

## **Policy: Investigational Drug Service Program**

### **Common Abbreviations:**

IRB: Internal Review Board

PI: Primary Investigator

IP: Investigational Product

IDS: Investigational Drug Service

### **Definitions:**

Vestigo®: A 21 CFR Part 11 compliant electronic accountability software application designed specifically for investigational pharmacy use and utilized by University of Utah Hospitals & Clinics Investigational Pharmacy Service. Refer to [www.mccreadiegroupp.com/vestigo/](http://www.mccreadiegroupp.com/vestigo/) for additional information.

### **Purpose:**

- A. This policy describes the scope and specific procedures for the Investigational Drug Service (IDS) Program for the University of Utah Hospitals & Clinics

### **Description:**

- A. The Investigational Pharmacy exists to specifically review new studies, train pharmacy personnel, and store, mix, and dispense study-specific investigational medications for clinical trials throughout the University of Utah Hospitals & Clinics.
- B. The IDS Clinical Pharmacists prepare study-specific information to facilitate handling of study drugs for the Investigational Pharmacy staff, and to train Pharmacists that may be handling study medications for after-hours studies at the University of Utah Hospital and Huntsman Cancer Hospital in situations when the IDS pharmacy is not open (i.e. after hours, weekends, holidays); and coordinates the inventory and drug control procedures. All protocol information and IDS instruction material containing protocol information is confidential. The IDS pharmacists are responsible for ensuring that investigational drugs are handled according to state and federal laws and regulations, hospital policy, institutional review board (IRB) policy, and sponsor protocol. All pharmacists and technicians must comply with this policy when handling investigational drugs.

### **Implementation:**

- A. Documentation of receipt, dispensation and return for each study drug maintained by the Investigational Pharmacy Services is recorded in electronic form using Vestigo®. The completed accountability, or a copy, must remain in the possession of the IDS pharmacy. The IDS pharmacist coordinates the handling of drug studies by the Department of Pharmacy Services. This includes:
  1. Meeting with investigators and/or study team to setup drug studies
  2. Meeting with IDS pharmacy personnel to discuss dispensing procedures, potential problems and protocol requirements
  3. Initiating a study by setting up a binder, training personnel, building the study in Vestigo®, creating and/or reviewing study-specific drug orders, and identifying a specific storage location for IP. Monitoring temperature in all investigational product storage areas
  4. Conducting quality improvement activities as assigned. (e.g. Root Cause Analysis, Failure Mode and Effects Analysis)
  5. Preparing reports as needed. This includes reports for:
    - a. P&T Committee
    - b. Pharmacy Department
    - c. Financial Purposes
    - d. Audits
- B. **To set up a drug study**, a lead IDS pharmacist will be assigned to review the IRB paperwork, protocol, available drug information, Pharmacy Manual, and discuss the study with the study sponsor (monitor), principal investigator (PI), or study coordinator to establish the following information:
  1. Name(s) and telephone number(s) of the PI, co-investigator(s), study coordinator(s) involved, and monitors (if applicable).
  2. Name and telephone number of emergency contact person.

3. The start date and expected conclusion date for the study, if known.
  4. The number of patients expected to participate in the study and the duration of therapy.
  5. Name, strength, dosage form and route of administration of the study drug(s). Packaging of the drug (i.e. patient specific, open label, blinded) will also be included.
  6. The source of the drug (i.e., supplied by pharmacy or investigator).
  7. Location and proper storage of the drug.
  8. Special handling requirements, if applicable (hazard category, etc.)
  9. Proper preparation and labeling of the study drug.
  10. Location of patients on the study
  11. Delivery of the drug to the patient care area.
  12. Disposition of empty study drug materials (i.e., save or discard).
  13. Pharmacy estimate for each study will be provided by Pharmacy Manager and information regarding who will be billed will be obtained. (i.e., patient expense or investigator). Investigational Pharmacy does not bill for patient-responsible medications.
  14. Person responsible for and method of ordering additional drug.
  15. Acceptable inventory levels of the study drug to meet study enrollment.
  16. Randomization and blinding procedures if applicable.
- C. IDS Pharmacist Responsibilities:** Based upon the information obtained from the PI and study protocol, the IDS pharmacist will complete study startup as outlined below.
1. Title of the study, name of PI, and IRB #
  2. Dispensing/labeling/record keeping instructions will include:
    - a. Location of study binders
    - b. Location and proper storage of study drug(s)
    - c. Information necessary on the prescription/order
    - d. Randomization of patients
    - e. Dose calculations and preparation
    - f. Proper labeling
    - g. Special handling requirements for the IP
    - h. Charging information (i.e., patient or investigator)
    - i. Handling drug returned by patients and returning or destroying drug as directed by sponsors
  3. Vestigo® will be utilized for all accountability records, which include:
    - a. Master Patient List
    - b. Receipt of IP
    - c. Expiration Date(s) of IP
    - d. Patient and IP Dispense information
    - e. Patient Returns
    - f. Disposition of used investigational product (IP)
  4. Investigators and study coordinators:
    - a. Name, telephone number and department of the PI, co-investigators, study coordinators, and external monitor(s). This will also include the emergency contact person(s) and telephone number(s).
  5. Medications
    - a. Drug name or number, strength, dosage form (vial, tablet, etc.), concentration
    - b. Source of the drug (i.e. supplied by the pharmacy or investigator)
    - c. Dosage and schedule (e.g., mg/kg, BID, etc.)
    - d. Reconstitution instructions and special handling precautions (if applicable)
    - e. Stability information Administration instructions and precautions
    - f. Drug Incompatibility information (if applicable and available)
  6. Concomitant medication information (if necessary)
  7. Unblinding information (if applicable)
  8. Information specific to the IDS pharmacist's ability to perform all responsibilities for IP management, storage, compounding, and dispensing(if necessary)
  9. IP ordering information, including:
    - a. Department or individual responsible for ordering additional drug.
    - b. Acceptable inventory levels for the drug, if applicable.

10. Date dispensing guidelines are prepared and date of any revisions.
  11. Study version or amendment number
  12. **Drug company contacts:**
    - a. Study monitor or contact person (if applicable)
    - b. Individual to contact for emergency drug information (name and phone number)
    - c. Individual to contact in emergency situations
    - d. Individual to contact for drug ordering
- D. Upon receipt of study drug,** the contents (drug name, strength, formulation, lot number, quantity) of the shipment will be verified against the packing slip. The date received (DD/MMM/YYYY) and time will be noted on the packing slip along with any expiration date information provided. The staff member will initial the sheet. The accountability of the drug receipt will be documented in Vestigo® only. Sponsor-provided accountability logs will not be used for inventory tracking. Confirmation of receipt (facsimile, email, IRT registration, temperature logger data verification) will be done as required by the sponsor.
1. Expiration or retest date: A mandatory disclosure of investigational product (IP) expiration or retest date, or date of manufacture is required by IDS. If no expiration date is available, IDS staff will follow-up on expiration date information again at suitable time intervals.
- E. Temperature Monitoring:**
1. Temperatures for all IP will be monitoring using an electronic temperature monitoring system. The system electronically records multiple temperature data points every minute for each device. The system provides the ability to set alerts to notify all investigational pharmacists when a device (refrigerator, ambient temperature, freezer) is getting close to the required temperature limit (e.g. close to the high point, or close to the low point) so that action can be taken prior to a temperature excursion occurring.
  2. Reports are generated each month outlining the high and low points for each device during a given month. This information is provided to the external monitor during the monitor visit, or to anyone else requiring the temperature information for a specific IP on a specific clinical trial.
- F. Dispensing study medication**
1. The investigational drug order must be transmitted to the pharmacy through a pre-approved method, such as Epic e-prescribing or IDS pharmacy-reviewed drug order templates. The orders must be signed by the PI or a Sub-I for each specific IP order. The drug shall not be dispensed until these four conditions have been met.
    - a. Study has received full IRB approval.
    - b. Approved investigators and study coordinators are listed in ERICA.
    - c. Pharmacy personnel have been fully trained on the study during the SIV, or by conversing with the PI, sponsor, monitor, or other personnel until all questions have been addressed and the primary pharmacist feels comfortable that the study may proceed.
    - d. On receipt of an initial order for an investigational drug, the Investigational Pharmacy requires a copy of the signature page of the informed consent for the patient enrolled in the study.
  2. **Upon dispensing study drug,** the prescription will be entered under the subject profile in Vestigo®. The first time a subject receives drug on a study, the subject will be entered into Vestigo® by name, MRN, and DOB. When a prescription is entered, the following information will be recorded in Vestigo:
    - a. Date dispensed (month/day/year)
    - b. Patient name or initials
    - c. Subject number or randomization number (if applicable to the study)
    - d. Lot number of IP
    - e. Amount dispensed
    - f. Inventory balance
    - g. User-name of verifying pharmacist
    - h. Name of prescribing physician
    - i. Prescription number (when necessary)

- G. Transport of Investigational Product to subjects:** The IDS pharmacy utilizes transport services from Huntsman Cancer Hospital, as well as couriers through the University of Utah Hospital for transport of investigational product. All couriers and transporters have been trained by hospital personnel on proper handling of investigational drug product. Each study drug delivered by a transporter is signed for, prior to leaving the pharmacy, by each transporter. The nurse or coordinator receiving study drug also signs upon receipt of investigational drug and is responsible for providing the medication to the patient. The IDS pharmacy ensures drug is packaged properly for transport.
- H. Used partial or empty vials will be destroyed per IDS Destruction Standard Operating Procedure, unless both of the following conditions are met:
1. The IP is not considered hazardous or biohazardous.
  2. The sponsor explicitly requires retention of the vials as discussed at the SIV.
- I. Returned IP from subjects will be counted and documented in Vestigo® and destroyed per IDS Destruction Standard Operating Procedure unless the sponsor explicitly requires retention of the returned IP as discussed at the SIV.
- J. **When study drug is returned** to the manufacturer due to expired drug, completion of study, drug recall, or when deemed appropriate, the following information will be recorded in Vestigo®:
1. Date (month/day/year)
  2. Study Name and IP
  3. Lot number
  4. Quantity returned
  5. Ending balance
  6. Initials of pharmacy personnel returning drug
  7. Name of person or manufacturer to who drug was returned
  8. Return information shall be electronically stored in Vestigo®
- K. **Monthly or bi-monthly inventory counts** will be completed and recorded in Vestigo®. Additional inventory checks will be done when deemed appropriate by the IDS Pharmacy Manager. The date of inventory count, quantity on-hand, and person conducting inventory will be recorded.
1. Any discrepancies between actual count and number recorded on the inventory control record will be remedied as soon as possible. The PI and coordinator will be notified of any discrepancies which cannot be remedied.
  2. Inventory records of all pharmacy activities related to drug studies must be maintained for a minimum of 2 years following: 1) the date a marketing application for the drug is approved for the drug for the indication which it is being investigated or 2) if no application is to be filed or 3) if the application is not approved for such indication until 2 years after the investigation is discontinued and the FDA is notified (21CFR312.62). Functionally, once a study is closed the drug accountability records and related study documents will be sent to Records Management or other suitable storage facility and labeled "Store indefinitely" under the direction of the IDS Pharmacy Manager, staff, and policies applicable to the study team.
- L. **Notification of expiration dates**, extensions, changes in storage requirements, etc. shall be noted on the inventory record in Vestigo®. Updates to study medication expiration date or retest date will be recorded in Vestigo®.
- M. **Destruction of investigational study drug** will be handled as biohazard or chemotherapy waste, or as appropriate per hospital policy if the drug has previously received FDA approval. Investigational study medications will be placed in the appropriate waste container. Documentation of destruction will be recorded in Vestigo.
- N. The PI is responsible for completing the Investigational Drug Data Form (IDDF) for studies involving investigational drugs.
- O. **A study binder** for each protocol will be prepared and will include:
1. Short instructions and/or dispensing guidelines (not available for review during monitor visits).
  2. A record of pharmacy staff training. All pharmacy staff working on a protocol will sign the training log.
  3. Study drug orders and other documented related to drug dispensation

4. Shipment documents
  5. Required forms
  6. Pertinent correspondence with the sponsor or monitoring company.
- The current study protocol and Investigator's Brochure (IB) will be stored electronically at the IRB's website (Electronic Research Integrity and Compliance Administration (ERICA)). No separate binder provided by the sponsor will be maintained.
- P. **Training to other pharmacy staff:** The lead IDS pharmacist for each protocol will be responsible for providing information and training to other pharmacists and technicians involved in dispensing the drug. Training is provided to IV Center staff for all after-hours studies performed at University Hospital.
- Q. **External Monitoring:** The following are requirements for external monitors performing study monitoring visits to the Investigational Drug Services pharmacy:
1. Utilization of electronic accountability system for all monitoring activities, including documenting findings, returns, destruction, and any notes.
  2. Performing subject IP returns for destruction or return, and expired IP during each monitor visit.
  3. Reviewing accountability information for the study while on site during the study visit
  4. If accountability records are required, a PDF can be created by the monitor and emailed to themselves using a company email (no personal emails can be utilized for investigational drug activities). IDS staff will not email drug accountability records outside of a monitoring visit unless pre-arranged at the site initiation visit.
  5. Requesting temperature logs during monitor visit.
  6. Scheduling monitor visits at least two weeks in advance.
  7. Requesting the appropriate time needed for each visit, within reason.
  8. Proper use of time while in the Investigational Pharmacy. No conference calls or work on other studies is allowed while monitoring.
  9. Temperature logs will only be emailed immediately following an on-site visit.
  10. **Remote monitoring is not supported** unless specifically requested and agreed upon during SIV. An additional fee applies.
- R. **Billing:** The IDS Pharmacy Manager or designee will bill each investigational drug study and submit it to the finance person or PI for each study on a monthly basis as generated in Vestigo®. Miscellaneous charges will be included (i.e. mailing costs, prepackaging, and compounding fees). These charges will be billed in Vestigo® as an "ad hoc" charge.
1. Prior to the start of a study, an account authorization form is sent to the PI and study team to complete and is returned to the IDS Pharmacy. IDS will maintain a copy of this account authorization form with the study file. An invoice will be created by IDS and sent electronically to the finance person or PI. Invoices will be kept electronically for each study in Vestigo®. At the time of billing, IDS will email a spreadsheet indicating the transfer of funds between accounts to the Accounts Payable Department at the University Accounting Office. A copy of the billing document will be retained by the PI or their department. Exceptions to the above outlined charging procedure are as follows:
  2. If for any reason the fees for a study are waived (for an emergency use protocol, for example) the IDS pharmacist will compile charges for reporting purposes and enter them into Vestigo®. However, the investigator or department will not be charged.
- S. **On-Call:** Solving problems or answering questions related to an investigational drug study after-hours:
1. There is an Investigational Pharmacist on-call every day. An email is sent to the staff at University Hospital Inpatient and HCH Inpatient Pharmacy (if applicable) to let them know who is on call and of any known pending or active study patients. The IDS pharmacist is available by paging through Smart Web or by contacting them directly via their cell phone. Cell phone numbers are provided in the daily email to other pharmacists working the weekend, holiday, evenings, etc.
  2. If for some reason, the Investigational Pharmacist does not answer a page, the IDS Pharmacy Manager may be contacted.
- T. Role of pharmacists in obtaining investigational drugs for **Emergency Use** (formerly Compassionate Use)

1. Emergency use protocol studies generally involve drugs that are not FDA approved but offer therapeutic options or are potentially lifesaving therapy for a particular disease state. An investigator may have both a treatment protocol and an emergency use protocol study for the same drug. These are separate studies with separate drug inventories and must not be used interchangeably.
2. Attending physicians may request emergency use protocol drugs directly from the potential supplier (usually a pharmaceutical company). The requesting physician must notify the IRB of emergency use protocol prior to drug use if possible or within 24 hours and complete the FDA EIND application
3. The IDS pharmacy will store, dispense, and account for EIND medications.
4. As with all investigational drugs, the patient must give signed informed consent prior to administration of the drug.