1.0 **Purpose**

The purpose of this SOP is to describe the procedure to ensure prompt reporting to the IRB, appropriate institutional officials, sponsor, coordinating center, and the appropriate regulatory agencies of unanticipated problems involving risks to participants or others.

2.0 **Definitions**

2.1 **Unanticipated Problems Involving Risk to Participants or Others.** This term is defined as an adverse event that is (1) unexpected, (2) serious, and (3) related or possibly related to participation in the research. Unanticipated problems also includes unexpected adverse events, regardless of severity, that the IRB determines represent risk to participants or others. Unanticipated problems also includes events that are not categorized as adverse events and are not directly related to an individual subject’s participation in a study, but represent risk to participants or others. 

*Example:* Events that could lead to a breach of confidentiality or privacy provisions such as the unanticipated loss or theft of files or that in anyway might subject the research participant to a higher degree of risk than anticipated in the research protocol.

2.2 **Adverse Event (AE).** This term is defined as any untoward physical or psychological occurrence in a human subject participating in research. An AE can be any unfavorable or unintended event including abnormal laboratory finding, symptom or disease associated with the research or the use of a medical investigational test article.

2.3 **Serious Adverse Event (SAE).** This term is defined as death; a life threatening experience; hospitalization (for a person not already hospitalized); prolongation of hospitalization (for a patient already hospitalized); persistent or significant disability or incapacity; congenital anomaly and/or birth defects; or an event that jeopardizes the subject and may require medical or surgical treatment to prevent one of the preceding outcomes.

2.4 **Unexpected Adverse Event (UAE).** This term is defined as any adverse event and/or reaction, the specificity or severity of which is not consistent with the informed consent, current investigator brochure or product labeling. Further, it is not consistent with the risk information described in the general investigational plan or proposal.

2.5 **Related.** An event is “related” if it is likely to have been caused by the research procedures.

2.6 **Substantive Action.** An action taken by an IRB that materially alters the substance and meaning of a protocol, informed consent form or process, or investigator status, including, but not limited to, restriction, suspension or termination of a study or...
investigator participation, and actions taken to prevent future occurrence(s) of the AE in research.

2.7 Unexpected Death. The death of a research subject in which a high risk of death is not projected, as indicated by the written protocol, informed consent form, or sponsor brochure. This definition does not include deaths associated with a terminal condition unless the research intervention clearly hastened the subject’s death. A subject’s death that is determined to be clearly not associated with the research is also not an “unexpected death” for purposes of the reporting requirements of these procedures.

3.0 Policy

It is the IRB’s policy to comply with Health and Human Services regulations at 45 CFR §46.103(b) (5) (1) (i) to have policies and procedures that ensure reporting of all unanticipated problems involving risk to participants or others to the IRB, regulatory agencies, and institutional officials.

3.1 The following problems must be reported to the IRB within 48 hours using the Problem Report form:

A. Any physical or psychological harm experienced by a participant, which in the opinion of the principal investigator, is both unexpected and related.

1. Harm is “unexpected” when its specificity and severity are not accurately reflected in the consent document.
2. Harm is “related to the research procedures” if in the opinion of the principal investigator, it is more likely than not to be caused by the research procedures or if it is more likely than not the event affects the rights and welfare of current participants.

B. Information that indicates a change to the risks or potential benefits of the research. For example:

1. An interim analysis or safety monitoring report indicates that the frequency or magnitude of harms or benefits might be different from those initially presented to the IRB.
2. A paper is published from another study that shows that the risks or potential benefits of your research might be different from those initially presented to the IRB.

C. A breach of confidentiality.

D. Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research participant

E. Incarceration of a participant in a protocol not approved to enroll prisoners.

F. An event that requires reporting to the sponsor.

G. Sponsor imposed suspension.

H. Complaint of a participant.
I. Protocol deviation.

3.2 IRB review of external reported problems.

A. The IRB Chair reviews problem reports and determines whether each is an unanticipated problem involving risks to participants or others. If the report is an unanticipated problem involving risks to participants and others, it is referred to the convened IRB for review. The IRB Chair also considers whether each report involves noncompliance. If so, the noncompliance policy is followed. If the IRB chair determines that the report is neither an unanticipated problem involving risks to participants or others nor noncompliance, it is filed and no further action is taken.

B. The IRB Chair will take all actions necessary to protect human participants including suspension or termination of the study (HRPP Policy #14.001). Investigators may also make changes to the research without prior approval by the IRB when necessary to eliminate apparent immediate hazards.

C. If referred for full IRB review, two (2) IRB reviewers are assigned to review the Report of Unanticipated Problem(s) or Adverse Event(s) Involving Risk. These members are provided and expected to review, in depth, copies of:
   2. The current consent document.
   3. The protocol application.
   4. The industry protocol (if one exists).
   5. The investigator’s brochure (if one exists).

D. All IRB members are provided and are expected to review, be familiar with, and be prepared to discuss copies of:
   1. The Report of Unanticipated Problem(s) or Adverse Event(s) Involving Risk and all submitted supporting materials.
   2. The current consent document.

E. The primary reviewers present the event or problem and lead the discussion. The IRB discusses and votes on whether the event or problem represents an unanticipated problem involving risks to participants or others as defined above. If the IRB determines by majority vote that the event or problem represented an unanticipated problem involving risks to participants or others, the SOP on Reporting to Regulatory Agencies and Institutional Officials will be followed (see HRPP policy #14.001 and #14.002). If the IRB determines that the problem is not an unanticipated problem involving risks to participants or others, the IRB determination overrules the determination of the chair and no further action is taken. The IRB determination of whether the problem is an unanticipated problem involving risks to participants or others is documented in the minutes.

F. The IRB considers the following actions on all reportable events or problems:
1. No action.

2. Modification of the research protocol.

3. Modification of the information disclosed during the consent process.

4. Additional information provided to past participants.

5. Notification of current participants (required when such information may relate to participants’ willingness to continue to take part in the research).

6. Requirement that current participants re-consent to participation.

7. Modification of the continuing review schedule.

8. Monitoring of the research.

9. Monitoring of the consent.

10. Suspension of the research.

11. Termination of the research.

12. More information sought pending a final decision or

13. Referral to other organizational entities (e.g., legal counsel, risk management).

Administrative Approval:

Dan R. Hoyt, Ph.D.
IRB Chair

Kimberly Andrews Espy, Ph.D.
Associate Vice Chancellor for Research