

## INVESTIGATIONAL DRUGS FOR HUMAN USE

### I. **PURPOSE:**

To delineate policies and procedures relating to the safe handling, dispensing, utilization and disposition of investigational drugs at the Portland VA Medical Center.

### II. **POLICY:**

The Research Pharmacy will control the storage, labeling and distribution of all investigational drugs for human use unless otherwise delegated in writing by the Research Pharmacy Program Manager to the investigator or another Pharmacy.

### III. **DEFINITION:**

- A. **DRUGS** include prescription medications, sample medications, herbal remedies, vitamins, nutraceuticals, over-the-counter drugs, vaccines, diagnostic and contrast agents used on or administered to persons to diagnose, treat or prevent disease or other abnormal conditions, radioactive medications, respiratory therapy treatments, parenteral nutrition, blood derivatives, intravenous solutions (plain, with electrolytes or drugs and any product defined by the Food and Drug Administration (FDA) as a drug.
- B. An **INVESTIGATIONAL DRUG** is defined as any drug or biologic used for the purpose of the research. This includes an approved drug that is being studied for an unapproved or approved use in a controlled, randomized or blinded clinical trial. (Any alteration in the content or ratio of active or inactive ingredients or dosage forms also renders a drug investigational.)

### IV. **RESPONSIBILITY:**

- A. The Research Pharmacists will be responsible for the day-to-day management of the Investigational Drug program as delineated in the functions listed within this document.
- B. The Research Pharmacy Program Manager or designee is responsible for resolving the identified discrepancies in inventory, documentation, and for ensuring that pharmacy employees follow the procedures for dispensing of investigational medications. The Research Pharmacy Program Manager is responsible for the integrity, security, and accountability of investigational drugs maintained within the pharmacy.

- C. The Chief, Pharmacy Service is responsible for ensuring that appropriate resources are available to maintain the Investigational Drug program.
- D. The principal investigator is responsible for the overall direction of all protocols involving the use of investigational drugs. These responsibilities include:
  - 1. Obtaining final Institutional Review Board (IRB) and Research and Development (R&D) Committee approval.
  - 2. Arranging investigational drug delivery and distribution through the Research Pharmacy.
  - 3. Obtaining and documenting informed consent and providing a copy to the Research Pharmacy.
  - 4. Providing approved protocols, investigator's brochures and other documents to the Research Pharmacy so that drug can be safely and appropriately dispensed.
  - 5. Providing a current, up-to-date signed copy of VA Form 10-9012 (Investigational Drug Information Record) to the Research Pharmacy with all authorized prescribers listed. The original will be kept with the R&D Service research study records. The research pharmacist will assist the investigator in preparing the 10-9012s.
  - 6. Complying with all VA regulations, AHRP standards, Joint Commission standards, FDA regulations and other Federal regulations regarding investigational drugs.
- E. The IRB Coordinators are responsible for providing approved protocols, Investigational Drug Information Records (VA Form 10-9012s), IRB and R&D Committee approval forms, amendments and other necessary paperwork as requested to ensure safe dispensing of investigational drugs.
- F. Staff Pharmacists are responsible for dispensing and assisting with randomization for investigational drugs on the rare occasions when the Research Pharmacists are not available.

V. **PROCEDURES:**

- A. Security and Storage.
  - 1. All Investigational drugs will be maintained in the Research Pharmacy to provide separation from non-investigational drugs. Exception: items that need to be kept at -20 degrees centigrade or below.
  - 2. Drugs that are standard of care and that are not provided by the research study sponsors may be stored and dispensed through Medical Center Outpatient Pharmacy and Inpatient Pharmacy procedures (i.e. comparator drugs).

3. Only Research Pharmacy staff and staff pharmacists have access to the Research Pharmacy.
4. Refrigerated medications will be stored in the Research Pharmacy refrigerator.
5. Drugs requiring refrigeration or room temperature storage conditions will be stored as defined by the United States Pharmacopoeia (USP) unless otherwise indicated by protocol. Refrigerated medications will be stored between 36 and 46<sup>o</sup>F. Room temperature medications will be stored between 68 and 77<sup>o</sup> F with infrequent excursions to 86<sup>o</sup> F. A temperature log will be maintained with temperatures recorded daily during the work week.
6. Drugs requiring special handling (refrigeration, frozen products, controlled substances, etc) will be identified by the Research Pharmacist in advance of receipt of drug product. The Research Pharmacist will determine the availability of space and/or equipment required for storing the product appropriately.

#### B. Receipt

1. All investigational drug supplies will be sent directly to the Research Pharmacy.
2. Investigational Drug supply will not be received into the Medical Center by anyone other than designated pharmacy personnel.
3. The Research Pharmacist will ensure that all receipt information for documentation required by the sponsor is completed. Receipts will be noted in the Research Pharmacy's computerized Investigational Drug Accountability log with date of receipt, quantity of receipt, expiration date and lot number.

#### C. Dispensing

1. Dispensing of investigational drug supply to study subjects will be coordinated through the Research Pharmacy.
2. Upon receipt of a medication/prescription order for an investigational drug product, the pharmacist will determine if a signed copy of the study subject's informed consent has been received. If an informed consent has not been received the pharmacist will request a copy of the informed consent from the investigator or his/her designee. The order will not be filled until a copy of the signed informed consent has been received by the Research Pharmacy. The Research Pharmacist will initial, and indicate the date and time that the

informed consent has been received in the pharmacy and reviewed by the pharmacist. The Research Pharmacist will review the signed informed consent and ensure that it is the most recently IRB approved informed consent form, and that both the subject, a witness, and the individual conducting the informed consent process has signed.

3. A list of active protocols will be maintained in the Research Pharmacy. Prior to dispensing an investigational drug, the Research Pharmacist will ensure that the protocol has received final R&D Committee and IRB approval.
4. If required by protocol, the Research Pharmacist will participate in the randomization process to assign a consented patient to a randomized treatment.
5. The Research Pharmacist will review the research study protocol and verify the correct drug and instructions for use according to the research study protocol. The Research Pharmacist will review the patient's medication profile after receipt of the order to ensure that the patient is not receiving medications that are contraindicated for the research study. The pharmacist will contact the investigator when drug interactions or contraindications are noted.
6. Prescriptions for ambulatory patients will be written or entered into the Computerized Patient Record System (CPRS) by authorized prescribers and will be filled by the Research Pharmacy using the Outpatient Pharmacy VISTA program. Whenever feasible two Research Pharmacy staff will check the prescription to provide additional safety in dispensing. Only authorized prescribers listed on VA Form 10-9012 for the research study may prescribe investigational drugs. Prescriptions/orders prescribed by other than authorized prescribers will not be filled.
7. Electronic medication orders for hospitalized patients will be entered under the Unit Dose, or IV Pharmacy VISTA computer program. If the drug is to be sent with the study patient upon discharge from the hospital, a prescription will be filled using the Outpatient Pharmacy Vista Program. Each drug sent to the ward will have a bar code attached so that it may be administered through utilization of the Bar Code Medication Administration (BCMA) program.
8. If the patient is receiving an investigational agent as part of a protocol from another institution, the Research Pharmacist will request a protocol from the involved institution. If the patient's physician wishes to continue the investigational drug during admission he/she will complete an Investigational Drug Information Record (VA Form 10-9012) for each investigational drug prescribed and forward the original of the completed form to the Research and Development for signatures. The Research Pharmacist will enter the

Policy and Procedure  
Investigational Drugs for Human Use  
Policy #55  
August 2007

Investigational Drug Information Record into the research patient's CPRS record and enter the drug into the Vista Computer. The physician will enter the order into the computer, which will be verified by the Research Pharmacist. A Bar code will be affixed to the investigational drug container and will be administered through the BCMA program.

9. The pharmacist will dispense the Investigational drugs utilizing the directions in the research study protocol and in accordance with Portland VA Medical Center pharmacy dispensing policies. An auxiliary label with instructions "Investigational Drug – Not for General Use" or "CAUTION - NEW DRUG: LIMITED BY FEDERAL LAW TO INVESTIGATIONAL USE." will be attached to the container as well as an expiration date. Expiration date will be one year from dispensing unless the manufacturer's expiration date for the drug expires before that time as per USP standards.
10. Pharmacy Service will maintain a perpetual inventory of each investigational drug on hand, indicating amounts received, dispensed, discarded, returned, etc., as appropriate in an investigational drug dispensing log. Additional documentation required by study sponsors will also be completed and maintained.
11. The Investigational Drug Record will include at minimum:
  - a. Name of drug, dosage form and strength
  - b. Manufacturer or other source
  - c. Date of Receipt of drug
  - d. Quantity received
  - e. Expiration date (memo from sponsor or noted in protocol from sponsor indicating that expiration is centrally managed is acceptable)
  - f. Control number, lot number or other identification number
  - g. Name of principal investigator
  - h. Protocol name and number
  - i. Date of final approval by the IRB and R&D Committee
  - j. Name of authorized prescriber writing the prescription
  - k. Name of subject or other subject identifier for individual receiving the drug
  - l. Serial Number of the Prescription (prescription number for outpatient prescriptions only)
  - m. Quantity dispensed
  - n. Recorders initials
  - o. Balance remaining after the transaction.
12. An Investigational Drug Information record (VA Form 10-9012) for each Investigational Drug will be placed in the patient's CPRS record by using the Investigational Drug Information progress note template. It can be accessed by reviewing the "Postings" section of the patient's CPRS record.

#### D. Disposition

1. Upon completion of a study involving an investigational drug the Research Pharmacist will remove the investigational drug from stock in accordance with written instructions from the investigator.
2. The investigational drug log will include a final entry when the use of the investigational drug is discontinued. This entry documents the date of termination of use of drug, quantity remaining, and action taken to dispose of the balance on hand.
3. The Investigational Drug accountability log will be closed out with the action taken for disposition recorded as the last entry in the log.
4. Excess stock will be returned to the sponsor or destroyed as per written instructions from the sponsor.
5. Any excess stock not returned to the manufacturer will be disposed of in a pharmaceutical waste bin and disposed of per the Medical Center Pharmaceutical waste policy. Any non-commercial investigational drug will be considered hazardous and will be disposed of in a disposable bulk hazardous waste container.

#### E. Records

1. All study protocols (original and including all current updates) will be maintained in a study specific binder. In addition the binder will contain the following elements:
  - a. Drug Information Record (VA Form 10-9012), which will designate the authorized prescriber list along with the approvals, received from the IRB and the R&D Committee.
  - b. Investigational Drug Accountability Record.
  - c. Pharmacy Copy of Patient signed Informed Consents.
  - d. Correspondence with Study Sponsor to include shipping receipts, audit reports and final disposition of study drug documentation.
2. Prescriptions for all study protocols will be maintained separately from the Outpatient Prescription records in the Research Pharmacy and maintained for at least 6 years or as specified by the sponsor or FDA.

F. Quality Assurance Monitors

1. The Research Pharmacist for investigational drug program will conduct an audit annually to assure compliance with regulations, standards and policies and report to the Research and Development Committee.
2. At a minimum, the pharmacist will report to the Research & Development Committee the following elements:
  - a. The number of prescriptions dispensed per quarter and that no prescriptions were dispensed without documentation within pharmacy of the patient informed consent.
  - b. Verification that the drug inventory on hand matches the recorded balance on the Investigational Drug Accountability Record and that all elements of dispensing were completed on the record.
  - c. Other Quality Assurance monitors as needed.

**VI. REFERENCES:**

VA Manual, M-2, Part I, Chapter 3, dated 1967.  
VHA Handbook 1108.4, dated October 14, 2005  
JC Accreditation Manual for Hospitals, Current Version (MM.7.40)  
Federal Register, Vol. 45, 1/18/80, pp 3758, para. 812.150;  
ASHP Guidelines for the Use of Investigational Drugs in Organized Health Care Settings; Amer. J. Hosp. Pharm., 1991, 48:315

**VII. RESCISSION:**

Pharmacy Policy and Procedures, Section #55, dated 8/02/04

**VIII. CONCURRENCES:** Endorsed by the Research & Development Committee

**IX. FOLLOW-UP RESPONSIBILITY:** Chief, Pharmacy Service