

CTO – SOP 4.4



ADVERSE EVENT REPORTING

INTRODUCTION

Subject safety is of the greatest importance for both the individual subject and the goals of the clinical study. Investigators are required to report to the sponsor all adverse events occurring locally during a study. If the event is serious and unexpected, prompt reporting to the sponsor and to the IRB of record is mandatory within 24 hours. This standard operating procedure describes the steps this clinical research team follows to fulfill the regulatory and clinical requirements for adverse event reporting.

SCOPE

This standard operating procedure describes the responsibilities of the research team for managing, reporting and documenting internal adverse events from the time an adverse event is identified until all follow-up activities associated with its resolution have been completed.

APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.32	IND safety reports
21 CFR 312.33	Annual reports
21 CFR 312.44	Termination
21 CFR 50.25	Elements of informed consent
21 CFR 56.108	IRB functions and operations
21 CFR 56.109	IRB review of research
21 CFR 56.115	IRB records
45 CFR 46.103	Assuring compliance with this policy-research

	conducted or supported by any Federal Department or Agency
45 CFR 46.109	IRB review of research
45 CFR 46.115	IRB records
45 CFR 46.116	General requirements for informed consent
FDA Information Sheets, October 1998	Continuing Review After Study Approval
May 1997	International Conference on Harmonization; Good Clinical Practice: Consolidated Guideline
October 2005	UNM CTO/NMCC Alliance Data Safety Monitoring Plan

July 2010 OHRP: Reviewing and Reporting Unanticipated Problems and Adverse Events (http://www.youtube.com/watch?v=hsUS0k3le_g_)

RESPONSIBILITY

This SOP applies to those members of the clinical and regulatory research teams involved in ensuring the appropriate management of internal adverse events. This includes the following:

- Principal investigator
- Co-investigator
- Research Nurse Manager
- Regulatory Manager
- Research Coordinator
- Research Nurse
- Regulatory Coordinator
- Data Coordinator
- Quality assurance auditors
- Study Pharmacists

PROCEDURES

Managing internal adverse events

<ul style="list-style-type: none"> • PI • Co-Investigator • Research Nurse/Coordinator 	<p>Follow a research subject who experiences any adverse change from baseline, ensuring that all appropriate resources are directed toward subject safety and well-being. Follow the subject until the event is resolved or stabilized and document accordingly.</p> <p>Discussion of adverse event grades and attribution will occur at each physician visit with the treating physician and research nurse/coordinator.</p>
<ul style="list-style-type: none"> • PI • Research Nurse/Coordinator • Study pharmacist 	<p>If necessary for the immediate medical care of the subject only, break the drug blinding after consultation (if possible) with the sponsor.</p>
<ul style="list-style-type: none"> • PI • Co-Investigator • Research Nurse/Coordinator • Regulatory Coordinator 	<p>Report Adverse Events per specific protocol and IRB requirements, in compliance with applicable. FDA reporting requirements Failure to report adverse events in a timely manner is considered non-compliance:</p> <p>For specific guidelines, follow:</p> <ul style="list-style-type: none"> • HRRC reporting policy for adverse events found at http://hsc.unm.edu/som/research/hrrc/Manual.html#eighttwo • WIRB reporting policy for adverse events found at: http://www.wirb.com/content/inv_adverse_events.aspx • NCI Central IRB reporting policy for adverse events found at: • http://www.ncicirb.org/AE_SOP_Memo_102810(4).pdf • http://www.ncicirb.org/AE_SOP_Memo_102810(4).pdf

	<ul style="list-style-type: none"> • http://www.ncicirb.org/CIRB_AE_Review_Process_Memo_040110.pdf • Sponsor reporting requirements as outlined in protocol • UNM CRTC CTO/NMCC Alliance Data Safety Monitoring Plan found at: http://hsc.unm.edu/crtc/intranet/ctoforms.asp
<ul style="list-style-type: none"> • Research Nurse/Coordinator • Data Coordinator • Regulatory Coordinator 	<p>Research Nurse/Coordinator record the details of the adverse event in the source documentation using the required AE & Con Med Flowsheet (Appendix A).</p> <p>Data Coordinator completes the appropriate CRFs.</p> <p>Research Nurse/Coordinator determines if the adverse event meets the reportable guidelines for a Serious Adverse Event (SAE).</p> <p>All SAE's event will be tracked in the Evelos system.</p> <p>All SAE's will be reported to the sponsor within 24 hours of knowledge of the event.</p> <p>A copy of the SAE sponsor and IRB report will be filed in the regulatory binder.</p> <p>All follow up reports related to a specific SAE will be similarly submitted to the sponsor and IRB, and filed in the regulatory binder.</p>
<ul style="list-style-type: none"> • Regulatory Coordinator 	<p>Keep originals or photocopies of all relevant documentation, including facsimile confirmations, and file in the study binder in a timely manner.</p>

Monitoring of internal adverse events

<ul style="list-style-type: none"> • Research Nurse/Coordinator • Regulatory Coordinator • Quality Assurance Auditors • PI • Co-Investigator 	<p>Adverse events are reviewed by study sponsors following submission of CRF's. With the exception of Investigator Initiated trials these are reviewed per the current Data Safety Monitoring Plan by the Data Safety Monitoring Committee (DSMC) .</p> <p>Reportable adverse events are reported to and reviewed by the PI (Co-Investigator), study sponsor</p>
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<ul style="list-style-type: none"> • DSMC Chairperson 	<p>and the IRB of record.</p> <p>Quality Assurance Auditors audit the patient records for accuracy of documenting and reporting adverse events for Investigator Initiated and Cooperative Group Trials per the current Data Safety Monitoring Plan.</p>
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<ul style="list-style-type: none"> • 	
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Identification, assessment and management of an internal adverse event

REGULATIONS	PROCEDURES
<p>Definition of an internal adverse event (AE):</p> <ul style="list-style-type: none"> • • An untoward or unfavorable medical occurrence in a human research subject, including any abnormal sign (abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in research, whether or not considered related to the subject's participation in the research. <p>Serious adverse events (SAEs) include:</p>	<p>Ensure that the following are appropriately investigated:</p> <ul style="list-style-type: none"> • Spontaneous reports by subjects • Observations by clinical research staff • Reports to research staff by family or medical care providers • Possible AEs documented in medical records and patient diary to include grade, attribution, start and stop date (if applicable), and outcome. • Reports of a subject death within four weeks after stopping treatment or during the protocol-defined follow-up period, whichever is longer, whether considered treatment-related or not <p>Research Coordinator documents adverse event by grade, attribution, length, and seriousness.</p>

- Death
- Life-threatening experience
- Inpatient hospitalization or prolongation
- Persistent or significant disability/incapacity
- Congenital anomaly/birth defect
- Events that would require medical or surgical intervention to prevent any of the above

Manage the adverse event to ensure that all appropriate resources are directed toward subject safety and well-being. Institute therapeutic intervention/support measures.

If applicable:

- Discontinue the investigational product, comparator, or placebo
- Unblind agent (as per protocol)
- Reduce dosage (as per protocol)
- Interrupt drug (as per protocol)
- Challenge (as per protocol)

Follow the subject and assess the adverse event until stabilized/resolved. Document resolution, end of event or other outcomes.

Report adverse event as indicated by sponsor, IRB guidelines and NM Cancer Care Alliance policy for reporting of external adverse events.

Approved: _____
CPDM/NMCCA Medical Director

Date: _____

SOP 4.4 - Adverse event reporting

Approved Date: 2/26/2004

Reviewed/Revised Date: 05/05, 8/05, 2/06, 9/08, 7/09, 12/10, 2/11, 6/11

Owner: Nurse Manager

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Research Coordinator Signature: _____

Physician Signature: _____

Note: AE/Con Med Flow sheet will be signed when the patient comes off treatment