North Florida Foundation for Research and Education (NFFRE)

Standard Operating Procedure

Adverse Event Reporting

1. PURPOSE

This Standard Operating Procedure (SOP) has been written to describe the procedure to be used by the investigator for the recording, management and reporting of Adverse Events (AEs), Adverse Reactions (ARs), Serious Adverse Events (SAEs), Suspected Serious Adverse Reactions (SSARs) and Suspected Unexpected Serious Adverse Reactions (SUSARs) which occur in subjects participating in Clinical Trials.

2. DEFINITIONS FOR ADVERSE EVENT (AE) REPORTING

Adverse Event (AE)

Any untoward or unexpected occurrence in a patient or clinical investigation participant where the occurrence does not necessarily have a causal relationship with the study intervention. An adverse event can therefore be any unfavorable, unusual and unintended sign, response, symptom, or disease where the outcome was not expected and has negative consequences for the patient or the caregiver.

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

- Death
- Life-threatening adverse event
- Inpatient hospitalization or prolonged existing hospitalization
- Persistent or significant disability/incapacity
- Congenital anomaly/birth defect

Important medical events that may not result in death, not be life-threatening, or not 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."

3. 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 readministered, 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.

University of Florida IRB Adverse Events – Reporting Instructions

You must report serious and unexpected adverse events that occur to subjects enrolled on the study listed below within 5 working days of discovery.

Sponsors may ask you to submit IND safety reports or other adverse events that occur to subjects enrolled at other sites on different protocols, but which involve the same test article (drug or device) being used in your study. IRB-01 does **not** accept these events unless all three of the following are true: (1) the event is serious and unexpected, (2) the event unexpectedly increases risk to the subjects in this study currently approved at UF, and (3) you/the sponsor provide substantive answers to questions 19.a. through 19.g.