THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

SOP-15: Investigational Product Management

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-15 describes the process for the receipt, storage, dispensing, reconciliation and return or authorized destruction of an investigational product (IP; e.g., drug or device). **Note: For all IP managed by Investigational Drug Service (IDS), please defer to IDS SOPs for IP management.** Attachment templates include:

A: Master Drug Accountability Log, B: Subject Drug Accountability Log, C: Subject Drug Diary, D: Study Drug Transport and Chain of Custody Form, E: Device Accountability 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

The PI is responsible for ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and 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 may delegate some or all of the Investigator's duties for managing IP accountability at the investigational site to an appropriate pharmacist or another appropriate individual who is under the supervision of the Investigator. The PI and delegated research team members will maintain a list of appropriately qualified staff members that have been delegated significant clinical research study-related duties. Additionally, delegated research team members engaged in the management of investigational product should be listed as key personnel with the IRB of record.

The PI and delegated research team members will be qualified by education, training, and experience to assume responsibility for the proper conduct of the study, will meet all the qualifications specified by the applicable regulatory and sponsor requirements, and will provide evidence of such qualifications through an up-to-date curriculum vitae and/or other relevant documentation requested by the sponsor, the IRB, and/or the regulatory authorities.

The PI and delegated research team members will:

- Ensure that the IP is used in accordance with the IRB approved protocol.
- Have all required documentation of completed training on handling and dispensing of IP.
- Explain the correct use of the IP to each subject and will check that each subject is following the instructions properly at intervals as defined by the clinical research study.
- In a randomized, double-blinded clinical research study, follow the study's randomization procedures, if any, and ensure that the randomization assignment is broken only in accordance with the protocol. (If the clinical research study is double-blinded, the investigator will promptly document and explain to the sponsor any premature unblinding of the IP such as accidental unblinding or unblinding due to a serious adverse event.)
- If emergency breaking of the study drug blind is medically necessary, the delegated research team member will document the reasons for breaking the blind and contact the study sponsor and other required regulatory authorities immediately.

Study Drug

A. Receipt and Inventory

Upon receipt of study drugs, a delegated research team member will review the shipment to ensure the information on the packing slip matches exactly what has been received at the site. This includes verifying the IP name, formulation, strength, quantity, lot numbers, expiration dates, supplies required for blinding the drug (if applicable) and that randomization assignment (if applicable) have been received. All information is to be tracked on a Master Drug Accountability Log *(See Attachment A: Master Drug Accountability Log)*.

If the sponsor includes a form to acknowledge receipt, the delegated research team member will obtain the appropriate signature and forward the form to the sponsor and retain a copy for the regulatory files. If any errors are identified, the delegated research team member will promptly document the errors and contact

the sponsor regarding the discrepancies. Copies of all invoices, drug dispensing and disposition records, randomization codes, and any other drug activity forms will be stored securely at the investigational site.

B. Safe Handling and Compounding

Study drug will be handled per the IP package insert, Investigator's Brochure (IB), protocol, pharmacy manual or Investigational Drug Service (IDS) guidelines. Specific precautions should be considered when handling hazardous drugs *(See Pharmacy Hazardous Drug reference in Applicable Regulation, Guidances and Policies section listed below)*.

Any research study that requires drug compounding is required to use IDS. IDS will make arrangements for sterile drug compounding.

Note: Utilizing sterile technique to reconstitute and/or withdraw drug from a vial for direct administration via IV push, subcutaneous injection, or intramuscular injection is not considered compounding and is permissible to be performed by delegated research team members.

C. Storage

The study drugs will be stored in a secure environment that is lockable, separate from commercial drug supply, with limited access for only delegated research team members. The site will ensure that study drugs are stored according to the storage requirements detailed in the protocol or supplied by the sponsor. This includes ensuring the study drug is stored at the appropriate temperature and a temperature log will be maintained, if required.

All refrigerators used for study drug storage will be plugged into outlets with back-up power where available. If the study agent is temperature sensitive, measures will be taken to capture the temperature continuously or at least daily. In the event that a temperature deviation is identified, the affected study drug will be immediately quarantined in the appropriate storage conditions and the sponsor will be contacted for further instructions. IP will not be dispensed until determined fit-for-use and all documentation of the event will be filed in the pharmacy binder.

No food, drink, or specimens will be stored in the same location as study drug.

The PI and delegated research team members will follow any special requirements for controlled substances required by the Controlled Substances Act at this investigational site in addition to those specified by the study drug regulations and institutional policies. It is strongly recommended that studies involving controlled substances be managed by IDS. If IDS is not a feasible option, additional education, training, and processes must be implemented due to the nature of the drug. The PI must contact IDS for consultation for specific guidance and training on controlled substances for research prior to study implementation.

D. Dispensing of Study Drug

Prior to dispensing study drug, the delegated research team members will ensure that study drug supplies are adequate and within an appropriate expiration date. If additional supplies are needed, the monitor or study sponsor will be contacted to request additional study drug. The Master Drug Accountability Log should be updated any time study drug inventory changes.

The PI is responsible for ensuring that study drug is appropriately dispensed and/or administered per protocol by delegated research team members.

The delegated research team members will ensure that each time a study medication is dispensed, the Subject Drug Accountability Log is completed *(See Attachment B: Subject Drug Accountability Log)*. Documentation should include:

- Amount dispensed
- Lot number/Bottle or kit number (if applicable)
- Name of individual dispensing study drug
- Subject ID number
- Subject's initials
- Date (and time, if appropriate) of dispensing
- Date (and time, if appropriate) and amount of study drug returned

If errors are made on the accountability form, there should be a single line through the error, with the initials of the person correcting the error and the date corrected. When recording the date, the month, day, and year will be recorded. For short stability agents, the preparation time and date as well as the dose time will be documented, if required by the sponsor. If study drug is wasted in error during preparation by the research team, this will be documented as a separate entry on the drug accountability form with reason for the error.

The delegated research team members will ensure that the correct study drug is used from the appropriate study supply and documented on the appropriate study drug accountability form. Study drug may not be used across protocols, and commercial drug may not be used in place of study drug.

It is recommended to provide diaries for administration of study medication at home to properly document use. The diary must be IRB approved. When the diary is returned to the site, the research team member will review the data for completeness. Source documentation should reflect but is not limited to amount of medication dispensed, bottle/kit number(s) dispensed, administration instructions, and subject education *(See Attachment C: Subject Drug Diary)*.

Discrepancies in the amount dispensed to the subject, used by the subject, or amount expected to be returned by the subject will be documented along with the reason for the discrepancies.

After the study drug has been dispensed, all containers and unused study drug should be returned by the subject to the site. The delegated research team member will document the date of return, drug name, lot number, quantity of unused study drug, and reason for missed doses, noncompliance or missing study drug.

E. Labeling of Study Drugs

All investigational drugs dispensed shall bear on the label "Investigational Drug: Limited by Federal Law to Investigational Use." Additional labeling information may include: subject name or initials, MRN or study sequence number, date of dispensing, study number, study drug name, directions for use, quantity, and name of PI and initials of dispensing staff. Investigational drug labels should not be obscured in any way.

F. Transport of Inventory to Satellite Site

Study drugs not managed by IDS may be transported to IRB approved satellite sites (as listed on the 1572) by a study team member. The chain of custody must be appropriately documented per sponsor requirements. Upon receipt, satellite staff will inspect the package and ensure receipt of documented items.

Receipt of study drug will be documented by satellite staff in satellite site drug accountability records. Storage conditions must be maintained during transport and meeting these requirements should be well documented *(See Attachment D: Study Drug Transport and Chain of Custody Form)*.

G. Mailing of Study Drug to Subjects

Study products may be mailed within the state of Ohio; however, all efforts will be made to avoid mailing study drug to subjects. If arrangements cannot be made, mailing of study drug to subjects within the state of Ohio is allowable as long as it is permitted per protocol, the sponsor and PI have given written authorization, and the mailing method is traceable (e.g., UPS or FedEx). Copies of shipping labels and permission from the sponsor and PI will be maintained in the subject's research record. If temperature monitoring is required, follow the instructions provided. If mailing across state lines, IDS must be contacted and provide approval.

H. Return/Destruction of Study Drug

At the conclusion of the study, the delegated research team member will ensure that all documentation regarding receipt, storage, dispensing, and return of used containers and unused study drug is complete, accurate, and ready for review for the termination visit.

Delegated research team members may appropriately destroy study drug at the site with written authorization and approval from the sponsor to do so. Destruction of study drug must follow institutional policies and procedures required by Occupational Safety and Health Administration (OSHA) and biohazard materials policies. IDS will assist with study drug destruction, as needed.

The delegated research team members will provide the sponsor with written documentation of the destruction of the study drug and maintain a copy for the regulatory files.

Study Device

A. Receipt and Inventory

Upon receipt of a study device, a delegated research team member must inspect the study device to verify the content, number of devices shipped, lot numbers and any other supplies received.

If there are any missing or damaged supplies, the delegated research team member will promptly document them and the sponsor and/or manufacturer will be notified to replace any missing or damaged supplies.

If the sponsor includes a form to acknowledge receipt, the delegated research team member will obtain the appropriate signature and forward the form to the sponsor and retain a copy for the regulatory files.

Copies of all invoices, device dispensing and disposition records, randomization codes, and any other device activity forms will be stored securely at the investigational site.

B. Labeling of Investigational Device

Upon receipt of investigational device, a label must be printed and attached to the box with the following statement: "CAUTION Investigational Device. Limited by Federal law to investigational use." The label will

describe all relevant contraindications, hazards, adverse effects, interfering substances or devices, warnings and precautions.

C. Storage

The study device will be stored in a secure environment with limited access for only delegated research team members. The delegated research team members will ensure that the study device is stored according to the storage requirements detailed in the protocol or supplied by the sponsor. The delegated research team members will follow any special requirements for devices required at this investigational site in addition to those specified by the study device regulations.

D. Assigning of Study Devices

Prior to assigning a study device, the delegated research team member will ensure device inventory and/or supplies are available. If additional supplies are needed, a research team member will contact the responsible party to request additional study devices.

The PI or Sub-Investigator is required to write an order in compliance with applicable legal, institutional and professional standards to utilize a study device for a study subject. The order may include the subject name, medical record number, subject study identification number, study name, protocol number or IRB approval number, and study device name.

The delegated research team member will ensure that each time a study device is dispensed, the Device Accountability Log is completed *(See Attachment E: Device Accountability Log)*. Documentation should include:

- Device dispensed with lot number or serial number, if applicable
- Name of individual dispensing the study device
- Subject ID number
- Subject's initials
- Date (and time, if appropriate) of dispensing/utilization of device
- Quantity dispensed
- Date of receipt
- Number of units returned or disposed, and reason

If errors are made on the accountability form, there should be a single line through the error, with the initials of the person correcting the error and the date corrected. When recording the date, the month, day, and year will be recorded.

The delegated research team member will ensure that the correct study device is used from the appropriate study supply and documented on the appropriate Device Accountability Log. The same device from a different study supply or from commercial supply may not be used.

E. Return of Study Device

At the conclusion of the study, the delegated research team members will ensure that all documentation regarding receipt, storage and dispensing/utilization of study devices is complete, accurate, and ready for review at the termination visit.

At the termination visit, the delegated research team member will ensure that the study device is available for the monitor to inventory and prepare for return shipment to the sponsor.

5. Applicable Regulations, Guidances and Policies

Regulation/ Guidance/Policy	Title
21 CFR 50	Protection of Human Subjects
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	Emergency Use of Investigational Drugs, Biologics or Devices
OSU Office of Responsible Research Practices HRPP	Event Reporting
OSU Office of Responsible Research Practices HRPP	Noncompliance
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	Research Involving Radiation
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
OSUWMC	Pharmacy Hazardous Drug Reference

OSUWMC Investigational Drug Services	IDS Policies and Procedures
COM Office of Human Resources	Training & Assessment Requirements
ICH GCP E6(R2)	Guideline for Good Clinical Practice: E6 Integrated Addendum
FDA Guidance for Industry	Current Good Manufacturing Practice for Phase 1 Investigational Drugs, July 2008
FDA Guidance for Industry	INDs for Phase 2 and Phase 3 Studies: Chemistry, Manufacturing and Controls Information, May 2003
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	Frequently Asked Questions- Statement of Investigators (Form FDA 1572), May 2010

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