Local Adverse and Serious Adverse Event Reporting Policy

I. PURPOSE/BACKGROUND
Under federal regulations for the protection of human subjects in research, investigators have an obligation to report certain adverse events (AE) occurring in research subjects. The Department of Health and Human Services regulations (45 CFR 46.103(b)(5)) require institutions to have “written procedures for ensuring the prompt reporting to the Institutional Review Board, appropriate institutional officials, and federal departments or agencies, any unanticipated problems involving risks to human subjects or others.” Although the requirements are similar not identical, the Food and Drug Administration (FDA), study sponsors and institutional policy also include requirements for reporting events that may affect the safety of human research subjects.

II. DEFINITIONS

Adverse Event (AE) – An adverse event is any undesirable experience associated with the use of a medical product in a patient.

Life-threatening adverse event or life-threatening suspected adverse reaction.
An adverse event or suspected adverse reaction is considered “life-threatening” if, in the view of either the investigator or sponsor, its occurrence places the patient or subject at immediate risk of death. It does not include an adverse event or suspected adverse reaction that, had it occurred in a more severe form, might have caused death.

Serious Adverse Event (SAE) or Serious Suspected Adverse Reaction - The FDA definition is:
An adverse event occurring at any dose that, in the view of either the investigator or sponsor, results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization (for ≥ 24 hours), a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

Suspected adverse reaction
Means any adverse event for which there is a reasonable possibility that the drug caused the adverse event. For the purposes of IND safety reporting, reasonable possibility means there is evidence to suggest a causal relationship between the drug and the adverse event. Suspected adverse reaction implies a lesser degree of certainty about causality than adverse reaction, which means any adverse event caused by a drug.

Unexpected Adverse Event – An adverse event is defined as being unexpected if the event exceeds the nature, severity, or frequency described in the current IRB application including the protocol, consent form and investigator brochure (when applicable).
Serious Adverse Event (SAE) is any AE that results in any of the following outcomes:

**Death**- Report if you suspect that the death was an outcome of the adverse event, and include the date, if known.

**Life-threatening adverse experience**- Report if suspected that the patient was at substantial risk of dying at the time of the adverse event, or use or continued use of the device or other medical product might have resulted in the death of the patient.

**Inpatient hospitalization or prolongation of existing hospitalization**- Report if admission to the hospital or prolongation of hospitalization was a result of the adverse event. Emergency room visits that do not result in admission to the hospital should be evaluated for one of the other serious outcomes (e.g., life-threatening; required intervention to prevent permanent impairment or damage; other serious medically important event).

**Persistent or significant disability/incapacity**- Report if the adverse event resulted in a substantial disruption of a person’s ability to conduct normal life functions, i.e., the adverse event resulted in a significant, persistent or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities and/or quality of life.

**Congenital anomaly/birth defect or cancer**- Report if you suspect that exposure to a medical product prior to conception or during pregnancy may have resulted in an adverse outcome in the child.

**Any other experience that suggests a significant hazard, contraindication, side effect or precaution that may require medical or surgical intervention to prevent one of the outcomes listed above.**

**Any event that changes the risk/benefit ratio of the study.**

**Local (on-site) vs. External (off-site) Adverse Events**

**Local (on-site) Adverse Events** are

- AEs that occur in study participants who were enrolled through UofL or a UofL affiliated study site, or
- AEs that occur in a study under the direct supervision of a UofL Principal Investigator (PI) and for which UofL is the Institutional Review Board (IRB) of record.

**External (off-site) Adverse Events** are:

- AEs that occur in study participants who are not enrolled at a UofL or a UofL affiliated study site. These AEs occur at sites that are under the oversight of another IRB.
- The PI typically receives notification of these events from the Study Sponsor and these AEs are usually referred to as Sponsor Safety Reports or Safety Memos (see External Adverse Event Reporting Policy).

The following definitions should be used to assess the AE relationship to study participation:
Definitely Related: An AE is definitely related to study participation if it is clear that the event was caused by study participation. A definitely related event has a strong relationship and an alternative cause is unlikely.

Probably Related: An AE is probably related when there is a reasonable possibility that the event is likely to have been caused by study participation. The AE has a timely relationship to the study procedure(s) and follows a known pattern of response, but a potential alternative cause may be present.

Possibly Related: An AE is possibly related when there is a reasonable possibility that the event might have been caused by study participation. A possibly related event may follow no known pattern of response and an alternative cause seems more likely. In other circumstances there may be significant uncertainty about the cause of the event, or a possible relationship to study participation cannot reasonably be ruled out.

Unrelated: The cause of the AE is known and the event is in no way related to any aspect of study participation. If there is any uncertainty regarding AE causality, then the event must be assessed as possibly related to research participation and reported to the IRB as indicated. Often, the cause of an unrelated AE is disease progression.

Important note: Information involving AEs determined to be unrelated to research participation must be retained in the investigator’s study files for follow-up, documentation and reference. The local AEs should be documented by a note to file or by the PI affixing signature to the AE log or according to the sponsor provided protocol.

To determine if the Adverse and/or Serious Adverse Event qualifies as a UPIRTSO please see UPIRTSO policy for full information.

III. POLICY

The University of Louisville (UofL) Institutional Review Board (IRB) will not accept local AEs or SAEs unless determined to be:

1. Definitely, Probably, or Possibly related and
2. Serious or Unexpected; and
3. Related to the Research Intervention.

AEs clearly not related to research should not be reported (i.e., subject involved in traffic accident or breaks leg while playing basketball).

Subject deaths occurring in non-interventional studies (i.e., surveys, interviews and observational-only studies) that are in no manner related to the research do not need to be reported.

If a local (on-site) AE is noted as “unresolved” at the time of initial reporting, a follow-up report will be required if the AE does not resolve as expected, or if the AE results in a chronic condition or death.
IV. **How to Report**

Use the chart below as a guide to determine which adverse events, other events, and safety information need to be reported to the UofL IRB.

<table>
<thead>
<tr>
<th>Type of Adverse Event</th>
<th>When to Report</th>
<th>iRIS Form</th>
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</thead>
<tbody>
<tr>
<td>Local Adverse Event PI determines to be:</td>
<td>Report within 10 working days of UofL site awareness</td>
<td>Adverse Event (AE) Reporting Form within iRIS</td>
</tr>
<tr>
<td>• Definitely, Probably, or Possibly related <strong>and</strong></td>
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**Subject:** Local Adverse & Serious Adverse Events  
**IRB Policy and Procedure**  
**Approved:** 1/31/2014  
**Author:** Institutional Review Board  
**Effective Date:** 2/17/2014  
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