 45 CFR Part 46 or the requirements or determinations of the IRB.

I. Investigator Responsibilities.
   A. It is the Investigator's responsibility to adhere to the IRB approved protocol and not to initiate any changes or amendments to the protocol prior to IRB review and approval of the change or amendment, unless there is an apparent need to minimize risk to the participants. In this case the Investigator must notify the IRB within 7 calendar days of the amendment (See HRPP Policy III.J and III.L).
   B. The Investigator is responsible for the ethical management, accurate documentation, and the protection of human participants in their research.
   C. Between IRB continuing reviews of a protocol and at the time of continuing review of a protocol, it is the Investigator's responsibility to keep the IRB Committee informed of any unanticipated problems involving risks to subjects or others or adverse events even if the event occurred at a location for which the VUMC IRB is not the IRB of record. The Investigator is responsible for the accurate documentation, investigation, reporting, and follow-up of all possible study-related adverse events. Investigators are also responsible for the accurate documentation, investigation, reporting, and follow-up of all unanticipated events to subjects or others, as appropriate (See HRPP Policy III.L).
   D. The Investigator complies with all requests from the IRB for further information or clarification regarding concerns or issues under investigation.

II. Regulatory Compliance Analyst (RCA) Responsibilities.
   A. When the RCA receives a report of alleged non-compliance the RCA verifies whether detailed explanation from the Investigator accompanies the report.
      1. If a detailed explanation from the Investigator accompanies the report the RCA forwards the information to the IRB Chair for review.
      2. If a detailed explanation from the Investigator does not accompany the report the RCA contacts the Investigator to request additional information.
   B. If the report contains no explanation from the Investigator or comes from a source other than the Investigator:
      1. The RCA forwards the information to the Chair of the appropriate Committee for review and determination; and
      2. The RCA notifies the HRPP Director and the HRPP Medical Director within 1 working day.
   C. If the report contains an explanation from the Investigator and comes from a source other than the Investigator the RCA forwards the information to the IRB Chair for review.
D. If the non-compliance is to be reviewed by the convened IRB, the RCA prepares the following documents to be forwarded to all members of the Committee for review:
   1. The audit report (investigation report);
   2. The alleged notification of potential noncompliance, if applicable;
   3. The last approval letter from the IRB;
   4. The last approved IRB application; and
   5. The last approved consent document.
   6. Additionally, the primary and secondary reviewers receive:
      7. The last approved protocol;
      8. The last approved Investigator’s Brochure, if applicable;
      9. The Grant, if applicable; and
     10. Any pertinent information (e.g., questionnaires, DSMB reports, etc.).
E. The RCA facilitates and maintains documentation of all communication between the Investigator and the IRB Committee. The RCA notifies the PI in writing of IRB determinations. The letter requires a signature of the IRB Chairperson or his/her designee.
F. The RCA maintains and updates the IRB database appropriately with current study information.

III. IRB Committee Responsibilities.
A. If at any point in the evaluation of an allegation or finding of non-compliance the IRB Committee Chair or convened IRB needs more information to make a determination, the IRB Committee Chair or convened IRB directs an investigation by a Regulatory Compliance Analyst. The Investigator is notified in writing of the directed investigation (audit). The RCA notifies the IRB in writing of the results of the investigation.
B. If at any point in the evaluation of an allegation or finding of non-compliance the IRB Committee Chair or convened IRB discovers allegations or findings of research misconduct, the IRB Chair will report this to the Dean of the investigator’s school.
C. When the IRB Committee Chair reviews an allegation of non-compliance, the Chair reviews the information and either:
   1. Determines the allegation has no basis in fact in which case no further action is taken;
   2. Determines the allegation has a basis in fact, in which case the report is handled as a finding of non-compliance.
D. When the IRB Committee Chair reviews a finding of non-compliance, the Chair either:
   1. Determines the information is not serious non-compliance and not continuing non-compliance, the IRB Chair:
      a) Formulates a corrective action plan;
      b) Forwards the corrective action plan to the Investigator; and
      c) Forwards the information to be included in the IRB agenda as an information item.
   2. Determines the information is serious or continuing non-compliance.
E. The RCA provides all IRB Committee Members with the protocol, consent document(s), most recently approved IRB application and supporting information to determine one of the following:
   1. There is no issue of non-compliance;
   2. There is noncompliance that is neither serious nor continuing;
   3. There is serious or continuing noncompliance. The HRPP will report this determination according to HRPP Policy II.D;
F. If there is no non-compliance, the IRB takes no further action.
G. If the non-compliance is neither serious nor continuing, the convened IRB can refer the matter to the IRB Chair or consider the actions below for serious or continuing non-compliance.

H. If the IRB Committee determines the non-compliance is serious or continuing, the IRB considers the following added protections:
   1. Verification that participant selection is appropriate and observation of the actual informed consent process by an RCA;
   2. An increase in monitoring of the research activity via a data safety monitor or board and intervention as necessary through steps such as visits to the activity site and continuing evaluation of the site by an RCA;
   3. Request an off-cycle data and safety monitor or board review;
   4. Request a directed audit of targeted areas of concern;
   5. Request a status report after each participant receives intervention from the Investigator;
   6. Modify the continuing review cycle;
   7. Request additional Investigator and staff education focused on human research protections from an RCA or other available sources (e.g., Institutional Biosafety Committee (IBC), OHRP conferences, NIH tutorial, human research protections seminars, IRB News You Can Use or Research Matters);
   8. Request a literature search from the clinical librarian at the Eskind Biomedical Library;
   9. Notify current subjects, if the information about the non-compliance might affect their willingness to continue participation;
   10. Suspend the study (See HRPP Policy II.B); or
   11. Terminate the study (See HRPP Policy II.B).

References
HRPP II.C - Investigating Any Non-Compliance, Serious, or Continuing Non-Compliance