

Department of Veterans Affairs  
Harry S. Truman Memorial Veterans' Hospital  
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Columbia, MO 65201

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## **INVESTIGATIONAL DRUGS**

1. **PURPOSE:** To establish policies and procedures governing the use of investigational new drugs (IND) at this Medical Center. To establish guidelines for the proper processing and dispensing of investigational drugs.

2. **POLICY:** Investigational new drugs for human use will be stored and dispensed through the Pharmacy Section at this Medical Center (except radioactive products), in accordance with all applicable federal laws and regulations and Veterans Health Administration (VHA) Handbook 1108 series. The Truman VA Pharmacy & Therapeutics Committee delegates all investigational drug protocol reviews required by VA Handbook 1108.08. The University of Missouri Health Sciences Institutional Review Board (HS-IRB) or the VA Central Institutional Review Board (IRB) and the VA Research and Development (R&D) Committees will review and must approve all protocols involving INDs, except as noted below for emergencies. The Food and Drug Administration (FDA) regulations CFR 56.102(d), 21 CFR 56.104(c) for the protection of human subjects and patients allow for an investigational drug or device to be used in emergency situations without prior HS-IRB approval. Emergency use is defined as the use of a test article (e.g., investigational drug or biologic) on a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is insufficient time to obtain HS-IRB approval. In this context, one time use of an IND for terminally ill patients, for emergency, and/or humanitarian use may be approved by the Chair of R&D, Chair of Pharmacy and Therapeutics (P&T) Committee, or the Chief of Staff (COS) without prior approval of the HS-IRB, or R&D Committee.

3. **DEFINITIONS:**

a. Investigational drugs are drugs in clinical stages of evaluation that have not been approved by the Food and Drug Administration (FDA) for general use and are not available for distribution through regular channels of interstate commerce.

b. An investigational drug is also a drug that has been approved for general use but has been placed in an Investigational Protocol, approved by the HS-IRB or VA Central IRB, to determine its effectiveness for new unapproved indications or in combination with another investigational agent.

c. An investigational drug is also a drug that has been approved for general use but has been placed in an HS-IRB or VA Central IRB approved Behavioral Sciences research protocol to determine its effectiveness for its approved intention and for the intent of being used in combination with an investigational non-pharmaceutical intervention.

d. A medication error is broadly defined as a dose of medication that deviates from the physician's order as written in the patient's medical record or as written on an outpatient prescription form. A medication error may also occur when the dose or process

deviates from the approved investigational protocol or from hospital policies and procedures for administering and dispensing medications.

4. **PROCEDURE:**

a. Approval of investigational drugs.

(1) Application for use of an IND, as part of an HS-IRB or VA Central IRB approved research study, must be made to the R&D Committee and HS-IRB or VA Central IRB using research application forms. Prior to R&D committee approval, the Principal Investigator will provide Pharmacy Service with VA Form 10-9012 to review. The 10-9012 will provide the Pharmacy Section with the names of those authorized to prescribe the drug(s). A copy of the research protocol and all IRB documentation (including IRB approval letter) will be furnished to the Pharmacy Section by the Research Office during the administrative review process. Only after review by the Pharmacy Section will the protocol be sent for review by the R&D Committee. Receipt by the Pharmacy Service of an R&D approval letter and VA Form 10-9012(s) signed and dated by the HS-IRB or VA Central IRB Chair or Member and R&D Chair from Research Service will denote approval of all required committees for the initiation of the research.

(2) Emergency and/or humanitarian use of an investigational new drug may be deemed exempt from review by the HS-IRB and R&D Committee for patients outside an approved research protocol provided all the following conditions are met:

(a) The subject is facing a life-threatening condition for which there is no standard acceptable treatment available.

(b) There is insufficient time to obtain HS-IRB or VA Central IRB approval prior to administration.

(c) The physician has legitimate access to a test article and believes there is reasonable likelihood that its use may be advantageous to the life-threatening condition.

(d) Emergency use of an investigational new drug must meet the requirements for an exception to informed consent. Exceptions to the requirement for informed consent can be found at the HS-IRB website (<http://research.missouri.edu/hsirb/policies.htm>).

(e) Written notification will be provided to the HS-IRB or VA Central IRB and the R&D Committee within five (5) days of the test article(s) administration.

(3) If possible, prior to the administration of a test article, the investigator must notify the HS-IRB Chair or the HS-IRB Administrative Office of the request for Emergency Use Approval and the intention to use an investigational test article. If the HS-IRB or Chair or HS-IRB Administrative Office cannot be contacted in advance, the investigator must notify the R&D Committee Chair, P&T Committee Chair, or COS to administer the drug as long as the individual notified reviews whether the six (6) conditions are met allowing the use of a test article without prior HS-IRB review. If the conditions are met, the reviewer can grant permission for the use to take place; otherwise, the reviewer must indicate that the use cannot take place.

(4) The following information must be provided when requesting emergency approval:

(a) Patient's name, social security number, and a brief medical history (including diagnosis) of the patient.

(b) Treatment for the life-threatening condition that has been attempted to date and results.

(c) The patient's prognosis.

(d) The principal investigator's rationale for intent to use the IND without prior HS-IRB review, including expected results.

(e) The IND name, IND number assigned by the FDA, and the principal investigators name and VA title.

(f) Literature reference source and authorized source of drug.

(g) The Chief, Pharmacy Service, must be provided the drug protocol, a copy of the signed approval letter, and a copy of the signed informed consent form before the IND can be dispensed.

(h) The emergency use of an IND must be reported by the principal investigator within five (5) working days to the HS-IRB and to the Associate Chief of Staff for Research and Development (ACOS/R&D).

(5) The HS-IRB and the R&D Committee will review each emergency use of a test article to determine whether the conditions allowing such use were met. If the conditions were not met, the matter will be handled under the non-compliance policy.

a. Custody and Dispensing of Investigational Drugs.

(1) Investigational drugs will be maintained in the Pharmacy by the Investigational Pharmacist, with the exception of radioactive agents.

(2) Drug accountability will be recorded on forms provided by the study sponsor and/or the Investigational Drug Dispensing Record form. These forms will be maintained by the Investigational Pharmacist in a protocol file. A record of each drug stored and dispensed will include the following:

(a) Name of drug, dosage form, and strength.

(b) Source of the drug (manufacturer, sponsor, and strength).

(c) HS-IRB/VA Central IRB/R&D Committee approved protocol (via approval letters and VA Forms 10-1223 [if study was IRB approved prior to March 31, 2011] and 10-9012(s)), HS-IRB/VA Central IRB number, approval dates (HS-IRB or VA Central IRB and R&D Committee), date protocol received, initial/continuing review dates of approval, and all versions of HS-IRB or VA Central IRB approved consents and the corresponding effective dates, and the Investigational Brochure.

(d) Amount and date received from source (including inventory notes).

(e) Expiration date, if any, for each prescription.

(f) Lot or control number, expiration, or retest date for each prescription.

Pharmacy will contact the study sponsor for retest date if the expiration date is not provided on the drug package or shipment records, and will document in the dispensing record the name and contact information for the person supplying the information. If the sponsor is unable to provide the information pursuant to their policies, (i.e., blinding of study drugs or continuous stability testing), the Investigational Pharmacist will request a statement to be filed in the dispensing record from a representative of the sponsor, the manufacturer or the distributor that attests that the expiration or retest dates are monitored centrally, and dispensing sites will be notified prior to the assignment or dispensing of any drugs that are approaching an expiration date.

(g) Date of authority to use.

(h) Serial number and date of prescription dispensed.

(i) Patient's name and hospital identification number for each Prescription.

(j) Notation confirming pharmacist's acknowledgement of appropriate consent form with proper signatures for each prescription.

(k) Amount dispensed for each prescription and remaining balance.

(l) Name of authorized prescriber(s) and initials of dispensing pharmacist for each prescription.

(3) Only physicians or dentists specifically authorized by the HS-IRB or VA Central IRB on VA Form 10-9012 (Investigational Drug Information Record) can prescribe an investigational drug.

(4) The Investigational Pharmacist will be responsible for the custody of all drugs involved in protocols approved by the HS-IRB or VA Central IRB and the R&D Committee, except this policy does not apply to drugs used within research laboratories for non-human purposes.

(5) Investigational drugs will be kept under double lock, separate from other pharmacy drug stocks, and dispensed only upon prescription of the provider specifically authorized to prescribe the drug. The prescription must be dated, signed, and bear the patient's name, actual quantities prescribed, and directions for use. Additionally, a copy of the patient's signed Informed Consent form must be contained within the Investigational Pharmacist's records and medical record. Upon request, the Investigational Pharmacist will provide a complete accounting to the HS-IRB or VA Central IRB for each protocol's Continuing Review or for audit purposes, including the names of all patients who received study drug(s) and the date the patient signed the consent form.

(6) A special investigational drug label, in addition to information required by law on prescription labels, will include the following legend, "FOR INVESTIGATIONAL USE ONLY," and other auxiliary, caution, or warning labels as indicated.

(7) Additionally, a file containing the approved protocol with amendments, the original signed Investigational Drug Information Record(s) (VA Form 10-9012), the Investigator Brochure, and copies of all subjects' signed Informed Consent forms (VA Form 10-1086) will be maintained for all active drug studies.

(8) The final entry in each study record will be the date of disposition of any remaining drug after the completion of the study. Records will be maintained using the most restrictive requirements, based on VHA Records Schedule 10-1 or FDA. The sponsor must authorize records to be destroyed prior to final destruction. Contact with the study sponsor will be made to determine disposition of unused study drug(s). Drugs authorized by the sponsor to be destroyed will be sent to a contracted vendor for destruction of drugs by methods which are in compliance with hazardous waste handling.

(9) Following receipt and review of informed consent documentation, the primary Investigational Pharmacist will dispense investigational drugs, when feasible. Other designated pharmacists who have completed training on investigational pharmacy policies and procedures may perform this function in the absence of the primary Investigational Pharmacist. Drugs that require special handling (example: chemotherapy) will be prepared by the Chemotherapy Pharmacist in the Pharmacy Service after all the required documentation has been received by the Investigational Pharmacist and the necessary information relayed to the Chemotherapy Pharmacist.

a. Consent for Use. The investigator will fully inform the patient about the study or use of investigational drugs, including possible known adverse reactions. The investigator will secure consent from the patient (or his/her legally authorized representative) by signatures on VA Form 10-1086. The signed/dated forms will become a permanent part of the patient's records (investigator and CPRS). The investigator or study coordinator will forward to the Pharmacy Section a copy of the signed consent form for each new patient. The pharmacy will not dispense an investigational drug until a copy of the consent form is received, with authorized signatures.

b. Administration of Investigational Drugs. The principal investigator will complete the Investigational Drug Information Record (VA Form 10-9012), with the original being retained in the pharmacy. (The Investigator will place the contents of VA Form 10-9012(s) in the patient's chart through the completion of a study specific research flagging note as an information sheet for the professional nurse responsible for the administration of the drug.)

c. Summary/Termination of Protocol. All records will be made available to the investigators and other authorized personnel while taking into consideration patient privacy rights.

d. Disposition of remaining IND stock. Unused stock will be returned or disposed of in accordance with the clinical trial protocol, FDA guidelines, Federal/State laws, and VA policy.

e. A Patient Incident Report (PIR), VA Form 10-54, 589A4 (revised 9/06), must be completed for each medication error, sentinel event, or close call to identify underlying causes and systems changes needed to reduce the likelihood of recurrence. The Patient incident form is located on the hospital intranet site and once completed is submitted to Performance Improvement via the VISTA email system. The employee who witnesses or who is the first to become aware of the medication event will initiate the incident report.

10) In instances when it is impractical for the drug to be dispensed from Pharmacy due to the immediacy of need (e.g. Surgery or Cath Lab) or lack of a Pharmacy at the location (e.g. outpatient clinics), the Chief, Pharmacy Service may delegate in writing to have investigational drug stored outside of the Pharmacy Service. In this instance the PI will sign a Delegation of Custody Agreement that outlines his/her responsibilities for investigational drug, as outlined in Handbook 1108.04. This delegation of custody document should adhere to the following requirements:

a. It must identify the location of the drug and the name of the investigator responsible for the storage and dispensing; be signed by the PI; and maintained in the pharmacy.

b. On a monthly basis, the Investigational Drug Pharmacist must verify by written audit that the storage location meets all security and storage requirements. Access to this storage area is to be restricted to appropriate study personnel only.

c. When investigational drugs are stored outside of the pharmacy, a real-time documentation of all drugs dispensed is required. This dispensing log provides a method for Pharmacy Service to inspect the investigational drug inventory and track all dispensing from the storage area.

d. The PI must comply with all dispensing and documentation requirements and these records must be made accessible to the investigational drug pharmacist when requested.

5. **REFERENCES:**

VHA Handbooks 1200.05, 1108.08, 1108.04, 1108.1, 1108.2, 1108.5, 1108.6, and 1108.7. 21 CFR 1300 series, 21 CFR 1400 series, and 21 CFR part 56 series.

6. **RECISSION:** HPM 589A4-123, Investigational Drugs, dated April 29, 2010.

APPROVED:

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