THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

SOP-13: Adverse Event Reporting

1. Objective

To ensure that the Principal Investigator (PI) and all research team members assisting in the conduct of clinical research are informed about their obligations and responsibilities as they pertain to Good Clinical Practices (GCP), the investigational plan, applicable regulations, guidances, and institutional policies. This Standard Operating Procedure (SOP) applies to the written procedures followed by all members of a clinical research team involved in the conduct of human subjects' research at The Ohio State University Wexner Medical Center (OSUWMC), hereafter called the investigational site. These detailed instructions promote compliance in conducting clinical research.

SOP-13 describes the process for adverse event reporting for clinical research. Attachment templates include:

A: Adverse Event Log
B: IND Safety Report Cover Letter
C: IND Safety Report Note to File

2. Responsibility

The College of Medicine Center for Clinical Research Management (COM-CCRM) develops, implements, and maintains SOPs. The need to write a new or revise an existing SOP is based upon changes to federal regulations, guidelines, institutional policies, or procedures. These documents will be provided to departments and research teams conducting human subjects' research. Departments or research teams may develop additional research SOPs or a Research Procedure Addendum (RPA) to expand on an existing SOP, however this need should be limited.

The PI is ultimately accountable for all clinical research activities and is responsible for the appropriate delegation of tasks to individuals with adequate training and education to perform such tasks. It is the responsibility of all members of the clinical research team involved in supervising, managing, or conducting study-related activities to follow the SOPs. The clinical research team may include but is not limited to the following members:

Research Team Members

Principal Investigator (PI)	Clinical Research Coordinator (CRC)
Sub-Investigator or Co-I (Sub-I or Co-I)	Clinical Research Assistant (CRA)
Clinical Research Manager (CRM)	Other Research Staff as appropriate
Clinical Research Specialist (CRS)	Administrative and Support Staff

3. Definitions

Please refer to the SOP Glossary document for detailed definitions of commonly used clinical research terminology.

4. Procedures

The PI is responsible for ensuring an investigation is conducted according to the signed investigator statement, the investigational plan, applicable regulations, and any conditions of approval imposed by an IRB or FDA, for protecting the rights, safety, and welfare of subjects under the investigator's care, and for the control of IP under investigation.

The PI and delegated research team members will conduct the clinical research study in compliance with the IRB approved protocol. The investigator/institution and the sponsor will sign the protocol or an alternative contract to confirm their agreement, as applicable.

The PI and delegated members of the research team will not implement any deviation from or changes to the protocol without agreement by the sponsor and prior review and documented approval from the IRB of an amendment, *except* where necessary to eliminate an immediate hazard to clinical research study subjects, or when the changes involve only logistical or administrative aspects of the clinical research study (e.g., change of monitor, change of telephone numbers). The implemented deviation or change should be submitted to the IRB for review and approval, to the sponsor for agreement, and (if required) to the appropriate regulatory authorities within the required timeframe.

The PI or delegated research team members will document and explain any deviation from the approved protocol and report the deviation promptly to the sponsor, IRB, and any other regulatory agency, as applicable.

The investigator should promptly provide written reports to the sponsor, the IRB, and where required by the applicable regulatory requirements, the institution on any changes significantly affecting the conduct of the clinical research study, and/or increasing the risk to subjects.

A. Adverse Events

The PI and delegated research team members will conduct a review of systems and document the subject's baseline state, per the protocol, prior to any clinical research study intervention. They will review the subject's systems at regular intervals as outlined by the protocol and document any adverse change in health or wellbeing.

All adverse events observed will be documented noting the event description, seriousness, severity, relationship to the clinical research study intervention, start date, outcome, stop date and any medical care given to manage the adverse event. All adverse events will be recorded on case report forms (CRFs) or as outlined in the protocol. The site will maintain any supportive documentation as source documentation *(See Attachment A: Adverse Event Log)*.

All adverse events will be reported to the IRB, sponsor, and other regulatory bodies (e.g., FDA) according to the reporting requirements and within the time periods specified by the protocol and applicable policies and regulations. Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluations should be reported according to the reporting requirements and within the timeline specified by the sponsor in the protocol.

During and following a subject's participation in a clinical research study, the PI should ensure that adequate medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the clinical research study.

The PI and research team members will follow up appropriately when a research subject experiences any adverse change from baseline or pretreatment condition, ensuring all appropriate resources are directed toward subject safety and well-being. The subject should be followed until the event has resolved, or as specified in the protocol.

The research team should follow the clinical research study's randomization procedures, if any, and should ensure that the code is broken only in accordance with the protocol. If the clinical research study is blinded, the investigator should promptly document and explain to the sponsor any premature unblinding (e.g., accidental unblinding, unblinding due to a serious adverse event) of the investigational product(s). If possible, the sponsor should be consulted before unblinding occurs.

B. Serious Adverse Events

A serious adverse event (SAE) may include, but is not limited to, an adverse event that is fatal or life threatening, permanently disabling, requires or prolongs hospitalization, or results in significant disability, congenital anomaly, or birth defect.

Events requiring prompt reporting to the IRB of record may be unanticipated problems involving risks to subjects or others such as:

- Adverse events or injuries that are serious, unexpected, and related.
- Adverse device effects that are unanticipated.
- Protocol deviations or violations involving risks or with the potential to recur.
- Events requiring prompt reporting according to the protocol or sponsor.

All serious adverse events observed will be documented noting the event description, seriousness, severity, relationship to the clinical research study intervention, start date, stop date (if applicable), outcome, any medical care given to manage the adverse event and the date the research team was notified of the serious adverse event.

The PI and the delegated research team members will immediately report all SAEs to the sponsor according to protocol requirements and will also comply with the applicable regulatory requirements related to the reporting of unexpected serious adverse drug/device reactions to the FDA and the IRB.

The initial report should be followed promptly by detailed, written reports. The immediate and follow-up reports should identify subjects by unique code numbers assigned to the clinical research study subjects and protocol number. Subjects should not be identified by name or initials.

For reported deaths, the investigator should supply the sponsor and the IRB with any additional requested information (e.g., autopsy reports, death certificates, and terminal medical reports).

Event reporting information and a link to the event reporting form for OSU's Office of Responsible Research Practices can be found at www.orrp.osu.edu/irb.

Event reporting information and a link to the event reporting form at WCG IRB can be found at www.wcgirb.com.

For all other reviewing IRBs, please refer to their event reporting guidelines.

The PI and delegated research team members will ensure the IRB is notified of all serious or reportable events occurring at this site during the approval period for the ongoing study. The PI should ensure all adverse events are reviewed as part of the site's periodic or annual reporting requirements.

C. Managing Safety Reports

The PI and research team will review all safety reports which are sent from the sponsor regarding SAEs experienced at other sites. All safety reports received from sponsors will be promptly submitted to the IRB according to the IRB's reporting requirements and timelines for review *(See Attachment B: IND Safety Report Cover Letter and Attachment C: IND Safety Report Note to File)*. The PI will sign and date each IND report as acknowledgement of review. In the case of electronic reporting, the PI will log in to the portal for acknowledgement and review. A copy of all safety reports will be maintained and filed appropriately with the regulatory files for each protocol.

5. Applicable Regulations, Guidances and Policies

Regulation/ Guidance/Policy	Title
21 CFR 50	Protection of Human Subjects
21 CFR 56	Institutional Review Boards
21 CFR 312	Investigational New Drug Application
21 CFR 812	Investigational Device Exemptions
45 CFR 46	Protection of Human Subjects
OSU Office of Responsible Research Practices HRPP	Additional Requirements for Clinical Research: ICH GCP
OSU Office of Responsible Research Practices HRPP	Data and Safety Monitoring
OSU Office of Responsible Research Practices HRPP	Event Reporting
OSU Office of Responsible Research Practices HRPP	Event Report Determination Guidance
OSU Office of Responsible Research Practices HRPP	IRB Actions and Communications

OSU Office of Responsible Research Practices HRPP	Research Involving Human Subjects
OSU Office of Responsible Research Practices HRPP	Research Involving Investigational Drugs
OSU Office of Responsible Research Practices HRPP	Research Involving Medical Devices
OSU Office of Responsible Research Practices HRPP	Responsibilities of Principal Investigators, Co-Investigators and Key Personnel
OSU Office of Research Compliance	Human Gene Transfer
OSUWMC	Use of Patient Information by Hospitals and Medical Staff
OSUWMC	Patient Information & HIPAA Requirements
ICH GCP E6(R2)	Guideline for Good Clinical Practice E6 Integrated Addendum
FDA Guidance for Industry	Investigator Responsibilities- Protecting the Rights, Safety, and Welfare of Study Subjects, October 2009
FDA Guidance for Industry	FDA Inspections of Clinical Investigators-Information Sheet, June 2010
FDA Guidance for Industry	Adverse Event Reporting to IRBs-Improving Human Subject Protection, January 2009
FDA Compliance Program Guidance Manual	Program 7348.11 Bioresearch Monitoring: Clinical Investigators and Sponsor-Investigators
FDA Guidance for Industry	Frequently Asked Questions- Statement of Investigator (Form FDA 1572), May 2010

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