ORLANDO HEALTH®

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Orlando, Florida 32806
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Type of Policy:	***PROTECTION OF HUMAN RESEARCH PARTICIPANTS***	Category:	**Orlando Health Institutional Review Board (IRB)**

Title:	***Reporting Serious Adverse Events***	Policy #:	**0330-1000**
		Replaced #:	ORMC IRB# 6000-0019 MDACCO IRB# 1000-0001-S
Page 1 of 3		Issued By:	Orlando Health Institutional Review Board (IRB)
Issue Date:	**7/19/95**	Approved By:	Philip Giordano, MD Institutional Official **SIGNATURE ON FILE**
Revision Dates:	1/1/01, 3/20/02, 11/12/07, 2/4/08, 1/1/09, 11/23/09, 7/29/11, 9/10/12, 8/14/14, 4/4/17, 4/21/20		

I. PURPOSE:

To maintain ethical and legal standards when reviewing adverse events.

II. DEFINITIONS:

A. Adverse event: Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally (the time between the study intervention and the adverse event) associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.

B. External adverse event: From the perspective of one particular institution engaged in a multicenter clinical trial, *external adverse events* are those adverse events experienced by subjects enrolled by investigators at other institutions engaged in the clinical trial. An IND safety report is an example of an external adverse event.

C. Internal (local) adverse event: With regards to a multicenter clinical trial, *internal adverse events* are those adverse events experienced by subjects enrolled by the investigator(s) at Orlando Health (OH) or any OH-affiliated site. In the context of a single-center clinical trial, all adverse events would be considered *internal adverse events.*

D. Possibly related to the research: There is a reasonable possibility that the adverse event, incident, experience or outcome may have been caused by the procedures involved in the research

E. Serious adverse event: Any adverse event temporally associated with the subject's participation in research that meets any of the following criteria:

1. results in death;
2. is life-threatening (places the subject at immediate risk of death from the event as it occurred);
3. requires inpatient hospitalization or prolongation of existing hospitalization;
4. results in a persistent or significant disability/incapacity;
5. results in a congenital anomaly/birth defect; or
6. any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the 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).

F. Unexpected adverse event: Any adverse event occurring in one or more subjects in a research protocol, the nature, severity, or frequency of which is:

1. Not consistent with the known, or foreseeable risk, of adverse events associated with the research procedures as described in protocol-related documents, such as the IRB-approved research protocol, the current IRB-approved informed consent document, and any other relevant sources of information (i.e., product labeling, investigator brochures, package inserts, etc.); or
2. Not consistent with the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.

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G. Life Threatening: is defined as the subject being at substantial risk of dying at the time of the unanticipated problem/adverse event or it is suspected that the study intervention or continuance of the study intervention would result in the subject's death.

H. Unanticipated Problem (i.e., unanticipated problem involving risks to subjects or others): any incident, experience, or outcome that meets **all** of the following criteria:

1. unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
2. related or possibly related to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
3. suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

III. POLICY:

Investigators will notify the IRB of all serious adverse events that occur at this institution and indicate their recommendations for the continuation, modification, or termination of studies involving the trial agent and/or research intervention. All unanticipated adverse events must be reported to the IRB within the required time frame described in this policy.

IV. PROCEDURE:

A. Reporting Local Serious Adverse Events:

1. **Prompt reporting:** All serious, unexpected, local adverse events definitely or possibly related to a trial agent must be promptly reported on the current OH IRB form to the IRB **within 5 working days** after site awareness. In addition, this type of event should be reported to the sponsor who will inform the Food Drug Administration (FDA), Office for Human Research Protections (OHRP) and/or National Institute of Health (NIH).
    i. Since it is unnecessary to include Protected Health Information, all patient information submitted regarding the adverse event must be de-identified on the IRB form. This is in accordance with HIPAA Guidelines' Minimum Necessary Standard.
    ii. Unanticipated risk may indicate that modifications to the investigational plan (which may also include changes to the informed consent form and/or plan to notify or re-consent enrolled subjects) are needed for the adequate protection of research subjects. These modifications may be submitted with the IRB form.

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iii. Upon review, the IRB will acknowledge the submission of the SAE. The IRB has the authority to recommend modifications to an approved study, suspend enrollment, or terminate the study in order to increase the protection of human subjects.

2. **At the time of Continuing Review:** All local serious adverse events that met or did not meet the prompt reporting criteria during the review period must be reported at the time of Continuing Review, using the appropriate IRB form.

B. Reporting External Safety Reports: The Office for Human Research Protection (OHRP) notes that reports of individual external adverse events often lack sufficient information to allow investigators or IRBs to make meaningful judgments about whether the adverse events are unexpected, related or possibly related. Individual adverse events should only be reported to the Orlando Health IRBs when a determination has been made that the events meet the criteria for an unanticipated problem. Ideally, external adverse events occurring in subjects enrolled in a multicenter study should be submitted for review and analysis to a monitoring entity (such as the research sponsor, DSMB/DMC, or statistical center) in accordance with a monitoring plan described in the IRB-approved protocol.

1. External Safety Reports do not need to be reported to the IRB unless they require a change to the protocol risks, the Investigator Brochure, the Informed Consent Form, or a change in the conduct of the study (e.g. temporary hold to enrollment). The changed documents should be uploaded with the Safety Report(s).
2. Only external adverse events that are identified by the sponsor in their report must be reported promptly to the IRB on the appropriate IRB form as an unanticipated problem under HHS regulation 45 CFR 46.103(b)(5). These reports should include both:
   i. a clear explanation of why the adverse event or series of adverse events has been determined to be an unanticipated problem; and
   ii. a description of any proposed changes to the investigational plan or other corrective actions to be taken by the investigators in response to the unanticipated problem.

V. DOCUMENTATION:

A. Serious Adverse Event Report Form
B. Internal Serious Adverse Event Log Sheet (Continuing Review)
C. Research Related IND Safety Report (External) Serious Adverse Event Line Listing form

VI. REFERENCES:

A. Office for Human Research Protection (OHRP) Guidance on Reviewing and Reporting Unanticipated Problems, January 15, 2007
B. Department of Health and Human Services (HHS) regulations 45 CFR part 46.103(b)(5)
C. IRBNet Template Library