Subject: Procedure for Reporting of Adverse Events, Serious Adverse Events, and Unanticipated Problems Involving Risk to Participants or Others

Procedure:
This procedure outlines the process for reporting of adverse events, serious adverse events, and unanticipated problems involving risk to participants or others.

I. Investigator Responsibilities.

A. The Investigator submits any serious adverse event that requires reporting according to this policy and any other adverse event that may represent an unanticipated problem involving risk to participants or others as follows:

1. A "Report of Unanticipated Problem Involving Risk to Participants or Others" is submitted to the IRB as soon as possible, but no later than 7 calendar days after the Investigator first learns of the event or problem.

2. This form contains the Investigator’s assessment of causality (related or not related to the study) and a description of the actual event;
   a) The form also contains an evaluation of whether the event meets the following criteria:
      (1) An event that suggests that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized;
      (2) Unanticipated (i.e., the event was not foreseeable); and
      (3) Related (i.e., likely to have been caused by the research procedures) and;

3. Any associated materials such as medical record notations or reports with the name and medical record number of the individual redacted (removed).

4. When applicable, a "Request for Amendment" indicating changes associated with the event or problem is submitted.

B. The Investigator is responsible for the accurate documentation, investigation, and follow-up of all unanticipated problems involving risk to participants or others that occur at the site in which the Investigator is responsible for the conduct of the research.

C. Investigators whose trials involve the use of recombinant DNA molecules in humans must also adhere to the reporting requirements outlined in the Institutional Biosafety Committee policy entitled: "Policy and Procedure for Reporting Serious Adverse Events Occurring on Human Gene Transfer Clinical Trials" (found at http://www.safety.vanderbilt.edu/bio/human-subjects-studies.php).
II. IRB Chair/Designated Committee Member Responsibilities.
   A. All reports made under the policy are provided to a Chair or a designated Committee Member for review within 2 working days.
   B. The reviewer is provided:
      1. A copy of the report and all attachments; and
      2. The IRB file.
   C. The Chair reviews the materials to determine whether the risk-potential benefit profile has changed.
   D. The Chair reviews the materials to determine whether the event represents an unanticipated problem involving risk to participants or others as follows:
      1. The Chair evaluates whether the event meets the following criteria:
         a) An event that suggests that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized;
         b) Unanticipated (i.e., the event was not foreseeable); and
         c) Related (i.e., likely to have been caused by the research procedures).
   E. If the Chair cannot make a determination for each criterion, the event will be forwarded to the full IRB Committee to make these decisions.
   F. If the Chair determines that the event meets all three criteria, then the event will be considered an unanticipated problem involving risk to participants or others and the event will be referred to the IRB Committee for further action.
   G. If participants are at immediate risk of harm and there is insufficient time to wait for review by the convened IRB, the Chair or designated Committee Member suspends the study according to HRPP Policy II.B.
   H. If the Chair determines that the event does not meet one or more of the three criteria, then the event will be considered not to represent an unanticipated problem involving risk to participants or others, the report will be accepted and signed by the Chair. However, if the event alters the IRB approved protocol, proposal, informed consent document or risk-potential benefit profile, the Chair or designee will determine the need for full IRB Committee review according to HRPP Policy III.K.

III. IRB Committee Responsibilities.
   A. If the Chair could not determine whether the reported event represented an unanticipated problem involving risks to participants or others, the IRB Committee will determine whether the event meets the following criteria:
      1. An event that suggests that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized;
      2. Unanticipated (i.e., the event was not foreseeable); and
      3. Related (i.e., likely to have been caused by the research procedures).
   B. If the IRB determines that the event meets all three criteria, then the event will be considered an unanticipated problem involving risk to participants or others.
      1. The event will be reported according to HRPP Policy II.D.
      2. The IRB will consider whether the event represents serious or continuing non-compliance according to HRPP Policy II.C.
      3. In the case of deviations from the protocol taken without prior IRB review to eliminate apparent immediate hazard to a research participant, the IRB will consider whether the changes were consistent with the rights and welfare of participants.
   C. If the IRB determines that the event does not meet one or more of the three criteria, then the event will be considered not to represent an unanticipated problem involving risks to participants or others, and the report may be accepted by the full Committee and signed by the Chair or designee with no further action.
IV. HRPP Regulatory Compliance Analyst (RCA) Responsibilities.

A. Upon receipt of a “Report of Adverse Events and Unanticipated Problems Involving Risk to Participants or Others,” the RCA facilitates review by the Chair or designated Committee Member within 2 working days.

B. The RCA will consult with the IRB Chair or designated Committee Member for assistance in determining the appropriate level of review for the “Report of Adverse Events and Unanticipated Problems Involving Risk to Participants or Others.”

C. Events reported that do not change the risk-potential benefit profile, study protocol, or informed consent documents are forwarded to the IRB Chair or designated Committee Member for review.

D. Unanticipated problems involving risk to participants or others that change the risk-potential benefit profile, study protocol, or informed consent documents are prepared for full IRB Committee review. The RCA places the items on the next available Committee agenda, assigns Reviewers, and attaches the appropriate documents in the database for the Committee. Documents for all Committee Members include:

1. The report of “Adverse Events and Unanticipated Problems Involving Risk to Participants or Others;”
2. The DSMB or safety report, if applicable;
3. Any attached supplemental material submitted with the report;
4. The current IRB approved application and informed consent document(s);
5. The sponsor’s protocol;
6. The Investigator’s Brochure; and
7. Any other pertinent materials such as advertisements, questionnaires, etc.

E. Committee action letters and final approval letters are drafted using the appropriate template and forwarded to the IRB Chair or designated Committee Member for signature.

F. Appropriate database entries are completed. If approved by expedited review, the notice is included on the next available agenda for the Committee’s notification.

References
HRPP III.L - Reporting of Adverse Events