THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

SOP-12: Protocol Compliance

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-12 describes the process for ensuring protocol compliance and documenting and reporting protocol deviations for clinical research. Attachment templates include:

A: Note to File
B: Protocol Deviation Log

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

A. Protocol Compliance

The PI's responsibility includes, but is not limited to the following:

- Ensuring that clinical research is conducted according to the signed investigator statement, the investigational plan, and applicable regulations and any conditions of approval imposed by an IRB, sponsor, or other regulatory body.
- Protecting the rights, safety, and welfare of subjects under the investigator's care.
- Control of investigational product.
- Accurate and adequate data and case histories.
- Timely reporting of adverse events and study data.
- Assurance of IRB review.

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 record, *except* where necessary to eliminate an *immediate* hazard to a subject, or when the changes involve only logistical or administrative aspects of the study (e.g., change of monitor, change of telephone numbers).

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

The PI or delegated research team members may implement a deviation from, or a change in, the protocol to eliminate an immediate hazard to clinical research study subjects without prior IRB approval. The implemented deviation or change should be submitted to the IRB of record for review and approval, to the sponsor for agreement, and (if required) to the appropriate regulatory authorities within the required timeframe.

Noncompliance with the protocol, SOPs, GCP, and/or applicable regulatory requirements by an investigator or by members of the research team may lead to prompt action by the sponsor, IRB, and/or FDA to ensure compliance.

If monitoring and/or auditing identifies serious and/or persistent noncompliance on the part of an investigator or members of the research team, the research may be terminated at the site. If investigational site participation is terminated because of noncompliance, the regulatory authorities should be promptly notified.

B. Preventative Measures

If not already provided by the sponsor, the delegated research team member will appropriately create worksheets, flow sheets, study calendars, electronic health record smart phrases, paper orders, electronic order sets and other tools to be used for source documentation and/or as a reminder to clinical research team members to perform protocol specific evaluations, assessments, and tests.

These tools will be developed and shared with key personnel and clinical support staff prior to protocol implementation to ensure that all key members of the protocol management team are trained and educated on the expectations of the protocol.

The delegated research team members will meet regularly with the key personnel and clinical support staff involved in the conduct of the clinical research study. This will ensure that the tools created are utilized appropriately and are successful in preventing protocol deviations. Delegated research team members will ensure tools remain current should protocol changes arise and that appropriate approvals are obtained by the IRB of record, if applicable.

C. Protocol Deviations

If the PI or Sub-Investigator foresees the need for a protocol deviation waiver, they must receive sponsor approval prior to the deviation and obtain approval, in cases where waivers are permissible, by the IRB of record. Protocol waivers should be used in very rare situations where compliance is not feasible and where the protocol cannot be amended in a timely manner to avoid the deviation.

The PI or Sub-Investigator may deviate from the protocol to eliminate immediate hazard to the patient without prior sponsor or IRB approval. The delegated research staff will document the deviation in a note to file or as part of the subject medical record as a research note and appropriately report the deviation to the sponsor and IRB *(See Attachment A: Note to File),* as applicable*.*

If a member of the research team discovers a protocol deviation or subject non-compliance, they will document the deviation as part of the study records, subject medical record, or research chart. They will appropriately report the deviation to the sponsor, IRB of record and other regulatory authorities, as applicable, and as specified in the reporting requirements of the protocol *(See Attachment B: Protocol Deviation Log)*.

Protocol deviations will be reviewed at regular intervals with the PI, delegated research team members and clinical support staff. If consistent deviations are noted, attempts should be made to implement a new process or create tools to prevent future deviations. If the implementation of a new process or tools is unable to correct the problem, the PI should work with the sponsor to assess whether a protocol amendment is feasible.

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

45 CFR 160	HIPAA Privacy Rule
45 CFR 164 Subparts A and E	HIPAA Privacy Rule
OSU Office of Responsible Research Practices HRPP	Additional Requirements for Clinical Research: ICH GCP
OSU Office of Responsible Research Practices HRPP	Event Reporting
OSU Office of Responsible Research Practices HRPP	Noncompliance Practices
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 Responsible Research Practices HRPP	Review of Research by Convened IRB
OSU Office of Responsible Research Practices HRPP	Suspension and Termination of IRB Approved Research
OSU Office of Research	Research Data Policy
OSU Office of Research Compliance	Research Misconduct
OSU Office of the Chief Information Officer	Institutional Data Policy
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	Screening Tests Prior to Study Enrollment Information Sheet
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	Oversight of Clinical Investigations-A Risk-Based Approach to Monitoring, August 2013
FDA Guidance for Industry	Sponsor-Investigator-IRB Interrelationship-Information Sheet

FDA Guidance for Industry	Frequently Asked Questions- Statement of Investigator (Form FDA 1572), May 2010

Issued: 20-FEB-2012
Revised:16-DEC-2013, 16-APR-2015, 30-JUN-2017, 10-SEP-2019, 12-SEP-2022