


Standard Operating Procedures for Clinical Research at USF Health Morsani CRC			
	ADVERSE EVENT REPORTING		
	SOP#: 204	Effective Date: 01/01/2015 Revision date:	Version#:1.0 Page: Page 1 of 6

PURPOSE: The purpose of this SOP is to ensure that adverse and serious adverse events of studies conducted at the CRC are defined, recorded, reported and evaluated as required by the USF IRB and the ICH guidelines.

SCOPE: This SOP applies to all potentially related study events favorable and adverse, serious and non-serious, that must be recorded in the research record Case Report Form (CRF).

RESPONSIBILITY: Research team members in contact with a subject are responsible for documenting events reported by the subject and making those known to appropriate staff (eg: research coordinator, research nurse, PI, etc). The Principal Investigator (PI) is responsible for the accuracy, completeness and timeliness of records and reports. The PI will review all reports before signature or transmission.

DEFINITIONS:


Adverse Drug Reaction (ADR): The World Health Organization (WHO) defines an ADR as “any response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for the modification of physiologic function.”

Adverse Event (AE): 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 associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research. AEs encompass both physical and psychological harms and are a subset of UPIRHSOs. One must determine whether the AE qualifies as an UPIRHSO by identifying if it meets the three criteria listed above.

Case Report Form (CRF): A paper or electronic questionnaire specifically used in clinical trial research. The CRF is the tool used by the sponsor of the clinical trial to collect data from each participating site. All data on each patient participating in a clinical trial are held and/or documented in the CRF, including adverse events.

Clinical Research Organization (CRO): An entity that assumes one or more of the obligations of a Sponsor, as an independent contractor to the Sponsor.

Internal Adverse Event: Any unfavorable event related to the research procedure(s) that occurs to a USF research participant in a study approved by the USF IRB (both single site and multi-center) and that has a USF or USF Affiliate institution's faculty, staff, or student acting as Principal Investigator.

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DEFINITIONS (cont.):

External Event: An event that occurs to a research participant enrolled at a study site under the jurisdiction of another IRB at another institution (non-USF or USF-Affiliate). A summary of these events are submitted to the USF IRB at the time of continuing review.

Institutional Review Board (IRB): An independent body constituted of medical, scientific, and non-scientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trial protocol and amendments and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.

Office for Human Research Protections (OHRP): An office within the U.S. Department of Health and Human Services (HHS) that provides leadership in the protection of the rights, welfare, and wellbeing of subjects involved in research. OHRP helps ensure this by providing clarification and guidance, developing educational programs and materials, maintaining regulatory oversight, and providing advice on ethical and regulatory issues in biomedical and social-behavioral research.


Serious Adverse Event (SAE): An adverse event occurring at any dose or level of intervention that results in any of the following outcomes:

- Death
- A life threatening event
- Requires or prolongs inpatient hospitalization
- Persistent or significant disability / incapacity
- A congenital anomaly or birth defect
- Medical important events

Source Documents: Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial.

Sponsor: An individual, company, institution, organization that takes responsibility for the initiation, management, and/or financing of the research.

Unanticipated or Unexpected Adverse Event: Any research-related event which in the opinion of the Principal Investigator was unforeseen at the time of its occurrence and involved risks to participants or others. An unanticipated event may be symptomatically and pathophysiologically related to an event listed in the labeling but differs because of greater specificity or severity (21 CFR 56 Preamble).

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DEFINITIONS (cont.):

Unanticipated Problems Involving Risks to Subjects or Others (UPIRHSO): The Office for Human Research Protections (OHRP) defines a UPIRHSO as any event or outcome that was previously unforeseen and indicates that participants or others are at an increased risk of harm. OHRP considers unanticipated problems in general to include any incident, experience, or outcome that meets all of the following criteria:

1. Unexpected: not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application);
2. Related or possibly related to participation in research (there is at least a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research; and
3. Increased risk of harm: suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Examples of UPIRHSOs are as follows:

- A single occurrence of a serious, unexpected event that is uncommon and strongly associated with drug exposure or is uncommon in the study population;
- An AE or SAE that is described or addressed in the investigator's brochure, protocol, or informed consent documents, but occurs at a specificity or severity that is inconsistent with prior observations;
- Breaches in confidentiality, including the loss of data on a computer or any electronic device which holds private or confidential information, or which places the participant or others at risk;
- Laboratory or medication errors that may involve risk to that individual or others;
- Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol;
- Incarceration of a participant when enrolled in a study not approved under subpart C provisions;
- Allegations of noncompliance

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PROCEDURE:


- At each study visit, the Investigator or Study Coordinator will inquire if the subject has had any new clinical experience, exacerbation, and/or deterioration of any existing clinical condition since the last study visit.
- If the subject reports an AE, the research nurse or coordinator evaluated the event with the Investigator, who then must evaluate the seriousness of the event. If possible, the nurse or coordinator should discuss the event while the study subject is at the investigative site.
- If the event is not serious, the information is recorded in the study subject's source documentation file, transcribed onto the adverse event CRF, managed medically as appropriate, and then followed until resolution.
- If the Investigator determines that the adverse event is serious/ unanticipated problem, the coordinator reports this event to the Sponsor and IRB (immediately upon becoming aware of it or) within their reporting requirements
- The Investigator is responsible for reviewing all completed adverse event forms for determination of serious events that require reports to the Sponsor and IRB.
- The Study Coordinator will forward current information available on the event (hospital records, lab tests, discharge summaries, etc) to the Sponsor, and as additional information becomes available, it will be forwarded to the Sponsor.
- The Study Coordinator will ensure that all reported AEs and SAEs are properly documented in the subject's chart and CRF, and that the appropriate forms are retained in the Regulatory Documents Binder.

Non-Serious Adverse Events (AEs): For reported AEs, the Study Coordinator will document the following in the subject's chart and CRF:

- Date and time (if applicable) the event started and ended
- Description of the event
- Severity of the event
- Outcome of the event
- Action taken
- Relationship to study drug

Serious Adverse Experiences (SAEs): The Study Coordinator should collect as much of the following information as possible for reporting to the Sponsor/ CRO and IRB:

- Subject number and initials
- Date of birth
- Subject demographics
- Date of the report
- Description of event, including relationship to study drug
- Determination of seriousness
- Possible cause of SAE other than trial medication
- Relevant medical conditions
- Concomitant medications
- Principal Investigator's name
- Name and telephone number of person reporting the event

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PROCEDURE:

For reported SAEs, notify the following people in the timeframes listed below:


- PI and Study Coordinator- immediately
- Sponsor/ CRO- in the timeframe stated in the protocol, but no later than 48 hours. If the SAE is life-threatening or a death, the sponsor/ CRO will be notified within 24 hours.
- IRB- immediately of the Investigator becoming aware of the event.

Internal Adverse Events

- Once aware of an internal adverse event, the Investigator will determine if the AE is unanticipated.
- If the Investigator deems the AE to be unanticipated, he/she must report the event to the IRB within 10 working days of the event.
- The Investigator must also report the AE to the monitoring entity (eg: sponsor, CRO, etc.).
- If the Investigator determines that an AE is not unanticipated, but the monitoring entity does find the AE to be unanticipated, the monitoring entity will submit reports to the Investigator and the External IRB.

External Adverse Events

The Investigator will be notified of external adverse events via reports by the sponsor or coordinating center of the multicenter clinical trials.

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REFERENCES:	OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events (January 15, 2007); FDA Guidance Clinical Investigators, Sponsors, and IRBs Adverse Event Reporting to IRBs-Improving Human Subject Protection (January 2009); 21 CFR 312.32; 21 CFR 56 Preamble; 21 CRF 56.108(b); 21 CFR 612.34	
RELATED POLICIES:	21 CFR 612.34; USF IRB and Relied Upon IRBs policies: Reporting Adverse Event and Unanticipated Problems involving Risk to Human Subjects or Others; SOP 501 Case Report Form Completion; SOP 502 Source Documentation	
APPENDICES:	Appendix L: Flow Diagram for AE Reporting Appendix O: Adverse Event Tracking Log	
REVISION HISTORY: Keep a running history of all revision dates		
Approval Date	Effective Date	Review/Revision Date
01/01/2015	01/01/2015	