Medications Used in Clinical Research

I. Purpose

The purpose of this policy is to establish standards for the control of medications used in clinical research.

II. Scope

This policy covers all areas of clinical research which involve the administration of Investigational medications to humans. This policy does not apply to non-drug related research or animal research.

III. Definitions

Investigational Drug- A chemical or biologic therapeutic product evaluated under a clinical research protocol. This agent may or may not have a previously established regulatory approval for a disease or condition.

Satellite Pharmacy- A pharmacy in an institution which provides medication services for the patients of the institution, and which is dependent upon the centrally located pharmacy for administrative control, staff training, and drug procurement.

IV. Policy Statements

A Ochsner’s Institutional Review Board (IRB) or other Ochsner approved Institutional Review Board must review and approve a clinical research study before an investigational medication is administered to an enrolled subject.

a Patients enrolled in a non-Ochsner clinical research protocol that has been approved by an outside IRB may continue the investigational medication at the discretion of the admitting physician. This medication should be treated as a “patient home med.”

B The Principal Investigator is responsible for the conduct of the research study in accordance with the clinical research protocol including verification that pharmacy staff is both trained and appropriately licensed (i.e., as a pharmacy technician or pharmacist).

C The Investigational Drug Service (IDS) will develop and maintain procedures to ensure appropriate and documented receipt, storage, preparation, dispensing, and destruction/return of investigational medications in accordance with a research study protocol.
Medications Used in Clinical Research

D Investigational medications used in clinical research will be stored in the pharmacy under appropriate storage conditions as defined in study protocol or on the medication label. This includes observance of any hazard precautions.

E The IDS will prepare and dispense Investigational medications or train other staff pharmacy members to control the preparation and dispensing if the medication cannot be handled directly by the investigational pharmacy.

F Pharmacy staff must ensure that any medication blind is maintained during dispensing or transport per the protocol by not disclosing the contents of a preparation to blinded staff.

G. Pharmacy and nursing personnel involved in the preparation, dispensing and administration of Investigational medications will receive appropriate education.

V. Procedures/Standards and Roles & Responsibilities

A Investigational medications will be administered according to the procedures outlined in the most current study protocol.

1 Deviation from the study protocol may result in a study protocol violation.

B Investigational Medication Storage

1 The investigational drug pharmacy or a designated inpatient or satellite pharmacy will store investigational medications for use in the hospital and infusion clinics, including studies where the medication will be initiated in the hospital and then transferred to the ambulatory setting. For patients who are admitted on an investigational drug from an outside institution, that medication will be stored as a "patient home med."

2 The Investigational drug pharmacy, outpatient pharmacy, or infusion pharmacy (depending on the site) will store Investigational medications that will be used in the ambulatory setting.

3 Investigational medications will be stored in a secure location under storage conditions specified by the research protocol.

4 Investigational medications may be stored in a patient care area and prepared by trained personnel when the timing of medication administration is critical to the success of the study, and it would be impractical for the Pharmacy to prepare the medication in the allotted time. Appropriate training on storage and preparation must be provided by the investigational pharmacy staff.
Medications Used in Clinical Research

C. Investigational Drug Preparation and Dispensing
   1. The Investigational drug pharmacy, or a designated inpatient or satellite pharmacy, as appropriate will prepare and dispense Investigational medications administered in the hospital and infusion clinics per preparation procedures in the study protocol.
   2. The Investigational drug pharmacy, outpatient Pharmacy, or the infusion pharmacy, as appropriate will dispense Investigational medications used in ambulatory patients per preparation procedures in the study protocol.
   3. For patients who are admitted on an investigational drug from an outside institution, that medication will be dispensed per institutional policy.

D. A Pharmacist will
   1. Receive Investigational medications for storage in the pharmacy and ensure appropriate storage conditions including continuous temperature monitoring.
   2. Maintain the accuracy of Investigational medication accountability logs.
   3. Close out clinical research studies and properly return or dispose of Investigational medications at the study sponsor’s directions.

E. Investigational Medication Education
   1. Pharmacy personnel involved in the preparation and dispensing of Investigational medications will receive education by the Sponsor on
      a. Proper preparation and administration
      b. Documentation requirements
      c. Safe handling and storage
   2. Investigational medications that will be administered in the hospital will be reviewed by nursing and pharmacy to agree upon safe handling and administration procedures.

F. Pharmacy will maintain study records for Investigational medications while the research protocol is active. When the research protocol is closed all pharmacy related study documents will be given to the principal investigator or designee for storage (either on-site or long term off-site) with the other study related clinical and regulatory documents.
Medications Used in Clinical Research

VI. Enforcement and Exceptions
   A. Failure to comply may result in progressive discipline for employees or termination of contract or service for third-party personnel, student, or volunteers. Exceptions may only be granted by the System Manager of Investigational Drug Services and/or Director of Pharmacy at the site after consultation with the Principal Investigator.

VII. Internal References
   -Attachment A, Procedures for Investigational Medication Storage and Accountability
   -Attachment B, Procedure for Dispensing Investigational Medication
   -Attachment C, Education for Investigational Medication
   -Attachment D, Procedure for Returning and Destroying Investigational Medications

   -OHS PHARM OS 046 Disaster Plan for Pharmacy Investigational Drug Services Ochsner Health System Emergency Preparation

   -OHS.PHARM OS 053 Transport of Investigational Medications

   -OHS PHARM 019 – Patient’s Home Medications

VIII. External References
   Code of Federal Regulations Title 45 Part 46-Protection of Human Subjects
   Code of Federal Regulations Title 21 Part 312 – Investigational New Drugs
   ASHP Guidelines for the Management of Investigational Drug Products American Journal of Health System Pharmacy Vol 75 (8) 2018

IX. Policy History
   Former Policy 8610pc-55 Investigational Drug Policy
   8610-PC-70 Investigational drugs for studies without approved protocols through nursing/pharmacy for inpatient care areas
   Investigational Medications

   [Approved and Reviewers on next page]
Medications Used in Clinical Research

X. Approved

______________________________
Warner Thomas, President and Chief Executive Officer

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Deborah Simonson, Pharm D, VP Pharmacy

Reviewers
Karl Gotzkowsky PharmD, Manager Investigational Drug Services
Stephanie Henderson, Manager Human Research Protection Program
I. A Pharmacist will receive investigational medications for storage in the pharmacy

A. Medications will be received directly from the study sponsor or designee at the initiation of and during the study

B. Medication may also be purchased by the investigational pharmacy through established vendors for research purposes if allowed by the study sponsor, study protocol and the study budget. This applies when medication is not being provided directly by the study Sponsor.

C. Medication will be immediately secured in the controlled access pharmacy at the appropriate temperature and storage conditions based on hazard level.

   1. Investigational medications will be stored separately from the pharmacy department commercial inventory. They will also be segregated by study protocol in order to mitigate dispensing errors such as selection of incorrect product.

D. Investigational medications will be re-ordered according to the study sponsor procedures allowing enough time to receive the medications so that the pharmacy does not run out of the investigational medication.

E. A pharmacy technician trained on a study may unpack shipments of investigational medication however final accountability must be by a pharmacist.

II. Temperature monitoring where investigational medications are stored

A. The ambient (i.e., room temperature), refrigerator, freezer, and/or cryo-tank temperatures will be continuously monitored.

   1. Temperature information must be reviewed once daily on working days to determine if a temperature excursion has occurred.

   2. Temperature information will be reviewed at the time of known temperature excursions.

B. In the event of a temperature excursion, the cause of the event will be documented in the pharmacy study record (i.e., power outage).

   1. A complete inventory of the affected product will be taken with attention to allowable storage conditions on the product label or in the protocol.

   2. Each study sponsor with affected medication will be notified of the temperature excursion on the day the excursion is noted. The exact reporting process is outlined by each study Sponsor. The study team should also be notified so that affected product is quarantined and not dispensed to a subject.

   3. A decision to allow either the use of the affected product or the destruction of the product will be at the discretion of the study sponsor via written communication.

C. Temperature records will be maintained for at least three years.
D A pharmacy technician may document daily temperatures on a temperature log as part of normal scope of practice. Noted excursions should be verbally relayed to the pharmacist upon discovery of the excursion.

III. The Pharmacy will maintain accurate investigational medication accountability logs

A Investigational medications will be entered onto the Investigational medication accountability log(s) when medication is received from the sponsor, dispensed to a patient, and when the medication is returned or destroyed. A pharmacy technician may make entries onto an accountability log, but a final verification and signature must be made by a pharmacist.

B Investigational medication accountability logs located in the Inpatient Pharmacy or Chemotherapy Infusion Pharmacy will be reviewed for accuracy at least monthly by a Pharmacist in order to maintain the accuracy of the information.

1. If a patient is actively receiving Investigational medication dispensed from the Inpatient Pharmacy, the Investigational medication accountability logs will be reviewed daily Monday through Friday.

2. If a discrepancy is found, it will be investigated and reconciled immediately.

3. If the discrepancy cannot be reconciled, the Director of Pharmacy will be immediately notified so that appropriate actions may be taken.

C Medication transfers will be documented on the Investigational medication accountability log along with the reason for the transfer (e.g., transfer medication from Inpatient Pharmacy to Outpatient Pharmacy).

1. The receiving Pharmacy will document that the medication has been received on the Investigational medication accountability log.

IV. Transporting Investigational Medications to Satellite Locations

A Research medications may be transported from a primary investigational pharmacy to a satellite location for use in a clinical trial. This procedure is outlined in OHS PHARM OS 053 Transport of Investigational Medications.
I. Dispensing Investigational Medications for Administration at Ochsner

A. Investigational Drugs will be ordered electronically by the provider through the EPIC system (or equivalent at a local site)

B. Orders for investigational medications will be entered into the computer system using an ‘INV’ code

1. The ‘INV’ code shows on the MAR designating the drug to nursing that it is an Investigational medication
2. The pharmacist is responsible for generating the request for a new investigational medication name preceded by “INV” to the IS team for inclusion in the computer system formulary
3. Some clinical trials utilize medications deemed standard of care or comparators which are not provided by the Sponsor nor provided free of charge. These medications will not be preceded by “INV” but rather should be ordered, dispensed, and billed as a regular formulary item

C. A Pharmacist will retrieve the Investigational medication from the appropriate storage area and complete the Investigational medication accountability log

D. The Investigational medication will be prepared and properly labeled by a Pharmacist or pharmacy technician for dispensing to the nursing unit

1. The Investigational pharmacy, inpatient pharmacy or chemotherapy infusion pharmacy will prepare parenteral medications
   a. Each dose must be prepared based on the process and stability data provided in the latest version of the study protocol
   b. The medication label must include a statement that the medication is an Investigational Drug. Use of an ‘Investigational Drug’ auxiliary label is allowed
   c. A Pharmacist must check the label and preparation for accuracy prior to dispensing
2. Oral medication will be packaged in a 24-hour supply unless protocol procedures or medication stability data mandate something different
   a. The medication label should state that the medication is an Investigational Drug
   b. A Pharmacist must check the label and product for accuracy prior to dispensing
3. Investigational Drugs will be picked up from the pharmacy by the investigator, clinical research coordinator or delegated designee. The pharmacy staff may however agree to a study specific process whereby the medication will be hand delivered to the nursing unit and given to the patient’s nurse, the charge nurse, or investigator. An example would include a weekend or after hours dispensing
II. Dispensing Investigational Medications for Outpatient use

A. The principle investigator or delegated ordering provider will order a research medication electronically through the EPIC system (or equivalent at a local site). Orders for investigational medications will be entered into the computer system using an 'INV' code, as described above.

B. The Pharmacist or trained pharmacy technician will obtain the research medication from the investigational pharmacy, satellite pharmacy, or outpatient pharmacy and prepare per study protocol.

C. A pharmacist or pharmacy technician will complete the Investigational medication accountability log to reflect the dispensing. A pharmacist must perform the final check and sign off.

D. The Pharmacist will dispense the medication to the investigator, clinical research coordinator, or delegated designee from the pharmacy.
I. Education of Pharmacy Personnel

A. Members of the investigational pharmacy team are responsible for completing all Sponsor mandated trainings for each research protocol prior to dispensing drug product.

B. Pharmacists and other members of the pharmacy staff who are to be identified on a study delegation log must complete Good Clinical Practice (also known as GCP, CITI) trainings assigned by the institution.

C. For each protocol, a research pharmacist or trained technician will prepare a pharmacy binder which includes at a minimum the latest version of the study protocol, accountability logs, shipment receipt documentation, and any other relevant manuals on preparation, storage, and dispensation of research drug.

D. The pharmacist will generate a drug information and procedure summary to include in the front of the pharmacy binder. This document may be used to train other pharmacy staff who assist on the research study.

E. If Pharmacy personnel are responsible for the randomization of patients enrolled in the study protocol, the procedures for completing the randomization process will be included in the study procedure.
   1. Passwords for electronic randomization systems are unique to each pharmacist. They must be securely stored and not shared between individuals.

F. The Investigational Drug Pharmacist will prepare study related in-service information for Pharmacy personnel if staff is utilized beyond the investigational pharmacy team.
   1. The Director of Pharmacy or designee and a member of the investigational pharmacy team will collectively determine the most appropriate method of education for Pharmacy personnel.
   2. Study-related education for Pharmacy personnel may include live in-service, team meeting or mailbox in-service.

II. Education of Non-Pharmacy Staff

A. Members of the investigational pharmacy team, clinical research team (such as a CRC), and/or nursing should determine whether an internal meeting is necessary to further review a new study prior to dispensing an investigational medication.
   1. The Pharmacist will present information and lead discussion on the Investigational medications and answer questions regarding the mechanism of action, safety, dose, formulation administration, product stability, and monitoring parameters following administration.
2. The CRC, nurse, or other clinical team representative will present information and lead discussion regarding study procedures, necessary ancillary supplies such as infusion tubing or infusion pump requirements, and answer questions regarding operational logistics on dispensing days.

B When needed for more complex trials or inpatient trials, members of the research team should present the trial to additional internal groups such as integration councils, safety committees, working groups or other local committees to obtain further guidance on best practices and process prior to initiating dosing. This is to ensure compliance with safety standards.

C Depending on the type and scope of the study, the investigational pharmacy department, the CRC, and/or a member of nursing leadership will determine the appropriate method for disseminating educational training onto personnel involved in the administration of the Investigational medication(s). This may include but is not limited to, in-services, staff meetings, one-on-one in-service when a study patient is enrolled, Huddle Helpers, or electronic in-services.
Procedure forReturning and Destroying
Investigational Medications
OHS PHARM 020 Medications Used in Clinical Research
Attachment D

I. Determination of Final Disposition of Medications Used in Research Trials

A. At the initiation of a study, the investigational pharmacist should establish with the Sponsor, Sponsor-Investigator, or Cooperative Group (e.g., National Cancer Institute) whether investigational medications (also called investigational product or IP) will be destroyed using a third-party waste management company or returned directly to the Sponsor designee. This applies to used, unused, expired, quarantined, or discontinued medications.

B. The IP inventory must first undergo accountability and reconciliation by the study Sponsor designee, either in person or through a remote visit. Interim and final inventories of all investigational IP will be reflected on accountability logs filed in the pharmacy binder for each respective study.

C. The research pharmacy may choose to document destruction of medications on a local destruction form should the Sponsor not require such documentation either on the accountability log or on a Sponsor provided destruction form.

II. Local Destruction of IP

A. Solid dosage form containers are to be placed into blue or black RCRA (Resource Conservation and Recovery Act) pharmaceutical waste bins located in each pharmacy based on hazard assessment. The bins are then collected by third party waste management company for off-site destruction by incineration.

B. Given the number of study medications placed simultaneously in a waste bin, the research pharmacists will not obtain an itemized Certificate of Destruction from the external vendor. The pharmacy record (accountability logs and/or destruction records) will serve as verification of offsite incineration.

III. Investigational Medications Returned by a Subject

A. Medications dispensed for outpatient use such as those for oral and topical administration may be returned to the research pharmacy. However, any used or empty infusion or injection related products such as IV bags, syringes, filter sets, sharps containers, infusion lines, transdermal patches, or other materials used in the process of administering prepared doses of IP will not be accepted by the research pharmacy.

B. To promote safety, study coordinators will perform the initial count of the returned product in their respective clinic or patient care areas in a dedicated, demarcated work area, while wearing appropriate personal protective equipment (PPE). This initial count of returned IP by coordinators may not take place inside the research pharmacy or outside of the pharmacy dispensing window.
Procedure for Returning and Destroying
Investigational Medications
OHS.PHARM 020 Medications Used in Clinical Research
Attachment D

C Specifically, coordinators must don 1 pair of ASTM D6978 gloves (and an N95 respirator if there is a reasonable risk of exposure to dust). A dedicated spatula and counting tray will be used to count returned oral medications. Only the number of tablets/capsules necessary to accomplish this task should be emptied from the bottle into the tray. Following the count, the coordinator should deactivate, decontaminate, clean, and disinfect after use and between products by wiping the work area and counting tray with Perdox®RTU followed by 70% isopropyl alcohol. Hands should be washed thoroughly with soap and water.

D Coordinators should don one new pair of ASTM D6978 gloves and place the medication container (even if empty) into a resealable clear plastic bag with yellow (chemotherapy, cytotoxic) HazD labeling or sticker, and transport to the pharmacy.

E Upon arrival the coordinator or designee will provide documentation of their count to the pharmacist.

F The research pharmacist will perform an independent count of IP returned to the pharmacy utilizing the process and PPE described in section C above. The count will be performed in a negative pressure receiving area, if available. If counts are discrepant, pharmacy will work with the coordinator to resolve the discrepancy and document on the pharmacy accountability log.

G Returned medications will be kept in the research pharmacy for 180 calendar days or until the next monitoring visit, whichever is sooner. If during a monitoring visit the medications are neither prepared for destruction nor returned to the Sponsor, the medications will be destroyed within 30 calendar days after written notification to the Sponsor.

IV. Investigational Medications Administered On-Site

A The research pharmacy reserves the right to refuse to retain a used medication container (ex., a vial) following preparation of a product if determined to be a hazardous (drug) product and/or a product used for an oncology trial. In this instance, the used container will be placed immediately in appropriate pharmaceutical waste disposal containers.

B The research pharmacy may agree to keep outer cartons or equivalent packaging as an alternative for reconciliation on a study-by-study basis.

C Partial or empty IV bags, syringes, filter sets, infusion lines, transdermal patches, PPE, or other materials used to prepare or administer medications will be immediately disposed of into appropriate waste disposal containers, such as black or yellow bins, red sharps containers, etc. This would take place in areas such as hospital floors, ambulatory clinics, or infusion clinics.

V. Expired IP and Unused IP at the End of a Study

A Expired IP or Unused IP remaining on site at the end of study notification will be either disposed of on-site or returned to the Sponsor designee based on prior agreement at the initiation of the trial.
B If the Sponsor or study monitor fails to acknowledge and/or arrange for final disposition of this IP within 180 days of initial request, the research pharmacy reserves the right to destroy the IP on site and document on a site generated destruction form.

VI. Destruction of Temperature Monitoring Devices

A Devices for monitoring the temperature of shipments will be stopped immediately upon opening the shipment, and the data from the monitoring device will be downloaded and either printed or saved electronically.

B Once temperature data is confirmed to be acceptable, the temperature monitoring device will be placed immediately in appropriate waste receptacle. Multi-use monitoring devices will be returned if requested, but at the Sponsor's expense.