CTO – SOP 4.4

New Mexico Cancer Care Alliance

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 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=hsUS0k3Ie_g_

RESPONSIBILITY

This SOP applies to those members of the clinical and regulatory research teams involved in ensuring the appropriate management of 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

• PI • Co-Investigator • Research Nurse/Coordinator	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. Discussion of adverse event grades and attribution will occur at each physician visit with the treating physician and research nurse/coordinator.
• PI • Research Nurse/Coordinator • Study pharmacist	If necessary for the immediate medical care of the subject only, break the drug blinding after consultation (if possible) with the sponsor.
• PI • Co-Investigator • Research Nurse/ Coordinator • Regulatory Coordinator	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: For specific guidelines, follow: • 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/invadverseevents.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 • 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
• Research Nurse/Coordinator • Data Coordinator • Regulatory Coordinator	Research Nurse/Coordinator record the details of the adverse event in the source documentation using the required AE & Con Med Flow sheet (Appendix A). Data Coordinator completes the appropriate CRFs. Research Nurse/Coordinator determines if the adverse event meets the reportable guidelines for a Serious Adverse Event (SAE). All SAE's event will be tracked in the Evelos system. All SAE's will be reported to the sponsor within required timeframe per the protocol and IRB requirements. Time begins when site is made aware of event. . A copy of the SAE sponsor and IRB report (if applicable) will be filed in the regulatory binder. All follow up reports related to a specific SAE will be similarly submitted to the sponsor and IRB, and filed in the regulatory binder.
• Regulatory Coordinator	Keep SAE originals or photocopies of all relevant documentation, including facsimile confirmations, and file in the study binder in a timely manner.

Monitoring of adverse events

• Research Nurse/Coordinator • Regulatory Coordinator • PI • Co-Investigator	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). Reportable adverse events are reported to and reviewed by the PI (Co-Investigator), study sponsor and the IRB of record.

Determining to Report Event to Either Sponsor or IRB

1) Determine if Adverse Event is reportable to sponsor. Reporting systems:
    a. Cooperative Groups: ADEERS
    b. Investigator Initiated Studies: Med Watch (Voluntary Form)
    c. Pharmaceutical Studies: Forms are sponsor specific
2) Determine if Event has to be reported to the IRB of record.
    a. HRRC (Cooperative Groups and Unfunded Investigator Initiated Studies).
        i. Reportable if the answer is yes to all three questions. Use the HRRC Event Form
            1. Was the patient put at risk
            2. Was the event caused by research
            3. Was the even related to
        ii. If Not Reportable (not all three questions above are not Yes): Use the Non-Reportable Tracking Log
    b. WIRB (Pharmaceutical and funded Investigator Initiated Studies)
        i. Reportable if the answer is Yes to these questions:
            1. Was the event unanticipated at the time of its occurrence?
            2. Did this even cause harm or place a participant or non-participant at increased risk of harm?
            3. Is it more likely than not that this event was caused by or probably caused by research?
        ii. Non-Reportable if the answer is No to any of the above questions.

Documentation of Serious Adverse Events (SAE)

- Key things to identify in your documentation:
    - Date apprised of the event.
    - Is the event reportable to the sponsor? If yes, date it was reported to sponsor.
    - Is the event reportable to IRB? If yes, date it was reported. If no, complete the tracking log for HRRC and for WIRB document this in notes.

- Include documentation of SAE on AE/Con Med Log (Appendix A)
- Enter in all SAE's into Evelos.

IRB's definition of adverse and serious adverse events

REGULATIONS	PROCEDURES
Definition of an adverse event (AE): • • 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.	Ensure that the following are appropriately investigated: • 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 Research Coordinator documents adverse event by grade, attribution, length, and seriousness.
Serious adverse events (SAEs) include: • 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: _____ Date: 2/17/12
CPDMI Medical Director

Appendix A: (Example of AE & Concomitant Med Flow sheet)

Appendix B: New Mexico Cancer Care Alliance Policy on Processing of External Adverse Event Safety Reports

Clinical Trials Office- Clinical Protocol & Data Management Department
Research Nurse Coordinator: _____

PATIENT: _____ **Protocol: _____**
MRN: _____ **Physician: _____**
PT STUDY #: _____

Cycle Dates					
Cycle 1	**Cycle 2**	**Cycle 3**	**Cycle 4**	**Cycle 5**	**Cycle 6**

Adverse Events and Con Med Flow Chart Using CTCAE 3.0
Attribution Codes: 1 = Unrelated, 2= Unlikely, 3= Possible, 4= Probable, 5= Definite
Study Drug Action Codes: 1= None, 2= Dose Reduced, 3= Interrupted, 4= Drug Discontinued

Adverse Event	Start Date	Stop Date	Grade	Attribution	Con Med	Dose	Start Date	Stop Date	Study Drug Action	SAE Yes/No

Research Coordinator Signature: _____ Physician Signature: _____
Note: AE/Con Med Flow sheet will be signed when the patient comes off treatment