

SOP# HRP 05.01
 Initial Approval Date: 2/14/08

RESEARCH AND INVESTIGATIONAL DRUGS

This SOP, originally approved on 2/14/08, was revised on 4/18/08 and has now undergone changes as summarized below:

Version	2.2	Origin	Version 2.1
Author	Jessica Mendoza		
Reviewed/ Revised by	Jessica Mendoza	Dates Reviewed / Revised	10/14/08
Changes	New content that PI must report study closure to Chief, Pharm Services through the IDP	New Version #	2.2
Approved	10/23/08 Leslie Katzel, R&D Chair	Approved R&D / Dennis Smith	10/23/08
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This amended version (2.2) will be submitted to the HRPOC Subcommittee and the R&D Committee at their next scheduled meetings.

 Leslie Katzel, MD, PhD
 Chair, R&D Committee

 Date

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RESEARCH AND INVESTIGATIONAL DRUGS

OBJECTIVE:

To outline policies and procedures to assure adequate safeguards to protect human research participants and to enhance the quality of the conduct of clinical trials.

SCOPE & POLICY:

All clinical trials (investigational drug, device or interventional studies performed on human subjects) must be carried out by qualified investigators under protocols approved by the VAMHCS Research and Development Committee.

Patients must be given complete information about the study objectives, risks, and benefits, and must give written, informed consent to participate in the study.

The principal investigator will obtain University of Maryland Baltimore (UMB) IRB and VAMHCS Research and Development Committee approval prior to the initiation of any investigational drug protocols within the VAMHCS.

The Chief, Pharmacy Service, the Investigational Drug Service Pharmacist or designee will review all protocols and amendments that involve the administration of drugs for research purposes and will be represented on the VAMHCS R&D Committee and/or on protocol review sub committee(s). The Investigational Drug Service Pharmacist will sign-off on all protocols or amendments prior to initiation of any human research protocols involving investigational research medications.

RESPONSIBILITIES:

1. The VA R&D Coordinator is responsible for:
 - assisting the PI in submission of the required documents for review and approval by the VA R&D Committee and applicable subcommittees;
 - ensuring that committee/subcommittee members receive all necessary documents in order to enable review of the protocols.
2. The Principal Investigator (PI) is responsible for:

- submitting all required documents for review and approval by the VA Pharmacy Service and the VA R&D Committee and applicable subcommittees prior to the initiation of any protocols at the VAMHCS that involve study drugs;
 - ensuring that inpatient nurses receive education and demonstrate competency related to the investigational drug prior to the administration of the study medication;
 - ensuring that a Research Subject Clinical Warning is entered into the electronic medical record (CPRS) per policy. (See SOP HRP 07.01);
 - notifying the Chief, Pharmacy Services, through the Investigational Drug Pharmacist, when a study has closed.
3. The VA R&D Committee is responsible for the final approval of VA protocols, including procedures involving research study drugs.
4. The Investigational Drug Service is responsible for approving the PI's pharmacy plan.

SEE ALSO:

IRB P&P I.5.C

VAMHCS SOP 119-010
VAMHCS Pharmacy SOP
VAMHCS Pharmacy Policy
IDS internal procedure

Emergency Use of Investigational or
Unlicensed Test Articles
Investigational Drug Section (IDS)
Controlled Substance Policy 119-018
Controlled Substance Handling 119-15
“Informed Consent Verification Procedure”

PROCEDURE:

1. The Principal investigator obtains a packet from the VAMHCS R&D Committee Coordinator. The packet currently contains the following forms related to the Investigational Pharmacy. It is possible that forms may change in the future; however these will be “built” into the new IRB protocol management system (“CICERO”) projected for sometime in 2008.
- Clinical Trials Data Sheet (provides information to the VA R&D Committee on VA resource utilization),
 - Research Methods Accountability Form (RMAF) (provides information from the PI to the investigational pharmacist and the VA R&D Committee on drug accountability, dispensing and authorized practitioners who can prescribe investigational medications for the protocol),
 - VA Form 10-9012 (Investigational Drug Information Record),
 - Pharmacy Fee Form (outlines payment to the VA Investigational Drug Service for storage and dispensing of investigational medications).

These forms, among others required for R&D submission, must be completed by the investigator/staff and submitted to the VAMHCS R&D Committee for review and approval prior to initiation of research at the VAMHCS.

1.1 When all study activities have ended, the investigator must send notification to the Chief, Pharmacy Services through the Investigational Drug Pharmacist.

2. Prior to the R&D Committee or subcommittee meeting, the Investigational Drug Pharmacist (IDP):
 - 2.1. is sent a copy of the agenda for review. This ensures that the IDP is aware of all investigational drug protocols coming before the VA R&D Committee.
 - 2.2. Is sent the protocol and pharmacy documents. This ensures that the IDP is familiar with the study procedures regarding the accountability and dispensing of study drugs. The IDP may meet with the investigator as part of the review process. The IDP must acknowledge an agreement with the investigator regarding the arrangements for IDS services.
3. All study drugs must be shipped to and dispensed by the IDS unless a pre-arranged written plan has been approved by the IDP and the Chief, Pharmacy Services.
 - 3.1. If a written agreement exists that permits the investigator to dispense study drug(s), the drug will be processed by the PI according to all applicable sections of IDS SOP 119-010. This includes consent form verification, drug accountability and dispensing.
4. Upon receipt of investigational drug protocol from the principal investigator, the pharmacist will set up an Investigational Drug Folder or binder according to IDS SOP 119-010, "Investigational Drug Section". Each folder will contain:
 - Copy of the approved protocol (unless available on-line),
 - IRB approval letter,
 - VA Form 10-1223 (Report of Human Studies (IRB) Approval),
 - VA R&D approval letter,
 - Dispensing instructions (if applicable),
 - Medication invoice, shipping receipts,
 - Copy of the VA Form 10-9012 (list of authorized prescribers),
 - Copies of the signed consent forms or signature pages or documentation of receipt of signed ICFs prior to dispensing (see IDS SOP 119-010),
 - Investigational Drug Dispensing Form(s).
5. Upon receiving the drug from the supplier, the pharmacy will verify the contents of the package with the invoice. A copy of the invoice will be placed in the Investigational Drug Folder. The pharmacy will indicate the invoice date, quantity received, and the current balance on the Investigational Drug

Dispensing Form or a sponsor specific dispensing form. The investigational medications are secured in the locked investigational pharmacy department. Access to investigational drugs is limited to the pharmacy staff only. The PI does not have access to investigational medications unless they are escorted into the pharmacy by pharmacy staff (per VAMHCS SOP 119-020, "Security of the Pharmacy"). Investigational medications will be stored according to sponsor requirements and are separated from general pharmacy stock.

6. The IDP processes study drugs according to VAMHCS SOP 119-010. This includes signed consent form verification, drug accountability and dispensing of study drug.
 - 6.1 Through the IDS' informed consent verification procedure, the pharmacist verifies that an IRB-approved 10-1086 consent form has been signed by the participant or LAR prior to dispensing the first dose of study drug.
 - 6.2 Drug accountability logs document all items required by VHA Handbook 1108.04 as well as Sponsor and other applicable requirements.
7. Disposition of unused stock:
 - 7.1 Unused stock will be disposed of by the pharmacy according to sponsor requirements.
 - 7.2 If disposition of unused stock is not outlined by the sponsor, at the termination of the protocol, the drug will be disposed of, after contacting the PI, at 1000 degrees Celsius per VA contractor.
 - 7.3 Documentation of disposition of unused stock will be kept in the Investigational Drug Folder.
8. Controlled Substances: The VA Pharmacy Service will adhere to the following policies and procedures to be followed when storing and dispensing controlled substances for investigational protocols in addition to any handling or accountability requirements by the sponsor:
 - VAMHCS Pharmacy SOP "Controlled Substance Policy" 119-018
 - VAMHCS Pharmacy Policy "Controlled Substance Handling" 119-15.
9. VA Cooperative Studies:
 - 9.1 The Cooperative Studies Program Clinical Research Pharmacy will be responsible for obtaining and distributing the investigational drug to the Chief, Pharmacy Service.
 - 9.2 Investigational medications will be controlled according to IDS policies and procedures.
 - 9.3 The Cooperative Studies Pharmacy will track expiration dates for investigational medications.

10. Pharmacy Service will immediately report all violations of the investigational drug policy, through the Research Compliance Officer to the Associate Chief of Staff for Research and Development and Medical Center Chief of Staff.
11. The Investigational Drug Logs are available to the VAMHCS Office of Research Compliance or the HRPO Quality Improvement Office as part of a routine or for-cause audit. The ORC performs a routine audit of the IDS so less than every two years.
12. Patients Transferred to the VAMHCS on Study Drug(s): When patients who are participating in a clinical study initiated elsewhere are admitted to the VAMHCS, VAMHCS SOP 119-010 will be followed.
13. Emergency Use Procedures:

Emergency use means “the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval”. [21 CFR 56.102(d)]. ***VAMHCS investigators must follow the IRB’s policies and procedures on “Emergency Use of a Test Article”***. A summary of the IRB’s procedures is as follows. Refer to the actual Policy for details*.

 - 13.2 Prior to the emergency use:
 - 13.2.1 The Investigator must make a request on behalf of an individual that is either confronted with a life threatening or severely debilitating condition, where the use of the investigational or unlicensed test article is needed, and there is no standard acceptable treatment available.
 - 13.2.2 The Investigator must contact the manufacturer of the drug, agent, or biologic to determine if the test article can be made available for the emergency use under the manufacturer’s IND or IDE; or whether the FDA will authorize shipment of the test article in advance of the IND submission.
 - 13.2.3 The Investigator must also contact the VAMHCS Investigational Drug Service Pharmacist (IDP) as soon as possible in order to arrange delivery or transfer of the investigational drug or biologic and to discuss the preparations and prescribing mechanism to be used.
 - 13.2.3.1 All investigational drugs or biologics must be delivered to and dispensed from the IDS unless otherwise arranged with the IDP and Chief, Pharmacy Services.
 - 13.2.3.2 The Investigator must complete an Investigational Drug Information Record (VA Form 10-9012) to be kept on file in the IDS.

* The current policy is UMB HRPP Policy and Procedure 11E: Procedure for the Emergency Use of FDA Regulated Products. However, as of 1/31/08, the UMB policies are in revision.

- 13.2.4 The Investigator must notify the IRB of the intent to use an investigational drug or biologic in an emergency situation (“Emergency Use Request”) via BRAAN/CICERO*.
- 13.2.4.1 If it is outside of regular business hours, the Investigator must contact the HRPO by telephone of the intent to use an investigational drug or biologic in an emergency situation (410-706-5037). The HRPO phone message provides a number to page the IRB Chair or Executive Committee Member after hours.
- 13.2.4.2 If possible, this notification should occur PRIOR to administration of the investigational drug or biologic. However, if, in extremely rare circumstances, it is not possible to communicate with the IRB before treating the patient, the welfare of the patient is the overriding priority and treatment may be administered without prior IRB notification. The practitioner must submit a written report to the IRB as soon as possible but within 5 working days. The investigator will be expected to justify to the IRB why communication prior to the use was not possible.
- 13.2.5 All efforts must be taken to obtain informed consent from the patient or the legally authorized representative (LAR) prior to the emergency use*.
- 13.2.5.1 If prior consent from the patient or LAR is not possible, refer to the IRB policy for details on alternative procedures.
- 13.2.5.2 Since the emergency use is prior to IRB approval, no IRB-approved consent form will exist. Use a hospital clinical consent form instead.
- 13.2.5.3 The consent form MUST clearly state that the drug or biologic is investigational.
- 13.3 The Investigator must document the following:
- 13.3.1 Enter an enrollment note in CPRS stating the circumstances of the emergency use and the consent process*.
- 13.3.2 Enter a “Research Subject Clinical Warning” (RSCW) into CPRS (even though the emergency use cannot be used for research data; see 12.5 below).
- 13.3.3 Immediately send a copy of the signed consent form to be scanned into CPRS.
- 13.4 After the emergency use:
- 13.4.1 The Investigator must notify the IRB, the VAMHCS Research Compliance Officer (RCO) and the Chair, R&D Committee as soon as possible but within five working days of the emergency use.
- 13.4.2 The Investigator must submit an Amendment in BRAAN/CICERO* providing a follow-up report to the IRB within five days of the emergency use of an investigational drug, device, or biologic.

- 13.4.3 The investigator should evaluate the likelihood of a similar need for the drug, agent, or biologic and if future use is likely, immediately initiate efforts to obtain IRB approval and an FDA approved IND for the drug, agent, or biologic's subsequent use.
- 13.5 **This use of the investigational drug may not be used to collect data for research purposes.**
- 13.6 **The Investigator may not use the investigational drug or biologic on future patients unless there is an approved protocol.**
Future uses of the test article requires IRB approval.

COMPLIANCE

Both the IDS and investigators are subject to routine or for-cause audits by the ORC, the HRPO, sponsors, and regulatory agencies. Audits may be announced or unannounced. The IDS is audited at least biannually.

REFERENCES:

VHA Handbook 1108.04	Investigational Drugs
IRB P&P I.5.A	Research Using Investigational or Unlicensed Test Articles
IRB P&P I.5.B	Control of Investigational Test Articles
IRB P&P I.5.C	Emergency Use of Investigational or Unlicensed Test Articles
IRB P&P I.5.C	Humanitarian Use Devices (HUD)
VAMHCS SOP 119-010	Investigational Drug Section (IDS)

APPROVAL

This SOP entitled "Research and Investigational Drugs" (Version 2.0) has been approved by the Medical Center Director, effective 2/14/08.