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

Definitions:

1. **Adverse Event**: There is no widely accepted common definition of an adverse event among regulatory entities. However, the FDA defines an Adverse Event as any undesirable experience associated with the use of a medical product in a patient.
2. **Related**: An event is “related” if it is likely to have resulted from participation in the research study.
3. **Risk-Potential Benefit Profile**: An evaluation of the risks and potential benefits that have occurred during the course of the study.
4. **Serious Adverse Event**: As defined by the FDA, any adverse event that results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse event when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.
5. **Unanticipated**: An event is “unanticipated” when it was unforeseeable at the time of its occurrence.
6. **Unanticipated Problems Involving Risk to Participants or Others**: Any event that was (1) unanticipated, (2) related, and (3) places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized.
7. **Unexpected Adverse Event**: As defined by the FDA, any adverse event, the specificity or severity of which is not consistent with the current Investigator Brochure; or, if an Investigator Brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the Investigator Brochure only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the Investigator Brochure only listed cerebral vascular accidents. Clarification Note: “Unexpected,” as used in this definition, refers to an adverse event that has not been previously observed (e.g., included in the investigator brochure) rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product and not listed in the Investigator’s Brochure.

Policy:

It is the policy of the IRB to require reporting of OHRP (the Office for Human Research Protections) and FDA (the Food and Drug Administration) defined events as follows:

1. The following requires reporting to the IRB within 7 calendar days of the VU or VUMC Investigator’s knowledge of the problem which includes serious adverse events, injuries, side effects, deaths, or other problems occurring at VU, VUMC or other locations in which the
Investigator is responsible for the conduct of the research and the VUMC IRB serves as the IRB of Record:

A. Any serious adverse event that in the Investigator’s opinion was unanticipated or unexpected, involved risk to participants or others and was possibly related to the research procedures; and/or
B. Any noncompliance with the IRB-approved protocol that increased risk or affected the participant’s rights, safety, or welfare.

II. Any unanticipated problem listed above in I.A and I.B requires reporting to the IRB even after the participant has completed the study or after the participant has withdrawn from the study including after study closure.

III. Study related events that do not occur at VU, VUMC or other locations in which the Investigator is responsible for the conduct of the research and the VUMC IRB does not serve as the IRB of Record do not need to be reported to the IRB unless, the event is related, unanticipated, and places subjects at a greater risk than previously known. In these instances, the PI will submit the event to the IRB via a "Request for Amendment". The amendment form must include the Sponsor and/or DSMB’s assessment of the event and the PI’s assessment of the event. Further, the amendment form should outline the necessary revisions to the IRB approved protocol and associated documents to incorporate the event’s impact on the risk-potential benefit profile of the study (See HRPP Policy III.K).

IV. All individual AEs are maintained by the Investigator. Adverse events may include a participant’s death as a result of a longtime illness (non-related), a breach in confidentiality or any complaint of a participant unless the risk involved is serious. In which case, the event is reported as an unanticipated problem involving risk to participants or others or as a serious adverse event at the time of occurrence.

V. Independent safety monitoring reports, interim analysis reports or Data and Safety Monitoring Board reports must be reported to the IRB when received by the PI. Individual outside safety reports are not required (See HRPP Policy III.K).

VI. For additional information regarding unanticipated adverse device effects, please refer to HRPP Policy XI.C.

References:
21 CFR 312.66
45 CFR 46.103(b)(5)
MedWatch – What is a Serious Adverse Event?
OHRP Guidance Document, "Guidance on Reviewing and Reporting Unanticipated Problems Involving Risk to Participants or Others and Adverse Events,” January 15, 2007