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| ***(Insert Research Team Name or Dept here)***  **Standard Operating Procedure (SOP)** | | |
| **SOP\_DrugDev** | **Accountability for Investigational Drugs and or Devices** | **Page 1 of 11** |
| **Date First Effective: xx/xx/xxxx** | **Revision Date: xx/xx/xxxx** | **Revision:** |
| **Site Authority (PI/Chair/Director):** | **Signature:** | **Date:** |
| **Approved By:**  **OCR Manager/Designee** | **Signature:** | **Date:** |

**PURPOSE**

To establish procedures for storing investigational products:

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

**RESPONSIBILITY**

1. The *principal investigator* (*PI*) is ultimately responsible 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:

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| 1. Maintain and monitor proper storage conditions 2. Secure investigational products and control access to storage areas 3. Maintain investigational drug/device inventory and accountability, including ordering and receipt, dispensing and disposition. 4. Perform weekly inventory counts of investigational product 5. Quality review of all DAR and accountability logs prior to distribution to outside parties |

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

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**PROCEDURES**

1. Control, Storage, and Monitoring of Investigational Product
2. Control
3. 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 padlocks.
   * 1. Only those employees that have delegated roles on the research team that require them to enter that area shall be allowed to do so.
     2. The *IPM* is the primary individual who provides appropriate research staff any codes or keys (the PI or *RT Coordinator* provide back-up).
4. Doors shall be locked at all times, whenever the *IPM* (or staff) is not in the area.
5. This area should only be accessed by the *IPM*, approved research staff, or UTHSA police.
6. 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 products 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.
7. Monitoring
8. The *IPM* monitors the temperatures of the storage areas at the beginning of each day using a Temperature Monitoring Log (SOP*\_TempLog,* see Appendix 1 for use when there is not a sponsor supplied form.)
   1. *[Modify as appropriate for your studies]*
      1. 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.
      2. 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 calibration records for temperature monitoring devices, or can obtain them from the facilities management where the IP is stored.
   4. The temperature logs and records shall be made available to study monitors upon request.
   5. The following temperature ranges are the standards:
      1. Room temperature: 15°C to 30°C
      2. Refrigerated temperature: 2°C to 8°C
      3. 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 may require an update to this SOP.
9. Accountability of Drugs – The *IPM* is responsible for the following:
10. Immediately record received drugs on the Drug Accountability Record and follow any procedures the sponsor requires to acknowledge receipt of investigational product. The DAR form is included as Appendix 2 for use when there is not a sponsor supplied form.
    1. Open and inspect contents to verify condition upon receipt of drug shipment.
    2. Compare invoice or packing slip to contents by lot number, dosage and quantity.
    3. Report any discrepancies to the sponsor immediately.
11. Maintain a separate DAR for each 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. Train staff on variable doses when applicable.
    3. Conversely, blinded or placebo-controlled drug is subject-specific and must be dispensed only to the subject to whom it has been assigned. Careful observation of assignment/randomization information on drug labels is required when dispensing consistent with the approved protocol and/or pharmacy manual.
12. 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 the retesting date and ensure no expired mediations are used.
13. Log a corresponding entry in the DAR each time an investigational medication is dispensed for a specific subject.
14. Complete the DAR; explanation as follows:
    1. Date: date transaction occurs, i.e. date medication dispensed, or date medication returned
    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 including milligram dose for oral medications
    5. Quantity Dispensed or Received: 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
15. Maintain all DARs for the duration of the study as part of the regulatory binder.
16. Immediately dispose of partially used or empty vials after preparation or administration using hazardous waste containers as per UTHSA hazardous waste policies. See Appendix 4 for more information on disposal of pharmaceutical products.
    1. Document any investigational inventory that has to be wasted (i.e. mixing errors, broken or cored vials) on the DAR.
    2. The destruction of partially used or empty vials will not be documented in a separate entry 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, and the label marked in a manner to designate that the container is no longer full.
    4. Do not reuse partial vials, unless specifically permitted by the protocol.
17. 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. Returned medications may not be reused for another subject since storage conditions and integrity of the medications can no longer be verified.
    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. If a sponsor requires returns to be saved, the *PI* must provide the special arrangements to the *IPM*.
18. Perform the investigational products inventory weekly. Resolve any discrepancies in a timely manner and document both the discrepancy and resolution.
19. The *IPM* will provide 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.
20. 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-see appendix 4) 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.
21. Accountability of Devices

The investigator is ultimately responsible for the control of the device(s) under investigation.

1. The device and its packaging shall have a label with the name and place of business of the manufacturer, packer, or distributor and include any warnings/precautions (e.g. contraindications, hazards, adverse effects, interfering substances/devices).
2. Upon receipt of the study device, the shipment should be inventoried. See Appendix 3 for use when there is not a sponsor supplied form.
3. Verify 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.
4. The sponsor/supplier should be promptly notified of any discrepancies.
5. Retain a copy of the shipping inventory, packing slips and document inventory in the study files.
6. 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.
7. Record daily any environmental requirements for storage, and record on the temperature log. Resolve and document any discrepancies.
8. Access to the storage area will be limited to essential research personnel.
9. Each time the device is distributed it will be reported on an accountability log 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. See Appendix 3 for use when there is not a sponsor supplied form.
10. Record any return, repair, or destruction of the device on the accountability log.
11. 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.
12. Retain all accountability documents during the conduct of the study and at the conclusion of the study forward to the RT Coordinator for retention in the regulatory binder.
13. FDA Requirements
    1. Ensure that all investigational products are labeled correctly. All investigational drugs are [required to be labeled](https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.6) with the following statement: “Caution: New Drug—Limited by Federal (or United States) law to investigational use.”
    2. Any prescribing physician/dentist in addition to the PI is required to be listed on FDA form 1572, and to have a separate signed form 1572 as their agreement with the sponsor that they will conduct the study in accordance with the current protocol and only make changes after notifying the sponsor, except where necessary to protect the safety, rights, or welfare of the subjects.
    3. All [investigational devices with IDEs are required to be labeled](https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.5) with the following statement: “CAUTION—Investigational device. Limited by Federal (or Unites States) law to investigational use”
    4. Any prescribing physician/dentist in addition to the PI is required to be listed on an agreement with the sponsor of the investigational device and agrees that they will conduct the study in accordance with the current protocol and only make changes after notifying the sponsor, except where necessary to protect the safety, rights, or welfare of the subjects.
14. **Transfers of Investigational Product**
    1. Investigational Product Transfer to Satellite Sites
       1. Prior to a transfer to satellite sites, the PI must obtain written documentation of the institutional approval for the transfer, or have documentation of the original institutional approval and provide this to the IPM.
       2. 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. An additional site visit will be required by the Office of Clinical Research if no site visit has been conducted at the new location.
    2. Investigational Product Transfer Between Protocols:
       1. Investigational product transfer between protocols will NOT occur unless the study sponsor approves and provides documentation for transfer.
       2. The *PI* must provide the IPM this documentation.
       3. The IPM records the investigational product transfer on the DAR’s of each protocol involved.
15. **Routine Verification of Compliance** – The *PI* ensures that the RT Coordinator conducts routine verification of the procedures. 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**

OCR Policy 1.1.2., Storage and Control of Investigational Drugs and Devices for Clinical Research

Clive, C. & Maynard, D. (2004). *Handbook of SOPs for Good Clinical Practice*. 2nd Ed., CRC Press. Print ISBN: 978-0-8493-2181-8. eBook ISBN: 978-0-203-49206-2

**ATTACHMENTS**

1. Appendix 1 – Yearly Temperature Log- (TempLog)
2. Appendix 2 – Sample Drug Accountability Record (DAR)
3. Appendix 3 – Sample Investigational Device Accountability Log (DevLog)
4. Appendix 4 – Disposal of Pharmaceutical Products

**Appendix 1.**

Temperature Log

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**Appendix 2.**

**Drug Accountability Record (DAR)**

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| **Protocol Title:** | | | | | | **Drug Name or Number:** | | | | |
| **Investigator Name:** | | | | | | **Dose Form and Strength:** | | | | |
| **IPM:** | | | | | | **Dispensing Area:** | | **Site Name and #:** | | |
| **Line#** | **Date** | **Subject initials** | **ID#** | **Dose** | **Quantity** | **Received/ Dispensed** | **Balance Forward** | | **Manufacturer, Lot# and Retest Date** | **Recorder’s Initials** |
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**Appendix 3**

**Investigational Device Accountability Log**

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| **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 |
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**Appendix 4**

**Disposal of Pharmaceutical Products**

Prior to disposal, verify whether the drugs are controlled substances at the following website:

<https://www.deadiversion.usdoj.gov/schedules/orangebook/c_cs_alpha.pdf>

1). Disposal of controlled substances (unused or expired) must be done through a DEA registered reverse distributor. Below is a list of reverse distributors located in Texas:

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| Med-Turn, Inc. (Collector) | (817) 868-5300 |
| Philip Reclamation Services-Stericycle Environmental Solutions, Inc. | (713) 679-2300 |
| Sharps Compliance, Inc. (Collector) | (903) 693-2525 |
| Veolia ES technical solutions, L.L.C. (collector) | (409) 736-2821 |

Full list of [DEA registered Reverse Distributors](http://www.nmbvm.org/wp-content/uploads/2018/04/Reverse-Distributor-List.pdf) for all states.

Or search for the location for public disposal of controlled substances closest to your research study site using the following link:

<https://apps2.deadiversion.usdoj.gov/pubdispsearch/spring/main?execution=e1s1>

2). If the drugs are not controlled substances, complete a request through the Environmental Health and Safety website:

<https://uthealthsa.sharepoint.com/Facilities/Pages/EHS.aspx>

a) Choose a chemical waste pickup from the Quick Links on the right side of the page

b) Label the drugs with a hazardous waste label prior to the pickup

Please allow at least one week for the pickup.