Investigational Drug Service Pharmacy

SOP 119-10

North Florida/South Georgia VHS
Gainesville, FL 32608

Service Line(s):
Research
Pharmacy

Signatory Authority:
Associate Chief of Staff, Research
Chair, Research & Development
Chief, Pharmacy

Effective Date:
March 9, 2022

Recertification Date:
March 9, 2027

Responsible Owner:
Pharmacy Service

1. PURPOSE AND AUTHORITY

a. The purpose of this standard operating procedure (SOP) is to delineate the procedures pertaining to the daily operations of the North Florida/South Georgia Veterans Health System (NF/SG VHS) Investigational Drug Service Pharmacies.

b. This SOP sets forth mandatory procedures and processes to supplement Veterans Health Administration Handbook 1108.04, Investigational Drugs and Supplies, dated February 29, 2012.

2. PROCEDURES

a. **Initial Protocol Review.**

(1) All clinical research protocols involving drugs are to be sent to the Pharmacist of Record for review and consideration prior to finalizing the study budget. A feasibility questionnaire must be completed at the time of the submission. If a protocol is not available at the time of the submission, the feasibility questionnaire must be provided, and the protocol will be submitted when it is available.

(2) Pharmacist of Record will review the protocol/questionnaire document for any details that affect NFSG Pharmacy Service and submit an Investigational Drug Service pharmacy feasibility report to the Principal Investigator or delegate. The report will include, but is not limited to:

(a) Protocol required Investigational Drug Service Pharmacy staffing needs outside of normal Investigational Drug Service Pharmacy business hours.

(b) Supplies/drugs that are not provided by the study sponsor.

(c) Legal/regulatory issues related to pharmacy operations.

(d) Current study workload regarding number of active protocols and current Investigational Drug Service Pharmacy staffing.

(e) Investigational Drug Service Pharmacy physical resources/equipment.

(3) Principal Investigator will provide any requested documentation to aid in Investigational Drug Service Pharmacy feasibility decisions.

(4) Investigational Drug Service Pharmacy staff will provide an estimate of the pharmacy charges for drug cost and services (based on the standard fee schedule), which will be reimbursed by the study sponsor. If the Principal Investigator requests a reduction/waiver of Investigational Drug Service Pharmacy fees, a written justification must be provided to the Pharmacist of Record for consideration. The Pharmacist of Record will provide a written response to the Principal Investigator.

(5) The Pharmacist of Record must receive a prepared Investigational Drug Information Record (IDIR/VA Form 10-9012) from the study team before Institutional Review Board (IRB) approval (if required). The study team will be responsible for obtaining needed signatures after Pharmacist of Record approval.

b. **Ordering Investigational Drug from the Study Sponsor.**

(1) The Principal Investigator/study team will provide all required documents to Investigational Drug Service Pharmacy staff before ordering study drug.

(2) The study team is responsible for ordering drug unless arrangements with Investigational Drug Service Pharmacy are made.

(3) The Principal Investigator/study team will order all drugs to be shipped directly to the Investigational Drug Service Pharmacy care of the Pharmacist of Record.

c. **Receipt and Storage of Investigational Drug.**

(1) Investigational Drug Service Pharmacy will receive and store investigational product promptly according to study sponsor requirements.

(2) Drug shipments designated as hazardous drugs must be received in clearly marked packaging. All receiving and storage of hazardous drugs will follow the NF/SG Standard Operating Procedure: Hazardous Drug Safe Handling Practices or equivalent standard operating procedures.

(3) Investigational Drug Service Pharmacy staff will review the investigational product shipment contents and confirm correct shipment, with the Pharmacist of Record signing the packing slip. These records will be stored in the pharmacy study records.

(4) The study accountability log/inventory will be updated to reflect the new supply of investigational product. Investigational Drug Service Pharmacy staff will complete study required electronic receipt records when required.

(5) Investigational Drug Service Pharmacy staff will quarantine any drug that arrives damaged or outside of protocol temperature requirements and report this to the sponsor immediately. The investigational product will be stored under the usual required conditions until the sponsor adjudicates the situation.

d. **Storage and Inventory of Investigational Product**

(1) All investigational products will be stored based on protocol specific requirements.

(2) Temperature monitoring will be maintained using both manual temperature logs and an overlapping continual electronic monitoring system.

(3) Investigational Drug Service Pharmacy staff will perform an inventory of all pharmaceutical investigational product monthly at regularly spaced intervals. The stocked quantity will be compared to the quantity in the continuous inventory column of the accountability log. Discrepancies with quantity will be reported to the Principal Investigator and the study sponsor immediately.

(4) Investigational Drug Service Pharmacy staff checks all investigational product expiration dates during the monthly inventory audit.

e. **Accountability for Investigational Product.**

(1) Investigational Drug Service Pharmacy staff will maintain a continuous inventory for all investigational product in the pharmacy. Lot number and expiration dates will be noted. If absent on the investigational product, the Principal Investigator is responsible for obtaining this information from the sponsor or providing documentation that this information is being centrally monitored by the sponsor.

(2) Investigational Drug Service Pharmacy staff will complete additional sponsor provided accountability logs if required by the sponsor.

(3) Pharmacist of Record will report any discrepancies in the accountability log to the sponsor immediately.

f. **Dispensing of Investigational Product.**

(1) Orders for Investigational Drugs:

(a) Orders will be accepted during Investigational Drug Service Pharmacy business hours, Monday-Friday, 8:00 am to 4:00 pm, excluding federal holidays.

(b) The Clinical Research Pharmacist will verify that the informed consent form (ICF) has been signed before the first investigational product dispensing. No exceptions unless approved by Associate Chief of Staff (ACOS) or Acting ACOS under FDA Emergency Use protocol.

(c) The Principal Investigator/study team must relay the participant specific identification number to the Clinical Research Pharmacist. This number cannot be reassigned to another subject.

(d) Only the Principal Investigator or Co-Investigator, may complete or modify investigational product orders for a clinical participant. Eligible investigators must be listed on the study delegation log and have authority to prescribe within the NF/SG VHS. The Principal Investigator/study team is responsible for providing all updated study documents needed to determine eligibility to Investigational Drug Service Pharmacy as they become available. Orders written by providers not on the study delegation log will not be filled.

(e) Investigators will prescribe using VA Form 10-2577F or the approved Investigational Drug Service Pharmacy electronic prescription blank. Medications for non-clinical protocols must be recorded on the Research Medication Supply Order form. All controlled substance orders must be on VA Form 10-2577F.

(2) Verification of Investigational Product for Dispensing:

(a) All investigational product dispensing will follow federal law, study protocol, and VA policies and procedures.

(b) Investigators will include the following in addition to the legal requirements of a prescription when ordering investigational product:

1 Patient identification number (protocol specific)

2 “INV” drug designation number

3 Protocol number

4 Treatment assignment (e.g., SID, or kit number, if applicable)

5 Randomization code (if applicable)

6 Protocol specific requirements (such as Body Surface Area or height and weight of subject)

(c) Clinical Research Pharmacist will review inclusion/exclusion criteria, protocol prohibited medications, completion of Research W(t) note template (or equivalent) by study team and signed informed consent form (ICF) for all new study subjects in addition to the standard pharmacist dispensing procedures.

(d) Investigators/study coordinators will report to the Pharmacy Administration office to pick up outpatient and inpatient medications for study participants following the chain of custody procedure. Investigational Drug Service Pharmacy staff will come to the office and meet with the study staff. If a study protocol designates blinded and unblinded staff, blinded staff are restricted from the Investigational Drug Service Pharmacy at any time when accidental unblinding could occur.

(e) Investigational Drug Service Pharmacy will only dispense drugs that are dispensed under the direction of a research protocol.

(3) Preparation of Investigational Product

(a) Investigational Drug Service Pharmacy staff will prepare investigational product following all applicable pharmacy quality standards, laws, and VA policy. The protocol preparation procedure will also be followed. Discrepancies between protocol preparation procedures and pharmacy standard, law, or policy must be addressed by the Principal Investigator before participant enrollment.

(b) Investigational Drug Service Pharmacy staff will follow United States Pharmacopeia 797/800/795 or other relevant standards where applicable to drug preparation.

(4) Labeling of Investigational Product:

(a) All investigational product dispensed from the Investigational Drug Service Pharmacy must be appropriately labeled containing:

1 Subject name

2 Drug name (including the “INV” prefix of the drug name)

3 Drug strength

4 Dosage

5 Route of administration

6 Quantity

7 Expiration date or beyond use date (if provided by manufacturer/sponsor)

8 Ordering investigator’s name

9 “Caution: New drug limited by federal law to investigational use” labeling

10 Unique study participant number

11 Applicable auxiliary labeling

12 VA prescription number

13 Pertinent manufacturer labeling will not be covered (ex. protocol number)

14 Any additional information required by the study protocol

(b) The Clinical Research Pharmacist will assure that all labeling is compatible with maintaining the study blind when applicable.

(c) The Clinical Research Pharmacist will obscure or remove any labeling that was placed by third-party pharmacy dispensing pharmacies prior to VA Investigational Drug Service Pharmacy verification/dispensing. This does not apply to study labeling from the drug manufacturer, except when directed by the protocol.

(5) Inpatient Dispensing for Subjects Enrolled in Inpatient Administration Protocols:

(a) Clinical Research Pharmacist will generate an inpatient medication label containing a Bar Coded Medication Administration barcode based on the prescription order from the investigator.

(b) Clinical Research Pharmacist will screen print the CPRS order for filing in the study records.

(c) Investigational Drug Service Pharmacy staff will coordinate pharmacy handling and blinding procedures described in the protocol.

(d) Study team must observe Investigational Drug Service Pharmacy hours of service unless prior arrangements have been agreed upon by Pharmacy Services.

(6) Dispensing to Subjects Enrolled in Outpatient Protocols While Admitted to the Hospital:

(a) Investigational Drug Service Pharmacy staff will alert the study coordinator when made aware of a research participant’s admission to the hospital.

(b) Study coordinator will notify the Principal Investigator of the hospital admission.

(c) The Principal Investigator will contact the subject’s attending physician-in-charge of medical care and discuss the condition of the patient, the study protocol, and the study drug. They will determine whether it is appropriate to continue the study drug. The Principal Investigator or the attending physician-in-charge of medical care will document the pertinent details of the discussion in the clinical record including the decision whether to continue IP. If the decision is to continue study drug, the Principal Investigator will write an order and present it to the Clinical Research Pharmacist. This procedure must be completed by the investigator promptly as the research pharmacist cannot dispense or repackage any investigational drug for inpatient use until all the above steps are complete and the Clinical Research Pharmacist has been notified.

(d) Clinical Research Pharmacist will determine if patient has their home supply of study drug at the hospital. If the study medication is brought to the hospital, the Clinical Research Pharmacist will receive the home supply of medication from the Study Coordinator for temporary storage in the Investigational Drug Service Pharmacy office during the subject's hospital admission.

e) The Clinical Research Pharmacist will create an inpatient order for the study drug upon receiving the investigator's written or electronic order if the home supply is available. Otherwise, Principal Investigator will issue a new order for a supply of study drug, dispensed through the research pharmacy, to be continued during hospitalization. The study coordinator will perform any necessary randomization procedures with the study sponsor, if needed, to issue a new investigational product supply.

f) Investigational Drug Service Pharmacy staff will dispense daily doses (or weekend/holiday doses) to the medical wards for administration as needed. The Investigational Drug Service Pharmacy staff will document all investigational product sent to the hospital ward on an accountability log and will return any home supply of investigational product to the patient at hospital discharge. Remaining drug from an additional supply prescription written by the Principal Investigator will be quarantined for destruction after discharge unless the protocol or Principal Investigator states otherwise.

(7) Dispensing and Storage of Investigational Chemotherapy:

(a) Investigational chemotherapy orders will be processed by the Clinical Research Pharmacist, but all compounding and dispensing portions will be performed by a clinical oncology pharmacist.

(b) Investigational Drug Service Pharmacy will store chemotherapeutic drugs. Hazardous investigational product that requires negative-pressure storage will be stored in the oncology area.

g. **Controlled Substances**

(1) Investigational Drug Service Pharmacy and research study staff will handle controlled substances in accordance with federal law, study protocol, and VA directives, policies, and procedures.

h. **Investigational Product Handling and Chain of Custody**

(1) Investigational Drug Service Pharmacy staff will ensure that the protocol requirements regarding investigational product handling are executed to assure investigational product quality.

(2) Investigational Drug Service Pharmacy staff will ensure that handling of investigational product follows the study's protocol blinding procedures (if applicable) while in the possession of the pharmacy.

(3) Pharmacist of Record will ensure that the chain of custody procedure will provide a smooth and well documented transfer of investigational product from arrival at the Investigational Drug Service pharmacy to the study subject.

(4) Investigational Drug Service Pharmacy staff will document the arrival of investigational product. The Principal Investigator, Co-Investigator or Study Coordinator only, will pick up investigational product from the Investigational Drug Service Pharmacy. Principal Investigator/Co-Investigator/Study Coordinator will sign for receipt when taking possession of dispensed investigational product.

(5) Principal Investigator/Study Coordinator will complete VA form 10-2638 for all controlled substance investigational product transferred to them and then to the subject, including administration. The form is returned to the Investigational Drug Service Pharmacy when complete and reviewed by the Clinical Research Pharmacist.

i. **Drug Administration by Non-Research Personnel**

(1) Registered nurses not on the study delegation log may administer medications when the needed skills are in their usual skill set unless prohibited by the study protocol.

(2) The Principal Investigator/Study Coordinator must provide any additional training that is needed to non-research registered nurses.

j. **Returning Patient Medications**

(1) The study coordinator will return all medication or empty packaging to the Investigational Drug Service Pharmacy when returned from a research subject. The pharmacy staff will inventory the returns and file them in quarantine, away from unused/new investigational product.

(2) Investigational Drug Service Pharmacy staff will not reissue sequestered investigational product that has been previously dispensed to another subject.

k. **Extended Investigational Product Expiration Dates**

(1) The study sponsor will notify the Investigational Drug Service Pharmacy of any extension in the expiration dates of investigational product. If this occurs, the new investigational product expiration date will be entered into the accountability log.

l. **Study Closure**

(1) The Principal Investigator/study team will notify the Investigational Drug Service Pharmacy of study closure with a formal study closure letter from the study sponsor. Until the formal closure letter is received, Investigational Drug Service Pharmacy will continue IDS pharmacy operations for the study. One exception exists where pharmacy will have no further role or auditing in the study and the integrity of the

study cannot be affected by pharmacy involvement. In this case, the study sponsor may authorize PHARMACY closure prior to full study closure in writing. The Pharmacist of Record will consider requests for investigational pharmacy closure of the study on a case-by-case basis. Any pharmacy records must be able to be transferred to the Principal Investigator at the time of pharmacy closure.

(2) The study coordinator will return any remaining investigational product to the Investigational Drug Service Pharmacy for final accountability/final disposition before formal closure.

(3) The Investigational Drug Service Pharmacy will compile all pharmacy records for the study at closure, combine into one folder/binder/electronic file and notify the Principal Investigator that the pharmacy records are ready for transfer. The Principal Investigator will report to the Investigational Drug Service Pharmacy and sign for receipt of pharmacy study records. The Principal Investigator will combine the pharmacy records with the study records for storage in the appropriate format.

(4) Any study records found to be stored in the Investigational Drug Service Pharmacy after the closure date will be returned to the Principal Investigator as soon as possible.

(5) The Investigational Drug Service Pharmacy will not be responsible for storage of study documents beyond the date that the completed records are released to the protocol's Principal Investigator.

m. **Final Medication Disposition**

(1) The study sponsor will authorize the destruction/disposal of any investigational product in writing to the Pharmacist of Record, who will sign VA form 2237 with a second approved pharmacist before the return or destruction of investigational product.

(2) The study sponsor will request onsite destruction or return of unused investigational product to the study sponsor site. Investigational Drug Service Pharmacy staff will utilize a sealed sharps container as a standard form of investigational product containment for destruction onsite unless other means are available and preferred. The study sponsor will provide prepaid shipping labels or reimbursement for shipping costs for investigational product if return to the sponsor for destruction is required.

n. **Code/Blind-Break Protocol**

(1) All staff involved in a blinded protocol will make every effort to protect the blinding of a study protocol from accidental unblinding.

(2) The physician directly responsible for medical care of a patient may request to break a study blind in an emergent medical situation. The physician will make every

effort to contact the Principal Investigator, Co-Investigator, Study Coordinator, or Clinical Research Pharmacist before breaking the blind. The Principal Investigator will discuss the case with the treating physician, and they will determine whether to proceed with the code break. The Principal Investigator or treating physician will contact the Clinical Research Pharmacist to notify them of the decision.

(3) The physician directly responsible for a patient's medical care may proceed with the code-break procedure in a medical emergency without the agreement of the Principal Investigator, as previously approved by the ACOS. The treating physician will attempt to contact the Clinical Research Pharmacist first. If the Clinical Research Pharmacist is not available, the covering pharmacist should attempt to reach the Pharmacy Research Manager. The Clinical Research Pharmacist will later notify the appropriate study personnel of the unblinding.

(4) The Principal Investigator may be required to break the blind of some studies where only the sponsor holds the blinding information. In these cases, neither the Clinical Research Pharmacist nor study coordinators will have access to the blinding codes. A treating physician may contact the study sponsor if needed in a crisis if the Principal Investigator cannot be reached.

(5) Any staff breaking the blinding code other than the Clinical Research Pharmacist will notify the Clinical Research Pharmacist within one working day of the code break by email and/in person/phone contact.

o. **Record Maintenance for Investigational Drug Protocols**

(1) Investigational Drug Service Pharmacy staff will store all study records in clearly labeled, study specific binders.

(2) Investigational Drug Service Pharmacy staff will record study records in permanent ink and avoid excessive striking through or correction fluid. Original study documents will not be restarted or discarded due to an error.

(3) Investigational Drug Service Pharmacy staff will not destroy any study records until written authorization is received from the study sponsor.

(4) The Principal Investigator will take possession of all study records after formal study closure.

p. **Quality Control/Quality Assurance Plan**

(1) The Pharmacist of Record is responsible for quality control in day-to-day activities in the Investigational Drug Service Pharmacy. Pharmacist of Record will report any errors to the NFSG VHS Medication Safety Committee and review process improvement recommendations from the committee.

q. **Investigational Drug Supplies for Non-Clinical Research Protocols**

(1) Investigational Drug Service Pharmacy will record dispensing and pharmacy cost documentation for each non-clinical investigator and report through the proper channels quarterly for reimbursement.

(2) Investigators will utilize a completed Research Medication Supply Order Form to request investigational drugs. The electronic form is available from the Investigational Drug Service Pharmacy staff upon request at (352) 548-3051. Orders can only be authorized by personnel involved in the study protocol who are also authorized to order the requested medication. The Clinical Research Pharmacist will verify all orders for accuracy before dispensing to study personnel.

r. **Emergency Processing of Research Medications**

(1) The Principal Investigator will arrange an alternate investigator to sign research prescriptions in their absence. The Clinical Research Pharmacist will accept a faxed, verbal, telephone order only in a life-threatening situation or where interruption of therapy would be detrimental to the subject's health. If this occurs, a study investigator will present a written prescription within five working days to replace the order.

s. **Non-VA Issued Investigational Drugs during Inpatient Admissions**

(1) The Clinical Research Pharmacist will notify the NF/SG VHS inpatient physician who will contact the Principal Investigator of the study and determine whether continuation of study drug is appropriate followed by writing a medical record note of the decision. The inpatient physician will request a copy of the subject's signed informed consent for the Investigational Drug Service pharmacy. The Clinical Research Pharmacist will enter a "Z-MISC" drug entry into the medical record for the study medication. The Clinical Research Pharmacist will dispense the medication following the procedures for *Dispensing to Subjects Enrolled in Outpatient Protocols While Admitted to the Hospital,* seen above. The medical team pharmacist will assure the remainder of the study medication is returned to the subject on hospital discharge. The inpatient physician will contact the Principal Investigator for further instructions if the subject does not have their home supply of investigational product at the hospital.

3. ASSIGNMENT OF RESPONSIBILITIES

a. The Chief, Pharmacy Service is responsible for the Investigational Drug Service pharmacy related duties as dictated by VA Handbook 1108.04

b. Associate Chief of Service, Research Service is responsible for the duties outlined in Handbook 1108.04 with respect to establishing the goals and objectives of the research service and ensuring proper oversight investigational studies within NF/SG VAMC.

4. DEFINITIONS

a. **Clinical Research Pharmacist.** Any pharmacist on a study delegation log who is performing study related duties within the Investigational Drug Service pharmacy.

b. **Controlled Substance.** Any substance that has been designated by the US Drug Enforcement Agency as a controlled substance in schedules C-I through C-V.

c. **Institutional Review Board (IRB).** May refer to a local IRB such as UF IRB-01, a central IRB (CIRB) or a commercial IRB for the purposes of this document.

d. **Investigational Drug Information Record (IDIR) (VA Form 10-9012).** A drug informational sheet containing information about investigational drugs used in a clinical investigational protocol.

e. **Investigational Drug Service Pharmacy** The division of Pharmacy Services responsible for investigational drug dispensing. This includes the Investigational Drug Service Pharmacy office and affiliated staff at the Malcom Randall VA Medical Center or Lake City VA Medical Center.

f. **Investigational Product.** Any drug that is being dispensed under a study protocol's direction.

g. **North Florida/South Georgia Veterans Health System (NF/SG VHS).** The health system for which this operating procedure applies, which includes the Malcom Randall VA Medical Center, Lake City VA Medical Center and all associated OPCs, and CBOCs.

h. **National Institute for Occupational Safety and Health.** The federal entity charged with regulating workplace safety.

i. **Principal Investigator.** The lead investigator for a research study or at a study site in a multicenter trial.

j. **Pharmacist of Record.** The lead pharmacist responsible for the operations of the Investigational Drug Service pharmacy or for a specific study protocol per the study delegation log.

k. **Study Coordinator.** A key member of the study team who is listed on the study's delegation log as a study coordinator.

l. **Study Team.** The clinical team affiliated with a study protocol which includes Principal Investigator, Co-Investigator, and SC. Does not include Investigational Drug Service Pharmacy staff for the purposes of this document.

5. REFERENCES

a. VHA Handbook 1108.04, dated February 29, 2012.

6. REVIEW

This SOP must be reviewed, at minimum, at recertification, and when there are changes to the governing document, VHA Handbook 1108.04.

7. RECERTIFICATION

This SOP is scheduled for recertification on or before January 24, 2027 In the event of contradiction with national policy, the national policy supersedes and controls this document.

8. SIGNATORY AUTHORITY

Keri Justice, Pharm. D.
Chief, Pharmacy NF/SGVHS
Date Approved:

KERI JUSTICE Digitally signed by KERI JUSTICE
Date: 2022.03.14 08:17:54 -04'00'

Joshua F. Yarrow, M.S., Ph.D.
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Date Approved:

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Scott Berceli, M.D., Ph.D.
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