Office of Clinical Research

Effective: June 1, 2009	Revised: June 3, 2016	Revision: 2
Responsibility: OCR		
Policy 1.1.2		

Policy: STORAGE AND CONTROL OF INVESTIGATIONAL DRUGS AND DEVICES FOR CLINICAL RESEARCH

1. BACKGROUND:
   Research accreditation standards of the Association for Accreditation for Human Research Protection Programs require the Health Science Center to ensure proper storage, inventory control, dispensing and tracking of investigational drugs and devices.

2. PURPOSE:
   To establish policies and procedures to ensure that the handling and storage of investigational products which are the subject of IRB approved research protocols meet the Health Science Center standards relating to inventory control, dispensing, and required documentation.

3. DEFINITIONS:
   a. ***Investigational drug*** includes any drug (approved or unapproved by the FDA) being used in research, other than the use of a marketed drug in the course of medical practice.
   b. ***Investigational device*** includes any device (approved or unapproved by the FDA) being used in research designed to evaluate safety and effectiveness of that device.
   c. ***Investigational product*** includes any investigational drug *or* investigational device or a combination of the two ("combination product") being used in a research designed to evaluate the safety or effectiveness of the drug, device, or combination.

4. REFERENCES:
   a. Applicable Federal Regulations include: 21 CFR §312.61, 21 CFR §312.62, 21 CFR §312.69, 21 CFR §812.100, 21 CFR §812.110, 21 CFR §812.140(a)
   b. Attachments provide sample standard operating procedures outlining responsibilities, required procedures and associated forms and logs.

5. RESPONSIBILITY:
   a. Investigators: All Investigators receiving and storing investigational drugs, investigational devices, or investigational products in their clinic or office areas outside of a hospital pharmacy, hospital designated service for devices, or the Investigational Drug Section of the Cancer Therapy and Research Center must:
      (1) Maintain proper environmental storage conditions with appropriate security of the items at all times.
      (2) Ensure and maintain inventory control and investigational product accountability including ordering, receipt, inventory, disposal/removal, and/or following procedures for transfer between institutions.
      (3) Maintain drug or device accountability documentation and reports.
      (4) Establish standard operating procedures (see attached example policy and logs for handling of investigational products) and provide for review to the Office of Clinical Research (OCR) Director or his/her designee for OCR approval. Any revision or modification to OCR approved policies must be reapproved by OCR.
      (5) For Department common storage locations, provide the following:
         (a) Identify the building, room location for the storage and management of test articles

(b) Identify the responsible person, position title, contact number for oversight of the test articles and their contact information

b. Office of Clinical Research (OCR):
   (1) Reviews and approves new/revised Standard Operating Procedures (SOPs) and related documents submitted from Investigators or HSC divisions, departments, and services.
   (2) Prior to SOP approval, OCR will inspect the HSC facilities where SOPs are to be implemented for the non-pharmacy storage of investigational products.
   (3) Documents the site inspection using the Drug/Device Storage Site Review checklist. This checklist also includes the option to waive physical inspection under special circumstances.
   (4) OCR may request a site inspection prior to institutional activation of a new protocol for any existing approved SOPs.

c. University Health System (UHS)
   (1) For investigational products stored on UHS premises, OCR will provide the UHS Research Office with a copy of the SOP for review prior to issuing final approval. Upon UHS review and where needed, a signed UHS Investigational Product Storage Authorization form will be provided to OCR for devices.
   (2) Prior to SOP approval, OCR will inspect the UHS facilities where SOPs are to be implemented for the non-pharmacy storage of investigational products. OCR will coordinate the inspection with the UHS Research Office. In some instances, site inspection may not be required. Details for not requiring inspection will be documented on the Drug/Device Storage Site Review form.

d. Monitoring of SOP adherence will be conducted by the Office of Research and Compliance (see VPR Policy on Study Reviews for Human Research).

e. After a study begins, investigators may choose to no longer hold and manage study drugs at their clinics but instead use an institutional pharmacy (e.g., UHS,STVHCS, CTRC Investigational Drug Section) where appropriate. This office rather than the investigator (division, department, or service director), will then be responsible for investigational product accountability and procedures.

(Insert Research Team Name or Dept here) Standard Operating Procedure (SOP)		
	Investigational Drug/Device Storage and Accountability	**Page 1 of 9**
Date First Effective:	Revision Date:	Revision:
Site Authority (PI/Chair/Director):	Signature:	Date:
OCR Approval By:	Signature:	Date:

PURPOSE

To establish procedures for storing investigational products for *Research Team/Department (RT/Dept)* studies:

1. Proper storage, temperature monitoring, and access for all investigational drugs/devices maintained by the investigator.
2. Maintaining investigational drugs/device inventory and accountability.
3. Transfer of investigational drugs/devices between protocols or sites.

RESPONSIBILITY

1. The *principal investigator* (*PI*) is ultimately responsible for *RT/Dept* procedures for handling of investigational product and ensuring research personnel comply with these procedures. The *PI* provides information as required per this SOP.
2. The *PI* appoints an *Investigational Product Manager*, *IPM*. As per this SOP, the *IPM* has the following primary responsibilities:

- Maintaining and monitoring proper storage conditions
- Securing investigational products and controlling access to storage areas
- Maintain investigational drug/device inventory and accountability, including ordering and receipt
- Perform weekly inventory counts of investigational product
- Maintain accurate drug accountability reports (DAR) and device accountability logs
- Remove investigational product from inventory when orders are processed
- Quality review of all DAR and accountability logs prior to distribution to outside parties

3. The *RT Coordinator* conducts routine verification that procedures are being followed.

REQUIRED ITEMS FOR STORAGE AND MONITORING OF MEDICATION:

- Shelving to store room temperature medication(s) in Rooms *X, Y, and Z*
- Refrigerator(s) to store refrigerated mediation(s): *#123* and *#456*
- Freezer(s) to store frozen medication(s): *#789*
- Storage bins to separate medication inventory
- Labels to identify inventory
- Certified/calibrated NSIT thermometers for storage rooms, refrigerators, and freezers
- Temperature Monitoring Log
- Drug Accountability Record (DAR)

PROCEDURES

1. Control, Storage, and Monitoring of Investigational Product
   a. Control
      1) The area where the investigational product, i.e. drugs and devices, are stored must be a limited access area. All storage rooms have key pad access; refrigerators and freezers have combination locks.
         i. Only those employees that have delegated roles on the research team that require them to enter that area shall be allowed to do so.
         ii. The *IPM* is the primary individual who provides appropriate research staff any codes or keys (the PI or *RT Coordinator* provide back-up).
      2) Doors shall be locked at all times, whenever the *IPM* (or staff) is not in the area.
      3) This area should only be accessed by the *IPM*, approved research staff, or UTHSCSA police.

   b. Storage
      1) Store all investigational products separately, by protocol. Where appropriate use individual bins (i.e. storage containers) for each protocol. The bins should be labeled with the name of the drug/device, the sponsor, and the protocol number, and the short title of the study.
      2) Store all investigational product according to the manufacturer's recommendations (either located in the study protocol or the package insert).
      3) The PI shall approve, prior to study start, the use of the controlled storage area for the investigational product ensuring that it will meet the temperature requirements (and any additional environmental controls) and that it has appropriate security.

c. Monitoring

1) The *IPM* monitors the temperatures of the storage areas at the beginning of each day using a Temperature Monitoring Log (see Appendix 1).

i. This log may be divided into weekly, monthly or yearly logs. This log will be placed on the outside of the area (i.e. room, refrigerator, freezer) being monitored.

ii. Electronic monitoring systems are used in rooms X and Z. Calibrated thermometers are used in all other areas.

2) The *IPM* reports any temperature excursions immediately to PI/Coordinators of the affected studies, manages the resolution of the problem, and documents the event.

3) The *IPM* maintains current certification to NIST* standards for all thermometers (electronic and other), to include coordinating the recalibration services. (*National Institute of Standards and Technology)

4) The temperature logs and records shall be made available to study monitors upon request.

5) The following temperature ranges are the standards:

i. Room temperature: 15°C to 30°C

ii. Refrigerated temperature: 2°C to 8°C

iii. Freezer temperature: -16°C to -30°C

6) If additional environmental considerations are required, the *IPM* must be notified.

7) The *IPM* will participate in establishing the routine procedures and documentation for monitoring the additional requirements.

8) Any storage conditions that extend beyond a single protocol should result in an update to this SOP.

2. Drug Accountability of Drugs – The *IPM* is responsible for the following:

a. Immediately recording received drugs on the Drug Accountability Record and any procedures the sponsor requires to acknowledge receipt of investigational product supply. The DAR form is included as Appendix 2 *(DAR*).

1) Opening and inspecting contents to verify condition upon receipt of drug shipment.

2) Comparing invoice or packing slip to contents by lot number, dosage and quantity.

3) Reporting any discrepancies to the sponsor immediately.

b. Maintain a separate DAR for every investigational drug.

1) Note that open-label study drug may come in more than one dose size, requiring separate storage areas and DARs for different dosages.

2) Training staff on variable doses is important when supplies arrive.

3) Conversely, blinded or placebo-controlled drug is subject-specific and must be dispensed only to the subject to whom it has been assigned. Carefully observe assignment information on drug labels.

c. Enter the strength and/or vial size of investigational medication(s) received for an investigational study individually onto a new DAR.

1) Verify information on the retesting dates of investigational drug. If the sponsor or manufacture does not provide this, contact the sponsor to obtain it.

2) Record of the retesting date and ensure no expired mediations are used.

d. Log a corresponding entry in the DAR each time an investigational medication is dispensed for a specific subject.

e. Complete the DAR; explanation as follows:

1) Date: date transaction occurs, i.e. date medication dispensed or date returned medication

2) Subject's initials: subject's first and last initials

3) Subject's ID No.: subject identification number; study number; and may include study arm information for multi-arm studies

4) Dose: dosage of medication dispensed and for oral medication will contain the total milligram dose

5) Quantity Dispensed or Received: identifies the amount received, dispensed, returned, and wasted.

6) Balance Forward/Balance: running balance

7) Manufacturer and Lot No.: will include bottle number, if applicable

8) Retest Date: when the investigational product must be retested as provided by the manufacturer/sponsor

9) Recorder's Initials: the person removing, wasting, or receiving the drug supply

f. Maintain all DARs for the duration the study conduct.

g. Immediately dispose of partially used or empty vials after preparation or administration using hazardous waste containers as per UTHSCSA hazardous waste policies.

1) The destruction of partially used or empty vials will not be documented in a separate entry on the DAR. Example follows:

- Subject's dose is 42.5 mg and the investigational product is provided as 10 mL vials, each with a concentration of 1 mg/mL (10 mg / 10 mL).
- Five (5) vials are required to prepare this subject's dose and 5 vials will be documented on the DAR.
- Based on this SOP the 4 empty and 1 partial vials will be disposed of immediately following preparation.
- No separate destruction record is necessary
- Study monitors may observe the first preparation of the investigational product to verify compliance to SOP.

2) Document any investigational inventory that has to be wasted (i.e. mixing errors, broken or cored vials) will be documented on the DAR.

3) Should the sponsor require that partially filled vials are saved; they should be stored in a separate bin/location from the investigational drug supply.

4) Do not reuse partial vials, unless specifically permitted by the protocol.

h. Document returned oral medications as outlined below.

1) Upon subject's return of oral investigational medication, document the number of tablets/capsules/etc. on the DAR as returned. Once disposed of, document as wasted on the DAR.

2) If a subject returns an empty bottle, it should not be documented in the DAR and the empty container should be placed in the biohazard waste container.

3) Due to safety concern and space limitations, it is not recommended that *PI*s save returned oral medications or empty returned oral medication bottles. Should a sponsor require returns to be saved, the *PI* must provide the special arrangements to the *IPM*.

i. Perform the investigational products inventory weekly. Resolve any discrepancies in a timely manner and document both the discrepancy and resolution.

j. The *IPM* provides the DAR(s) for each study monitor visit covering the time period between monitoring visits. The *IPM* should have adequate time to review the DAR to ensure the information contained in the report is accurate.

k. Upon study completion the *IPM* will either return remaining medication to the study sponsor or destroy on site after written approval from the study sponsor.

1) Document the return/destruction of the investigational product on the DAR.

2) Complete a final DAR (initial drug receipt through final disposal) after the inventory remaining is zero.

3) The *PI* and the *IPM* will sign original, final DAR as well as the individual(s) performing the site close out visit.

4) The *IPM* provides a copy to the sponsor. The original DAR(s) are provided to the RT Coordinator for retention.

3. Drug Accountability of Devices

As with investigational drugs, the investigator is ultimately responsible for the control of the device(s) under investigation. The IPM follows section 1 of this SOP, for investigational devices, and

a. The device and its packaging shall have a label with the name and place of business of the manufacturer, packer, or distributor. The device must have labeling that clearly states it is for investigational use and include any warnings/precautions (e.g. contraindications, hazards, adverse effects, interfering substances/devices).

b. Upon receipt of the study device, the shipment should be inventoried (see log at Appendix 3), verifying that the receipt date, lot number/serial or model number (sometimes date of manufacture), device type/batch number or code mark, and quantity on the packing slips match what was actually received. See the Device Accountability Log at Appendix 3.

c. Promptly bring any discrepancies to the attention of the sponsor/supplier of the device(s).

d. Retain a copy of the shipping inventory, packing slips and document inventory in the study files.

e. The devices will be stored in a secure environment according to the requirements listed in the protocol or in the investigator's brochure. For example, the temperature or any other environmental requirements for the storage area.

f. Record daily any environmental requirements for storage. Resolve and document any discrepancies.

g. Access to the storage area will be limited to essential research personnel.

h. Each time the device is distributed it will be reported on an accountability log (see Appendix 3) containing the following information: the date the study device is dispensed/used; where it is dispensed/used; by whom it is dispensed/used; and the date and signature or initials of the person dispensing/using the study device (plus information dictated by the study protocol.

i. Record any return, repair, or destruction of the device on the accountability log (see Appendix 3).

j. Record a note of explanation why and how many device units are returned to the sponsor, repaired or otherwise disposed of; when a device is disposed of, note the identification of the person responsible.

k. Retain all accountability documents during the conduct of the study and at the conclusion of the study forward to the RT Coordinator for retention.

4. Transfers of Investigational Product

a. Investigational Product Transfer to Satellite Sites

   i. Prior to a transfer to satellite sites, the PI must obtain written documentation of the IRB approval for the transfer and provide this to the IPM.

   ii. The *PI* must provide the IPM information on the satellite site's investigational drug pharmacist and/or PI to include, name, title, complete mailing address, telephone numbers for normal business hours, and an e-mail address.

b. Investigational Product Transfer Between Protocols:

   i. Investigational product transfer between protocols will NOT occur unless the study sponsor approves and provides documentation for transfer.

   ii. The *PI* must provide the IPM this documentation.

   iii. The IPM records the investigational product transfer on the DAR's of each protocol involved.

5. **Routine Verification of Compliance** – The *PI* ensures that the RT Coordinator conducts routine verification of the procedures prescribed by this *RT/Dept*. The review must be documented and any discrepancies documented along with the resolution, and procedures updated as warranted. The PI reviews all verifications (signs and dates).

REFERENCES

Office of Clinical Research Policy, Storage and Control of Investigational Drugs and Devices for Clinical Research

ATTACHMENTS

1. Appendix 1 – Sample Yearly Temperature Log
2. Appendix 2 – Sample Drug Accountability Record (DAR)
3. Appendix 3 – Sample Investigational Device Accountability Log

Appendix 1.

Temperature Log

Year: _____

	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
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Appendix 2.

Drug Accountability Record (DAR)

Protocol Title:						Drug Name or Number:			
Investigator Name:						Dose Form and Strength:			
IPM:						Dispensing Area: Bldg/Room#/Clinic		Site Name and #:	
Line#	Date	Pt initials	ID#	Dose	Quantity	Received/ Dispensed	Balance Forward	Manufacturer, Lot# and Retest	Recorder's Initials
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Appendix 3.

Investigational Device Accountability Log

DEVICE REPORT					DEVICE USE				DEVICE RETURN/REPAIR/DESTRUCTION						
Date Rec'd	Initials of Reciever	Lot No. /Serial or Model No.	Device Type/Batch No.	Notes	Date Used	Initials of Device Dispenser	Subject ID	Notes	RET=Returned DES=Destroyed REP=Repaired	Date	Initials	Auth No.	No. of Units	Reason	Notes