DEFINITIONS FOR ADVERSE EVENT (AE) REPORTING

A **serious adverse event** is any adverse event that results in any of the following outcomes:

- death,
- a life-threatening adverse event,
- inpatient hospitalization or prolonging 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, the event may jeopardize the patient or subject and/or may require medical or surgical intervention to prevent one of the outcomes listed in the definition above.

An **unexpected adverse event** is any adverse event that is not consistent with the current investigator brochure, protocol, consent form, or is not part of the normal disease progression. In addition, known adverse events may occur more frequently than expected. If so, then this event meets the definition of "unexpected" and must be reported to the IRB.

Full Board Protocols: IRB-01 considers all local deaths and non-local deaths (considered by the local PI or project Study Chair to be related or possibly related to study participation) to be Serious and Unexpected, even if it is a possible outcome of disease progression. These events must be reported within five working days of discovery. A non-local death considered to be unrelated can be reported at the time of CR on the cumulative AET.

Expedited and Exempt Protocols: IRB-01 considers all local deaths or non-local deaths (that is related or possibly related to study participation) to be Serious and Unexpected. These deaths must be reported within five working days of discovery. If the PI determines a non-local death is not related to participation in the protocol, the death can be reported at the time of CR on the cumulative AET.

A **local adverse event** is an adverse event that occurs in a subject enrolled in a protocol that is under the supervision of a University of Florida Institutional Review Board approved Principal Investigator. It does not matter where the subject experiences the adverse experience or where the subject may be treated for that adverse experience, the adverse event is still considered "local."

CAUSAL RELATIONSHIP OF ADVERSE EVENTS TO STUDY INTERVENTIONS:

"Related" A "related" causal relationship between a study intervention and an adverse event exists when the reaction follows within a reasonable time after the administration of the study drug or intervention, follows a known response pattern to the suspected study intervention, and is confirmed by improvement when the study intervention has stopped and the reaction reappears when the intervention is re-administered, or the patient has documented toxic concentrations of the study drug or evidence of the intervention in the blood or other fluid. A "related" causal relationship exists for drug overdoses in a patient with consistent symptoms, exhibits documented toxic concentrations in blood or other fluids, or responds to a specific antidote.

"Cannot be ruled out" A "cannot be ruled out" causal relationship exists when the reaction follows a known response pattern to the study intervention and is confirmed by improvement when the intervention is stopped, cannot be reasonably explained by the known characteristics of the condition being treated or, when the reaction follows within a reasonable time after the administration of the study drug or intervention, follows a known response pattern to the suspected intervention but could have been caused by the condition being treated or by other interventions.