Investigational Products: IP Management and Accountability

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Investigational Drug Service

Department of Pharmacy
Learning Objectives

- Describe the Code of Federal Regulations (CFR) and Good Clinical Practice (GCP) guidelines as they pertain to study drugs.
- Describe national and state standards and laws applicable to study drugs.
- Describe the lifecycle of an investigational drug.
- Explain how the Investigational Drug Service (IDS) can help Investigators/Study Coordinators fulfill these requirements.
Regulations and Standards

- Code of Federal Regulations (CFR)
- Good Clinical Practice (GCP)
- NY State Regulations
- Hospital Policy (IRB)
  - The Joint Commission (TJC)
  - American Society of Health System Pharmacists (ASHP)
  - Hematology Oncology Pharmacy Association (HOPA)
Code of Federal Regulations
General Responsibilities of Investigators

312.60 An investigator is responsible for ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; for protecting the rights, safety, and welfare of subjects under the investigator’s care; and for the control of drugs under investigation.
Investigator Record Keeping and Retention

312.62(a) An investigator is required to maintain adequate records of the disposition of the drug.

312.62(b) An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation.

312.62(c) An investigator shall retain records for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated, or until 2 years after it is D/C and FDA is notified.
Handling of Controlled Substances

312.69 If the investigational drug is subject to the CSA, the investigator shall take adequate precautions, including storage of the investigational drug in a securely locked, substantially constructed cabinet, or other securely locked, substantially constructed enclosure, access to which is limited, to prevent theft or diversion of the substance into illegal channels of distribution.

Cabinet must meet NYS regulations – NYS likely to inspect

NYS requires that the site/PI obtain a Class 4 Researcher’s license
Good Clinical Practice
What is Good Clinical Practice?

1.24 A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.
Roles and Responsibilities

4.6.1 Responsibility for *investigational product(s) accountability* at the trial site(s) rests with the investigator/institution.

4.6.2 Where allowed/required, the investigator/institution may/should assign some or all of the investigator’s/institution’s duties for investigational product(s) accountability at the trial site(s) to an appropriate pharmacist or another appropriate pharmacist or another appropriate individual who is under the supervision of the investigator/institution.
Record Keeping and Retention (IP Related)

4.6.3 Maintaining records of the product’s delivery to the trial site, inventory at the site, use by each subject, and the return to the sponsor or alternative disposition of unused product(s). These records should include:

- Dates
- Quantities
- Batch/serial numbers
- Expiration dates
- Unique code number assigned to the product and trial subject
Record Retention (All)

4.9.5 Essential documents should be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents should be retained for a longer period, however, if required by the applicable regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator/institution as to when these documents no longer need to be retained.
Drug Accountability
Drug Accountability Lifecycle

Supply → Delivery → Inventory → Use → Return/Destroy

- Sponsor
- Enrolling Site
- Enrolling Site/Sponsor
Investigational Drug Delivery

- Date of arrival
- Packing invoice
- Temperature tracker
- Acknowledgement of receipt

CLINICAL SUPPLIES SHIPPING REQUEST

Request ID: 60857  X  Shipment Request  Date Processed: 08-Jun-2015
Consignment No.: IPS02 Consignment No: 100326
Requested By: EO255369  Requested Ship Date: 10-Jun-2015
Requestor’s Telephone: 610-576-3432
Trial ID: AD1334 (AD1334)
Ship To: Attn: Stephen Bean  Site ID: 840017
Address: University of Rochester School of Medicine & Dentistry
          601 Elmwood Ave, Box 597
          Rochester, NY
          United States  14620
Telephone: 685-275-6153  Fax No.: 
Comments: IPS02 Consignment No: 100326
Packed By: I0257697  Approved By: I0257697  Actual Shipment Date: 10-Jun-2015

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<th>MFG_LOT</th>
<th>ORD_LOT</th>
<th>Item ID #</th>
<th>QTY</th>
<th>Item Description</th>
<th>Use By Date</th>
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Temperature Monitoring (Onsite)

▪ Storage conditions must be monitored
▪ Secondary monitoring system should be in place
▪ In the event of a temperature excursion the site must be able to
  ▪ IDS utilizes a Min/Max manual recording system for each area
  ▪ Considered to be the minimum accepted by most sponsors
  ▪ provide details to sponsor including when, how long it lasted (ideally),
  ▪ and the “out of range temperatures” reached during the excursion

▪ Temperatures must be monitored on a daily basis
▪ Records must be readily available to study monitors upon request
  ▪ A continuous monitoring system with 24/7 alert functionality preferred
    ▪ IDS system records temperatures every 15 minutes via Mobileview
      by Stanley Healthcare
        ▪ Alerts IDS pharmacists via text messages in the event of an
          excursion
### IDS Continuous Temperature Monitoring

**Temperature History**

<table>
<thead>
<tr>
<th>Report run by: Steve Bean, Mon 18 Nov 19 14:22:26</th>
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</thead>
<tbody>
<tr>
<td>Period: Tue 01 Oct 19 00:00:00 - Mon 18 Nov 19 14:22:25</td>
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</table>

<table>
<thead>
<tr>
<th>Asset Name:</th>
<th>PHARM_SMH_IDS1_REF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asset ID:</td>
<td>CMT-104PHID-003</td>
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<tr>
<td>Description:</td>
<td>S8725 IDS Fridge #1 (A)</td>
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<tr>
<td>Category:</td>
<td>Medication Refrigerators</td>
</tr>
<tr>
<td>Range:</td>
<td>2.0 °C to 8.0 °C</td>
</tr>
<tr>
<td>Department:</td>
<td>SMH, SMH IDS Pharmacy</td>
</tr>
</tbody>
</table>

![Temperature Graph]

- **PHARM_SMH_IDS1_REF**
- **High Range**
- **Low Range**
## IDS Temperature Log (min/max log)

### Investigational Drug Services: Strong Memorial Hospital
All medication storage areas need to be checked for proper temperature range on a daily basis.

**Storage area ID = Refrigerator #2, room 5-6725**

**Temperature range:** 2 to 8 degrees C  
**High/Low Thermometer Details**  
**SN:** 140495006  
**Calibration due date:** 07/22/16

### Temperature Log

**Month:** June, 2015

<table>
<thead>
<tr>
<th>Date</th>
<th>Low Temp</th>
<th>High Temp</th>
<th>Current Temp</th>
<th>Time Recorded</th>
<th>Reset (Y/N)</th>
<th>Initials</th>
</tr>
</thead>
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<td>6/7/2015</td>
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<td>6/8/2015</td>
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<td>16:00</td>
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<td>GC</td>
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Investigational Drug Inventory

- Inventory log - at minimum must capture
  - Date received, dispensed, returned by patient, returned to sponsor or destroyed onsite (i.e. the lifecycle)
  - Subject information (dispensing's and returns)
  - Bottle/Kit number (if applicable)
  - Lot number
  - Expiration/Retest date (if applicable)
Investigational Drug Use – Subject Specific Product Accountability

Dispensing
- Subject ID
- Date dispensed
- Dose/quantity dispensed
- Lot number/package identifier
- Initials of study staff

Return
- Date of return
- Quantity returned
- Initials of study staff

May be required in addition to the overall drug accountability log
# Drug Accountability Record: Inventory Log

**Protocol Title**  
Master Drug Accountability Log

<table>
<thead>
<tr>
<th>Investigator/ Site:</th>
<th>Package Size:</th>
<th>Storage Temperature:</th>
</tr>
</thead>
</table>

| Investigational Drug: | |

### RECEIVED

<table>
<thead>
<tr>
<th>Shipment Number</th>
<th>Lot/Kit Number Received</th>
<th>Date Received</th>
<th>Expiration Date</th>
<th>Receipt Verified by Site (initials)</th>
<th>Date Dispensed</th>
<th>Subjects #/Initials</th>
<th>Dispensed by</th>
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<tbody>
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</tbody>
</table>

### DISPENSATION

<table>
<thead>
<tr>
<th>Verified by Monitor (initials and date)</th>
<th>Lot/Kit Number Returned</th>
<th>Comments (e.g., unused, used, damaged ID, expired)</th>
<th>Returned to Sponsor (Monitor initials/date)</th>
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**UR Medicine**  
*Medicine of the Highest Order*
Investigational Drug Return/Destruction

- Written approval from the sponsor for ultimate disposition
  - Return to sponsor
  - On-site disposal/destruction
    - Must have formal SOP for on-site destruction
Investigational Drug Return/Destruction

Return to Sponsor

- Date of (return) shipment
- Detailed listing of contents of the shipment
  - Often via use of sponsor’s return form
- Name/initial of study staff
- Place copy of return form in shipment and in study file/binder

Destroy Onsite

- Sponsor must provide authorization and guidelines
- Date, quantity, means of destruction
- Name/initial of study staff
- If a controlled substance → NYS, federal regulations apply as well
# Investigational Drug Destruction Record

**Wilmot Cancer Center**

**James P. Wilmot Cancer Center Pharmacy**

**Investigational Drug Services**

**INVESTIGATIONAL AGENT DESTRUCTION RECORD**

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Day</th>
<th>Date</th>
<th>Lot</th>
<th>Component</th>
<th>Vials</th>
<th>Vial Status</th>
</tr>
</thead>
</table>

I certify that the agent(s) referenced above has been disposed of or otherwise destroyed in a manner consistent with institutional policy/Cancer Center Investigational Drug Service policy and procedure.

---

**NAME / TITLE**  
**SIGNATURE**  
**DATE**

---

**WITNESS NAME / TITLE**  
**SIGNATURE**  
**DATE**
## Drug Accountability Record: Inventory Log

### Protocol Title
Master Drug Accountability Log

**Investigator/Site:**

**Investigational Drug:**

**Package Size:**

**Storage Temperature:**

### Table: Drug Accountability Record

<table>
<thead>
<tr>
<th>RECEIVED</th>
<th>DISPENSATION</th>
<th>RETURN/DESTRUCTION</th>
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<tbody>
<tr>
<td>Shipment Number</td>
<td>Lot/Kit Number Received</td>
<td>Date Received</td>
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**Medicine of the Highest Order**

**UR Medicine**
Study Team Tools/References

OHSP Study Documentation Tool Box

NCCIH Clinical Research Toolbox

NIDCR Toolkit for Clinical Researchers

NCI – Pharmaceutical Management Branch Investigational Drug Accountability Training Videos
PI Initiated “In-House Study” Thinking Points

- Where does the drug come from?
  - Who is responsible for ordering the drug?

- Who can prepare blinded dose forms?

- How to prepare blinded dose forms?
  - Is it even possible to blind doses?
    - Too bulky, hazardous, chemical instability

- What is required for control/storage of the drug?
  - Security
  - Temperature
  - Documents
PI Initiated “In-House Study” Thinking Points Cont.

- Preparing and dispensing to the patient
  - How/who prepares/dispenses the product?
  - Is maintenance of study blind required?
    - If so then what is dispensing plan?
  - Is it possible to ship the product to the patient at home?
    - Generally discouraged

- Drug returns by the patients

- Disposition/destruction of unused/expired/patient returned drugs
What is an Investigational Drug Service?

The IDS is a division of pharmacy ensuring that the handling, storage, packing, labeling, distribution, and inventory maintenance of investigational agents comply with Good Clinical Practices (GCP), Federal and State regulations, The Joint Commission (TJC) Standards, as well as per the recommendations of the American Society of Health-System Pharmacists (ASHP) and the Hematology Oncology Pharmacy Association (HOPA)
Responsibilities

- Reviewing study protocols before their submission to the institutional review board (IRB)
- Development of guidelines for appropriate dispensing of the study drug
- Development of drug information resources for use by health professionals involved with dispensing and/or administration of the drug (cancer center and inpatient based studies)
- Ensuring that supplies of investigational drugs are stored properly and kept in a secure pharmacy area separate from regular drug supplies
- Maintenance of accurate drug lifecycle and temperature records
- Managing study drug inventory
Services Provided

- Drug and Record Storage
  - Access limited to IDS staff
    - Enhances security and maintenance of blind
  - Archiving of study files via Iron Mountain
- Inventory Control via the “Vestigo Automated Accountability System”
  - Receipt
  - Returns/Destruction
  - Quality Assurance
- Patient randomization
- Dose Calculation/Preparation/Delivery
- Determine the budget for the study
Services Provided Cont.

- Regulatory forms
- Study Meetings
  - SEV/SIV/Monitoring/Close Out
  - Planning/design (in-house)
- Miscellaneous
  - Randomization schemes (with limitations)
  - Odd dosage form preparations
  - Drug packaging/shipping (with limitations)
References


Medicine of the Highest Order