FAST FACTS

5.1 - Investigational Drugs for Human Use

Main Changes/Updates:

- **This policy provides an overview of the procedures and responsibilities of the investigational drug division of the pharmacy department, as well as related responsibilities of principle investigators and the IRB analysts.**
- **Still followed 8/2019 – E.W.**

1. PURPOSE:

The purpose of this policy is to delineate policies and procedures relating to the safe handling, dispensing, utilization and disposition of investigational drugs at the VA Portland Health Care System.

2. SCOPE:

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 Supervisor to the investigator or another Pharmacy.

DEFINITIONS:

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.)

3. RESPONSIBILITIES:

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 Supervisor or designee** is responsible for the integrity, security, and accountability of investigational drugs maintained within the pharmacy. Specific responsibilities also include the following:
   1. Resolving any identified discrepancies in inventory, documentation, and for ensuring that pharmacy employees follow the procedures for dispensing of investigational medications.
   2. Following procedures detailed in the PVAMC IRB Standard Operating Procedures with regard to FDA and Pharmacy Benefits Management Warnings.

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.
6. Complying with all VA regulations, National Committee on Quality Assurance (NCQA) standards, Joint Commission on Accreditation of Health Care Organizations (JCAHO) standards and other Federal regulations regarding investigational drugs.
7. Adhering to all other responsibilities as described in the PVAMC IRB Standard Operating Procedures.

E. The **IRB Analysts** 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.

4. PROCEDURES:

A. Security and Storage.

1. All Investigational drugs will be maintained in the Research Pharmacy to provide separation from non-investigational drugs.

2. Drugs that are standard of care and that are not provided by the research study sponsors may be stored and dispensed through 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. 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°F. Room temperature medications will be stored between 68 and 77° F with infrequent excursions to 86° F. A temperature log will be maintained with temperatures recorded daily per institutional processes.

5. 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 supply 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. 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 review the signed informed consent to ensure compliance with regulations, and will electronically document this review.
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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 received final initial IRB approval and initial approval from the ACOS/R&D and that IRB approval is current and the study is in active status.

4. If required by protocol, the Research Pharmacist will participate in the randomization process to assign a consented subject to a randomized treatment.

5. The Research Pharmacist will review the study protocol and verify the correct drug and instructions for use. The Research Pharmacist will review the medication profile after receipt of the order to ensure that the subject is not receiving contraindicated medications and will contact the investigator when drug interactions or contraindications are noted.

6. Prescriptions for ambulatory patients will be written by authorized prescribers and filled by the Research Pharmacy 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 computer program. If the drug is to be sent with the study patient upon discharge from the hospital, a prescription will be filled according to Outpatient Pharmacy procedures. Each drug sent to the ward will have a bar code attached so that it may be administered through utilization of bar code scanning and verification program.

8. If the patient is receiving an investigational agent as part of an IRB-approved protocol from another institution, and the attending VAPORHCS physician determines it is in the best interests of the patient to continue the investigational drug, the Research Pharmacist will obtain and enter the Investigational Drug Information Record into the research patient's electronic record and enter the drug into the drug database. 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 to aid in administration. Data will not be collected while the investigational medication is administered during hospitalization. However, if it is determined that data is to be collected while investigational drug is administered, the protocol must be reviewed and approved by the PVAMC IRB and R and D Committees. The local investigator is responsible for ensuring all pertinent documents are submitted, approved and all applicable regulations are followed.

9. The pharmacist will dispense the Investigational drugs in accordance with study protocol VA Portland Health Care System 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.,. Additional documentation required by study sponsors will also be completed and maintained.

11. The Investigational Drug Accountability Record will include at minimum:
    a. Name of drug
    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)
    g. Date of final approval by the IRB and R&D Committee
    h. Name of authorized prescriber writing the prescription
    i. Name of patient receiving the drug
    j. Serial Number of the Prescription (prescription number for outpatient prescriptions only)

k. Quantity dispensed and
l. 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 electronic record .
13. Research Pharmacy staff will follow USP Guidelines and Good Clinical Practices when compounding of investigational medications. Research Pharmacy staff will be trained on the usage of compounding equipment and processes of documentation as described in the Research Pharmacy Compounding Policy and Procedure.

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 or sponsor.

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 Record 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.

5. Any excess stock not returned to the manufacturer will be disposed of in a bio-hazardous waste bin and sealed prior to leaving the pharmacy. This is sealed in another bio-hazardous waste box and removed by Facilities Management. The sealed box is escorted to the incineration site and destruction is witnessed by a Medical Center representative.

E. Records

1. Electronic versions of study protocols (original and all updated versions) will be maintained in a study specific folder on the Research Pharmacy network drive. This secure, password protected network drive is located behind the VA firewall and is only available to designated Research Pharmacy staff. At the pharmacists' discretion, certain sections of the protocol will be printed and filed in a study specific binder for quick reference by research pharmacy staff 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 Dispensing Record to be created by Research Pharmacists. This will include summary information on the protocol, dosing and preparation instructions, drug disposal and other details to

assist research pharmacy staff on specific procedures. When needed, this document will be shared with outpatient or inpatient pharmacy staff.

c. Investigational Drug Accountability Record. Electronic copies of drug accountability record will be stored on the Research Pharmacy network drive under the study specific folder.

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.
3. Upon study closure, research pharmacy staff will follow archiving procedures as outlined in Research Pharmacy Archiving Policy. Original shipping and inventory records are given to Principal Investigator and electronic copies will be maintained in Research Pharmacy network drive.

F. Quality Assurance Monitors

The Research Pharmacist for investigational drug program will conduct an audit quarterly to assure compliance with regulations, standards and policies. Reported deviations from regulations and policies will be documented and sent to appropriate oversight committees and personnel

5. FOLLOW-UP RESPONSIBILITY:

6. EXPIRATION DATE: August 2022

7. APPROVING OFFICIAL: Chief, Pharmacy Service

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Signature Date

8. REFERENCES:

i. VAHandbook 1200.05 October 15, 2010.
ii. VHA Handbook 1108.04
iii. JCAHO Accreditation Manual for Hospitals, Current Version (MM.7.40)
iv. Federal Register, Vol. 45, 1/18/80, pp 3758, para. 812.150;American Society of Health-Systems Pharmacists. ASHP Guidelines on Clinical Drug Research. Am J Health-Syst Phar. 1998:55:369-76
v. NCQA Standards version 2.1
vi. FDA Guidance Document *Use of Investigational Products when Subjects Enter a Second Institution-Information Sheet 1/1998..*

9. RESCISSION: Pharmacy Operations Manual, Section N