INVESTIGATIONAL DRUG MANAGEMENT OVERVIEW

FDA/IRB/Institutional Approval

STUDY FEASIBILITY
- Drug Info
- Plans

PROCUREMENT
- Order
- Receipt
- Storage

DISPENSATION
- Preparation
- Administration

DISPOSAL
- Return
- On-site Disposal

Subject Enrollment Prescription/Order
Subject Return Expiration Study Completion

NORTHWELL HEALTH
OFFICE OF RESEARCH COMPLIANCE
STUDY FEASIBILITY AND APPROVAL

Where can I learn about the investigational drug?
- Protocol
- Investigator’s brochure
- Product insert or prescribing information
- Pharmacy manual
- Sponsor or manufacturer

What should I know about the investigational drug?

<table>
<thead>
<tr>
<th>Drug Information</th>
<th>Management Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage form and drug strength</td>
<td>Procurement process</td>
</tr>
<tr>
<td>Package size</td>
<td>Security requirements</td>
</tr>
<tr>
<td>Dose schedule</td>
<td>Storage conditions</td>
</tr>
<tr>
<td>Dose preparation</td>
<td>Blinding and randomization</td>
</tr>
<tr>
<td>Product stability</td>
<td>Transport requirements</td>
</tr>
<tr>
<td>Ancillary products</td>
<td>Disposal procedures</td>
</tr>
</tbody>
</table>

What else should I do?
- Determine storage and dispensation location.
- Secure necessary resources.
- Delegate responsibilities.
- Establish necessary procedures.

If a Northwell Health Pharmacy stores and dispenses investigational drugs (ID),

<table>
<thead>
<tr>
<th>The research team needs to...</th>
<th>The Department of Pharmacy needs to...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiate feasibility meeting.</td>
<td>Assess feasibility.</td>
</tr>
<tr>
<td>Provide essential documents.</td>
<td>Secure necessary resources.</td>
</tr>
<tr>
<td>Notify the Pharmacy of IRB approval.</td>
<td>Establish an investigational drug (or pharmacy) binder.</td>
</tr>
</tbody>
</table>
PROCUREMENT – ACCOUNTABILITY - STORAGE

If the Department of Pharmacy orders and receives investigational drugs (ID),

<table>
<thead>
<tr>
<th>The research team needs to…</th>
<th>The Department of Pharmacy needs to…</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Notify (if necessary) the Pharmacy of subject enrollment or screening to secure investigational drug(s).</td>
<td>▪ Order investigational drug(s) according to the protocol and sponsor’s instructions.</td>
</tr>
<tr>
<td></td>
<td>▪ Receive and verify investigational drug(s).</td>
</tr>
<tr>
<td></td>
<td>▪ Record the receipt of ID in a DARF.</td>
</tr>
<tr>
<td></td>
<td>▪ Store ID according to the protocol.</td>
</tr>
</tbody>
</table>

I received an investigational drug package. How do I confirm it is the correct package?

Verify the following information in the shipping document and confirm the actual investigational drug supply.

- Protocol, PI and research site information
- Subject information
- Drug name, dosage form and drug strength
- Package size and quantity
- Lot or batch number
- Kit, bottle or vial numbers
- Expiration or retest date
- Temperature during transit
- Damage and discrepancy

What is the Drug Accountability Record Form (DARF)?

It is an auditable log of drug management. The sponsor may provide the following DARFs:

- Protocol-specific DARF
- Subject-specific DARF
- Sponsor-specific DARF [e.g., National Cancer Institute (NCI) Cancer Therapy Evaluation Program (CTEP) DARF, AIDS Clinical Trial Group (ACTG) DARF]

If the sponsor does not provide a DARF or you are involved in an investigator-initiated study, please use the DARF template in the HRPP website.

What should I record in the DARF?

<table>
<thead>
<tr>
<th>Study Information</th>
<th>Drug Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protocol title</td>
<td>Name</td>
</tr>
<tr>
<td>IRB or protocol number</td>
<td>Dosage form and drug strength</td>
</tr>
<tr>
<td>Hospital or Medical Center</td>
<td>Package size</td>
</tr>
<tr>
<td>Dispensing location</td>
<td>Inventory or dispensing unit</td>
</tr>
<tr>
<td>Investigator name</td>
<td>Storage temperature</td>
</tr>
<tr>
<td>Investigator or site number</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Management</th>
<th>For Each Entry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Receipt</td>
<td>Date</td>
</tr>
<tr>
<td>Dispensation</td>
<td>Subject initials and study ID</td>
</tr>
<tr>
<td>Distribution or transfer</td>
<td>Dose and quantity</td>
</tr>
<tr>
<td>Periodic inventory verification</td>
<td>Balance</td>
</tr>
<tr>
<td>Subject return</td>
<td>Lot or batch number</td>
</tr>
<tr>
<td>Return to sponsor</td>
<td>Kit, bottle or vial number</td>
</tr>
<tr>
<td>On-site disposal</td>
<td>Expiration date</td>
</tr>
<tr>
<td></td>
<td>Recorder initials</td>
</tr>
</tbody>
</table>

When do I use a separate DARF sheet?

You need to use a separate DARF sheet for:

- Each protocol
- Each drug under the same study
- Each dosage form
- Each drug strength
- Each lot number
- Each storage and preparation location

*Incorrect DARF entries should be crossed out with a single line and corrected with the date and initials of the recorder. No erasure or masking fluid is allowed.*

*File a note if necessary to provide further explanation of any issues and place it in the binder.*

*Schedule periodic inventory verification to reconcile any discrepancies, secure sufficient supplies for upcoming subject visits and dispose of any expired drugs.*
How should I store investigational drugs?

- Establish controlled access to investigational drugs by only authorized personnel. Access to keys or pass codes to investigational drug storage should be limited accordingly.

- Store investigational drugs in dedicated storage shelf, cabinet, refrigerator and freezer space separate from non-research drugs and clinical supplies.

- Label storage compartments with study and drug information.

- Establish separate compartment for each drug, strength and lot under the same study.

- Store used, returned and expired drugs separate from working stock.

- Establish safeguards for drugs with the same name for multiple protocols.

How can I ensure adequate storage temperatures?

- Monitor and record storage temperatures continuously (e.g., alarm and continuous recording system).

- Install back-up power generators for refrigerators and freezers storing investigational drugs.

- Establish procedures for any temperature excursions.

- Plan for emergency situations.
PREPARATION – DISPENSATION

If the Department of Pharmacy prepares and dispenses investigational drugs (ID),

<table>
<thead>
<tr>
<th>The research team needs to...</th>
<th>The Department of Pharmacy needs to...</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Notify (if possible) the Pharmacy of subject enrollment and subject dosing schedules prior to actual dosing dates.</td>
<td>▪ Verify authorized prescribers.</td>
</tr>
<tr>
<td>▪ Provide necessary documents for dispensation.</td>
<td>▪ Verify subject’s signed informed consent.</td>
</tr>
<tr>
<td>▪ Coordinate picking-up investigational drug(s).</td>
<td>▪ Verify treatment arm assignments.</td>
</tr>
<tr>
<td>▪ Provide subjects education (medication guide, dosing instructions on labels, sponsor-provided materials, demonstration in clinic).</td>
<td>▪ Verify doses per protocol.</td>
</tr>
<tr>
<td></td>
<td>➢ Dosing schedule?</td>
</tr>
<tr>
<td></td>
<td>➢ Dose modification?</td>
</tr>
<tr>
<td></td>
<td>➢ Product change?</td>
</tr>
<tr>
<td></td>
<td>▪ Verify assigned unique identifiers for ID.</td>
</tr>
<tr>
<td></td>
<td>▪ Prepare the investigational drug(s) according to protocol and pharmacy manual.</td>
</tr>
<tr>
<td></td>
<td>▪ Record dispensation in DARF.</td>
</tr>
<tr>
<td></td>
<td>▪ Complete protocol-specific forms.</td>
</tr>
</tbody>
</table>

What documents do I need prior to preparation?

- Signed informed consent form
- Treatment arm assignments
- Kit, bottle or vial assignments
- Drug order and/or prescription
  - Appropriate inpatient or outpatient forms
  - Only from authorized prescribers listed in
    - FDA Form 1572
    - Delegation of responsibilities
    - Individual investigator agreement

For investigational drugs stored and dispensed on site: Maintain prescriptions or other types of documentation containing investigational drug and subject information, which an authorized investigator reviews and signs at each dispensation. This record will show that only authorized prescribers have ordered the investigational drug.

What requirements do I need to follow for preparation?

- Protocol-specific documents
  For example,
  - Subject-specific dispensation records
  - Dose calculation sheets
  - Original drug label sheets
INVESTIGATIONAL DRUG MANAGEMENT OVERVIEW

- **Compounding**
  - Resources specified for compounding (e.g., ancillary products, administration set)
  - Compounding instructions and logs
  - USP 797 for compounding sterile preparations

- **Packaging**
  - Requirements for immediate container (e.g., child proof, light protection, blinding)
  - Bottle opening policy and dispensing unit (e.g., bottle vs. tablets or capsules)

**What information should dispensing labels contain?**

- “Caution: New drug-limited by federal law (or US) to investigational use”
- Study identifier (e.g., IRB number)
- Prescription or drug order number
- Subject name
- Subject address or location in facility
- Subject study identification number
- Investigational drug name (or placebo)
- Investigational drug dosage form and strength
- Dispensing quantity
- Administration instructions including dose
- Directions for storage and other relevant information
- Preparation or dispensing date and/or time
- Expiration date and time
- Name of prescribing investigator
- Name of preparing health professional or pharmacist
- Dispensing location name, address and phone numbers

Label template is available in the HRPP website.

What requirements do I need to follow for dispensation?

- **Dispensation and on-site administration**
  - Only qualified, NYS-licensed and delegated staff should perform a final-check on investigational drugs prior to dispensation or administration.
  - Any staff involved in administration need to meet protocol-specific requirements.
  - Two independent checks are recommended.

- **Subject education**
  - Any sponsor-provided materials
  - Product insert or medication guide
  - Instructions on dispensing label
  - Demonstration and teach-back in clinic

- **Subject compliance**
  - Subject dosing diary or drug calendar
  - Record quantity of returned investigational drug in DARF and other required forms.

*Retrieve both used and unused investigational drugs including empty bottles from subjects for subject compliance check and safe disposal.*
DISPOSAL

If the Department of Pharmacy disposes of investigational drugs (ID),

<table>
<thead>
<tr>
<th>The research team needs to...</th>
<th>The Department of Pharmacy needs to...</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Return any used or unused drugs.</td>
<td>▪ Follow sponsor's policy on disposal.</td>
</tr>
<tr>
<td>▪ Notify pharmacy of the study and subject status for drug reconciliation.</td>
<td>▪ Obtain approval for return or on-site disposal.</td>
</tr>
<tr>
<td>▪ Provide pharmacy with any relevant communications from sponsors (e.g., drug expiration, drug recall).</td>
<td>▪ Dispose of investigational drug(s) according to the institutional or facility policy.</td>
</tr>
<tr>
<td></td>
<td>▪ Record return or on-site disposal in DARF.</td>
</tr>
<tr>
<td></td>
<td>▪ Record return or on-site disposal in protocol-and subject-specific forms.</td>
</tr>
</tbody>
</table>

How can I dispose of used, unused or expired drugs?

- Return to the sponsor

- On-site disposal
  - Obtain written approval from the sponsors.
  - Comply with policies at each facility.
  - Follow additional procedures for controlled substances.

- Documentation and records
  - Retain approval from the sponsors.
  - Enter return or on-site disposal in Drug Accountability Record Forms (DARFs).
  - Enter return or on-site disposal in subject-specific dispensation records.
  - Record return or on-site disposal in any other sponsor-provided or on-site forms.

Ask the sponsor regarding the disposition of prepared but non-dispensed investigational drugs.

Remove any Protected Health Information (PHI) before disposal.
DOCUMENTATION

Investigational Drug (or Pharmacy) Binder

Study Feasibility & Initiation
- IRB Approval (and Renewal) Letter
- FDA Form 1572
- Delegation of Responsibilities
- Individual Investigator Agreement
- Contacts
- Approved Protocols
- Investigator’s Brochure
- Pharmacy Manual
- Randomization Charts
- Unblinding Packets

Throughout the management of ID
- Read Essential Documents
- Retain Documentation
- Record Accountability
- Remember Regulatory Compliance

Procurement, Accountability and Storage
- Order/Shipping Documents
- Delivery/Receipt Confirmation
- Drug Accountability Record Forms
- Temperature Logs

Preparation & Dispensation
- Signed Informed Consent Forms
- Treatment Arm Assignments
- Kit, bottle or vial assignments
- Prescriptions/Orders
- Dose Calculation Sheets
- Drug Label Sheets
- Dispensation Records
- Drug Pick-up Records

Disposal
- Subject Return Records
- Return to Sponsor Records
- On-site Disposal Records

There are additional requirements for clinical research involving controlled substances. Contact the Office of Research Compliance (orc@northwell.edu) for more information.