

University of Texas Health Science Center San Antonio

Vice President for Research
Office of Clinical Research

Issued: May 2009
Effective: Aug 1, 2009

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 of investigational or unlicensed test articles meets the Health Science Center standards relating to pharmacy, inventory control and documentation of investigational articles in IRB approved research protocols.

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.

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 and required procedures and associated forms and logs.

5. RESPONSIBILITY:

- a. Investigators: All Investigators receiving and storing investigational drugs or investigational devices 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:
 - i. Maintain proper environmental storage conditions with appropriate security of the items at all times.
 - ii. Ensure and maintain inventory control and investigational test article accountability including ordering, receipt, inventory, and removal.
 - iii. Maintain drug or device accountability documentation and reports.
 - iv. Establish standard operating procedures (see attached detailed examples for handling of investigational drugs and devices).
 - v. Provide their policies and procedures for storage, control, and dispensing for review to the Assistant Vice President for Research Operations.
 - vi. See 5.b and 5.d listed below as alternatives.
- b. Department Chairs: Ensure all storage areas are properly registered and approved (see 5.a and 5.c) A Division, Department, or Service may decide to designate a location and a responsible person to oversee the management of test articles to include the receipt, inventory control, dispensing accountability, and storage of these test articles for multiple investigators in a specific clinic or division/department location under your specified

policies. The Division, Department, or Service should provide the items listed below to the Assistant Vice President for Research:

- i. Identify the building, room location for the storage and management of test articles.
 - ii. Identify the responsible person, position title, contact number for oversight of the test articles and their contact information.
 - iii. Provide the specific policies and procedures for the designated clinic, service, department, or division.
 - iv. Provide a list of investigators currently using test articles under approved protocols in this location.
- c. Assistant Vice President for Research Operations:
- i. Review documents submitted from Investigators or HSC divisions, departments, and services and forward as appropriate for approval to:
 - a) *Investigational drugs* - Director, Investigational Drug Section, Scott Soefje, Pharm D. Reviews policies and provides approval number for sites involving drugs.
 - b) *Investigational devices* - Director, Office of Clinical Research, Holly Nolan, MS. Reviews policies and provides approval number for sites involving devices.
 - d. Investigators may also choose to no longer hold and manage study drugs at their clinics but instead use the UHS Purchasing office for Devices, UHS Pharmacy, STVHCS Pharmacy, or the CTRC Investigational Drug Section where appropriate. This office rather than the investigator or division, department, service director, is then responsible for investigational product accountability and procedures.
6. Director, Office of Clinical Research:
- a. Conduct periodic review of investigational drug and device procedures as part of the clinical study process assessment (monitoring). Provide reports to:
 - i. Director, Investigational Drug Section (re: investigational drug product accountability)
 - ii. Director, Institutional Review Board
 - iii. Assistant Vice President for Research Operations
 - iv. Quarterly summary reports of monitoring results to Assistant Vice President for Regulatory Affairs & Compliance

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1.0 **PURPOSE:**

- 1.1 To establish a procedure for proper storage, temperature monitoring, and access for all investigational drugs/devices maintained by the investigator.
- 1.2 To establish a procedure for maintaining investigational drugs/device inventory and accountability.
- 1.3 To establish a procedure for delivery of investigational drugs/devices for clinical trials to treatment sites other than where the drug is stored.

2.0 **RESPONSIBILITY:**

- 2.1 The investigator is responsible for maintaining proper storage conditions for both investigational drugs and/or devices.
- 2.2 The investigator is responsible for maintaining appropriate access for both investigational drugs and/or devices.
- 2.3 The investigator or the investigator’s designee has following primary responsibilities:
 - 2.3.1 Maintain investigational drug/device inventory and accountability, including ordering and receipt of investigational product
 - 2.3.2 Perform weekly inventory counts of investigational medication.
 - 2.3.3 Generate drug accountability reports (DAR) and device accountability logs for review by study monitors and/or auditors
 - 2.3.4 Remove investigational product from inventory when orders are processed.
 - 2.3.5 Quality assurance review of all DAR and accountability logs prior to distribution to outside parties.

3.0 **REQUIRED ITEMS FOR STORAGE AND MONITORING OF MEDICATION:**

- 3.1 Shelving to store room temperature medication(s)
- 3.2 Refrigerator(s) to store refrigerated medication(s)
- 3.3 Freezer(s) to store frozen medication(s)
- 3.4 Storage bins to separate medication inventory
- 3.5 Medication labels to identify medication inventory
- 3.6 Certified/Calibrated Thermometers
- 3.7 Temperature Monitoring Log (see Appendix 1).
- 3.8 Drug Accountability Record (DAR)

4.0 **PROCEDURE FOR STORAGE AND MONITORING OF MEDICATION:**

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- 4.1 A UTHSCSA investigator (non-CTRC) may store investigational drug/device products in an area other than a pharmacy, but they assume responsibility for the investigational product.
- 4.2 The investigator shall designate an area for the storage of investigational drugs/device that will meet the temperature requirements and ensure the security of the area.
- 4.3 The area where the investigational product is stored will be considered a limited access area. Only those employees that have a requirement to enter that area shall be allowed to do so.
- 4.4 Doors shall be locked at all times, whenever the investigator or in the investigator’s designee is not in the area.
- 4.5 This area should only be accessed by the investigator, the investigator’s designee, or UTHSCSA police.
- 4.6 All medication/devices should be stored separately by protocol. Where appropriate individual bins/storage containers should be used for each protocol.
 - 4.6.1 The bins should be labeled with the name of the drug/device, the sponsor, and the title of the study.
- 4.7 All medications/devices will be stored according to the manufacturers recommendations either located in the study protocol or the package insert.
- 4.8 Temperatures will be recorded at the beginning of each work day on a Temperature Monitoring Log. This log may be divided into weekly, monthly or yearly logs. This log will be placed on the outside of the item being monitored. Electronic monitoring systems are encouraged, but not required. An example of a yearly temperature log is provided in the appendix. This log shall be made available to study monitors upon request.
- 4.9 The following temperature ranges will be the standards:
 - 4.9.1 Room temperature: 15°C to 30°C
 - 4.9.2 Refrigerated temperature: 2°C to 8°C
 - 4.9.3 Freezer temperature: -16°C to -30°C

5.0 PROCEDURE FOR DRUG ACCOUNTABILITY DOCUMENTATION

- 5.1 A separate drug/device accountability report (DAR) shall be maintained for every investigational drug/device. Examples of a DAR are included in the appendix and can also found at <http://ctep.cancer.gov/forms/docs/accountability.pdf>
- 5.2 All receipts of drugs shipped to the investigator should be saved for the duration that the documentation for the study is saved. Received drugs should be immediately documented on the DAR and any procedures the sponsor requires followed to acknowledge receipt of investigational product supply.

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- 5.3 Each strength and/or vial size of investigational medication(s) received for an investigational study will be entered individually onto a new DAR.
 - 5.3.1 It is the responsibility of the pharmaceutical sponsor to provide sufficient notification regarding retesting dates of investigational drug(s), therefore if retest dates are not provided; the sponsor should be contacted to obtain this information.
- 5.4 A corresponding entry will be made in the DAR each time an investigational medication is dispensed for a specific patient.
- 5.5 If the sample form is not used, the DAR header should contain at a minimum the following information:
 - 5.5.1 Name of the Institution/Department
 - 5.5.2 Protocol number
 - 5.5.3 Agent name
 - 5.5.4 Dosing form and strength
 - 5.5.5 Protocol title
 - 5.5.6 Principle investigator
 - 5.5.7 Dispensing area/storage area
- 5.6 If the sample form is not used, the DAR, the column headers and the information contained within each column should contain at a minimum:
 - 5.6.1 Date: date transaction occurs, i.e. date medication dispensed or date returned medication is entered into system.
 - 5.6.2 Patient's Initials: patient's first and last initials
 - 5.6.3 Patient's ID number: patient identification number; study number; and may include study arm information for multi-arm studies.
 - 5.6.4 Dose: dosage of medication dispensed and for oral medication will contain the total milligram dose.
 - 5.6.5 Quantity dispensed or received: identifies the amount dispensed, returned, wasted, and received.
 - 5.6.6 Balance forward: running balance
 - 5.6.7 Manufacturer and Lot number: will include bottle number if applicable
 - 5.6.8 Recorder's Initials: The person removing, wasting, or receiving the drug/device supply.
- 5.7 It is recommended that the investigator **not keep partially used or empty vials** of investigational medication.
 - 5.7.1 Partially used or empty vials will be disposed immediately after preparation or administration via hazardous waste containers as per UTHSCSA hazardous waste policies
 - 5.7.2 The destruction of partially used or empty vials will not be documented in a separate entry on the DAR.
 - 5.7.2.1 Example: Patient'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).
 - 5.7.2.2 Five (5) vials are required to prepare this patient's dose and 5 vials will be documented on the DAR.
 - 5.7.2.3 Based on IDS policy the 4 empty and 1 partial vials will be disposed of

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immediately following preparation.

5.7.2.4 No separate destruction record is necessary.

5.7.2.5 Study monitors may observe the first preparation of the investigational product to verify IDS compliance to this standard operating procedure.

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

5.7.4 Should the investigator choose to save partially filled vials; they should be stored in a separate bin/location from the investigational drug supply.

5.7.5 Partial vials should not be re-used, unless specifically permitted by the protocol.

5.8 Due to safety concern and space limitations, it is not recommended that investigators **save returned oral medications or empty returned oral medication bottles**. Oral return medications will be documented as outlined below. Should a sponsor require returns to be saved, the sponsor should contact the investigator to make special arrangements.

5.8.1 Any oral investigational medication returned by a patient will be documented and the number of tablets/capsules/etc. will be documented as wasted. The number wasted will be entered into DAR as returned, then immediately entered as wasted.

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

5.9 Inventory of investigational products should be performed every week by the investigator or their designee. Discrepancies should be resolved as soon as possible.

5.10 The DAR will be provided for each study monitor visit covering the time period between monitoring visits.

5.10.1 The investigator or their designee should have adequate time to review the DAR to ensure the information contained in the report is accurate prior to distribution.

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

5.11.1 This will also be documented on the DAR.

5.11.2 A final and complete DAR (initial drug receipt through final disposal) will be completed after the inventory remaining is zero.

5.11.3 The original will be signed by the investigator and the individual(s) performing the site close out visit. This document will be filled with all the investigator records pertaining to the study.

5.11.4 A copy will be provided for the company.

5.12 Investigational Drug Transfer Between Protocols:

5.12.1 Investigational drug transfer between protocols will not occur unless the study sponsor approves and provides documentation for transfer.

5.12.2 Documentation of the investigational drug transfer will be recorded on the DAR's of each protocol involved.

5.13 Investigational Drug Transfer to Satellite Sites:

5.13.1 Prior to investigational drug transfer to a satellite site, the investigator should require:

5.13.1.1 Written documentation of the IRB approval at the satellite.

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5.13.1.2 Documentation identifying the satellite site's investigational drug pharmacist and/or Principal Investigator including: name, title, complete mailing address, telephone numbers for normal business hours and an e-mail address.

6.0 **PROCEDURE FOR STORAGE AND MONITORING OF DEVICES:** As with investigational drugs, the investigator is responsible for the control of the device(s) under investigation. 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).

6.1 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.

6.2 Promptly bring any discrepancies to the attention of the Sponsor/supplier of the device(s);

6.3 Retain a copy of the shipping inventory, packing slips and document inventory in the study files;

6.4 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:

6.4.1 Routinely record (e.g. daily) any environmental requirements for storage.

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

6.5 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).

6.6 Any return, repair, or destruction of the device will also be recorded on the accountability log (see Appendix 3).

6.7 At the conclusion of the study, all documentation regarding receipt, storage, dispensing, and return/repair will be verified for completeness and accuracy;

6.8 A note of explanation will be recorded of why and how many device units are returned to the Sponsor, repaired or otherwise disposed of; when a device is disposed of, the identification of the person responsible should be noted; and

6.9 A copy of all accountability documents will be maintained in the study regulatory files.

7.0 **APPENDIX:**

7.1 Appendix 1 – Yearly Temperature Log

7.2 Appendix 2 – Sample Drug Accountability Record

7.3 Appendix 3 – Sample Investigational Device Accountability Log

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Appendix 1: Temperature Log For Year: _____

	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
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Appendix 2: Sample DAR

Public reporting burden for this collection of information is estimated to average 6 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. **An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.** Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to: NIH, Project Clearance Branch, 6705 Rockledge Drive, MSC 7974, Bethesda, MD 20892-7974, ATTN: PRA (0925-0240). Do not return the completed form to this address.

OMB No. 0925-0240
Expires: 02/28/2011
NIH-2564

National Institutes of Health National Cancer Institute	Division of Cancer Treatment and Diagnosis Cancer Therapy Evaluation Program	PAGE NO.
Investigational Agent Accountability Record		CONTROL RECORD <input type="checkbox"/>
		SATELLITE RECORD <input type="checkbox"/>

Name of Institution:	NCI Protocol No.:
Agent Name:	Dose Form and Strength:
Protocol Title:	Dispensing Area:
Investigator Name:	NCI Investigator No.:

Line No.	Date	Patient's Initials	Patient's ID No.	Dose	Quantity Dispensed or Received	Balance Forward	Manufacturer and Lot No.	Recorder's Initials
						Balance		
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