

**RESEARCH PHARMACY STANDARD OPERATING PROCEDURES (SOP)
Controlled Substances Utilized in Animal Research**

1. **PURPOSE:** To establish a standard operating procedure for the handling of controlled substances utilized in animal research at the South Texas Veterans Health Care System (STVHCS).
2. **POLICY:** It is STVHCS policy that the Research Pharmacy will handle controlled substances utilized in animal research in accordance with Hospital Policy Memorandum *Drug Enforcement Agency (DEA) Registration*, local Pharmacy Service Policy Memorandum *Controlled Substances, Standard Operating Procedures for Balance Adjustments for Controlled Drugs* and *Standard Operating Procedures for Procuring and Receiving Controlled Substances* which comply with the Department of Veterans Affairs (VA) and Federal regulations regarding controlled substances.
 - a. **Definitions**
 - (1) Compounded preparations: Any alteration in the packaging or dosage form of a commercially supplied medication (i.e. bulk to unit dose preparation or ampules to diluted syringes).
3. **ACTION:**
 - a. **Responsibilities**
 - (1) The Director is responsible for:
 - (a) Disseminating information to “providers” including veterinarians and scientific investigators regarding DEA registration requirements for those individuals that perform and/or conduct research with respect to, administer, or use in teaching or chemical analysis, a controlled substance.
 - (b) Authorizing in the animal research area, also known as the Veterinary Medical Unit (VMU), a designated provider to be responsible for ensuring the appropriate security, handling, and storage of all controlled substances.
 - (c) All responsibilities as described in Pharmacy Service Policy Memorandum *Controlled Substances*.
 - (2) ACOS for Research is responsible for:
 - (a) Ensuring all requirements for receipt, handling, storage, security, administration, waste, and destruction or return of controlled substances used in animal research are followed in accordance with *Controlled Substances, Standard Operating Procedures for Balance Adjustments for Controlled Drugs, Standard Operating Procedures for Procuring and Receiving Controlled Substances* unless otherwise stated in this SOP.

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- (b) Assisting investigators in complying with applicable rules and regulations regarding DEA registration. This includes educating researchers about the requirements, assisting them as necessary during implementation, and providing regular oversight to insure compliance is being maintained.
 - (c) Ensuring documentation of receipt, administration, and the wasting of controlled substances used in the VMU.
 - (d) Ensuring all required inventory verification is performed, security of controlled substances is maintained and the room is appropriately secured in the VMU.
 - (e) Ensuring principal investigators are appropriately educated on this SOP.
- (3) **The Chief, Pharmacy Service** is responsible for:
- (a) Ensuring the medical facility Director is notified of the need to authorize a Designated Provider to ensure security, handling, and storage of the controlled substances in the VMU.
 - (b) All responsibilities as described in Pharmacy Service Policy Memorandums *Controlled Substances, Standard Operating Procedures for Balance Adjustments for Controlled Drugs and Standard Operating Procedures for Procuring and Receiving Controlled Substances.*
- (4) **The Principal Investigators** are responsible for:
- (a) Ensuring compliance with Hospital Policy Memorandum Drug Enforcement Agency (DEA) Registration.
 - (b) Requesting to use controlled substances on laboratory animals by completing the appropriate section in the Safety Survey and the ACORP forms in order to obtain IACUC approval.
 - (c) Ensuring appropriate implementation of this policy and procedure on handling of controlled substances utilized in animal research including inventory, record keeping, security, and disposal provisions.
 - (d) Ensuring laboratory technicians and all other study staff, defined as authorized agents of the DEA registrant (PI), are in compliance with all local policies and procedures and federal regulations related to controlled substances. The registrant is required to screen those employees prior to authorization. As part of the screening process, a questionnaire (Attachment 1) which includes the following questions (21 CFR 1301.90) must be completed for each non-practitioner having access to DEA controlled substances:
 - 1. Within the past five years, have you been convicted of a felony, or, within the past two years, any misdemeanor, or, are you presently charged with committing a criminal offense?

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2. In the past 3 years, have you knowingly used narcotics, amphetamines, or barbiturates other than those prescribed to you by a physician?
 - (e) Fill out one questionnaire for each employee (non-practitioner) who is authorized by the registrant to handle DEA controlled substances under his or her direction. The registrant should maintain this documentation for the duration of the employee's employment. In the event an employee provides a "YES" response on the questionnaire, the registrant (investigator) is advised to contact the ACOS for Research to discuss how to proceed.
 - (f) Notifying the Research Pharmacist of requests for controlled substances to be utilized in animal research pursuant to a study protocol.
- (5) **The Research Pharmacist** is responsible for:
- (a) Stocking the Automated Dispensing System (ADS) as described within this SOP
 - (b) Ensuring the VistA Controlled Substances Package is the primary storage mechanism for controlled substances forms and transactions. VA Forms 10-2321 and 10-2638 will be completed in ink and signed by the principal investigator, laboratory technician, VMU designated provider and/or research pharmacist and filed separately in the research pharmacy in a numerical file once completed.
 - (c) Resuming custody of controlled substances returned by the VMU ADS once notified to do so by the VMU designated provider.
 - (d) Reviewing expended VA Forms 10-2638 for errors, losses and/or waste upon receipt from the VMU designated provider.
 - (e) Ensuring all controlled substances returned to the research pharmacy are posted on the Controlled Substance Destruction menu in VistA and held for destruction.
- (6) **The Animal Research Designated Provider** is responsible for:
- (a) Appropriately securing, handling, storing, wasting, issuing and inventorying all controlled substances within the VMU ADS.
 - (b) Ensuring laboratory technicians' or Principal Investigators' (PI) documentation of receipt, administration, and the wasting of controlled substances used in animal research is appropriate.
 - (c) Performing inventory verification and discrepancy resolution as required in Pharmacy Service Policy Memorandum *Automated Dispensing System Policy for Pharmacy Automated Dispensing System Machines*.
 - (d) Returning controlled substances to the research pharmacy as described in the section titled disposition.

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b. Procedures

(1) Ordering

- (a) The Research Pharmacist, with the concurrence of the ACOS for Research, will place a request to Pharmacy Procurement for the purchase of a controlled substance to be utilized in animal research pursuant to a principal investigator's study protocol.
- (b) The Chief of Pharmacy will initiate the order of all purchase requests through Pharmacy Procurement.
- (c) All controlled substances for use in animal research are then purchased through pharmacy utilizing the hospital DEA license.

(2) Opening shipments, Receiving and Verification of Posting in VistA

- (a) All procedures described in *Standard Operating Procedures for Procuring and Receiving Controlled Substances* are to be followed as written unless otherwise stated below.
- (b) All controlled substances being tested or evaluated in study protocols will be delivered directly to either the inpatient or outpatient vault and remain unopened awaiting reconciliation and processing by the research pharmacist and accountable officer (AO).
- (c) The source of controlled substances may be from a prime vendor, a non-prime vendor, or directly from a study sponsor.

- 1. In the instance of a prime vendor receipt, pharmacy procurement personnel or designee will place the controlled substance in the vault. The procurement staff member, or designee, will sign the wholesaler's manifest (shipping list) documenting receipt of the drug shipment. The procurement staff member downloads the McKesson invoice for the controlled substances purchased, and then uploads this into the VistA system via the PSA McKesson invoice upload program. The research pharmacist will act as the receiving official (RO). The Accountable Officers (AO) and RO will reconcile the controlled substance shipment received with the controlled substance INVOICE ORIGINAL and DENOTED COPY. Both the INVOICE ORIGINAL and DENOTED COPY will be signed and dated by the AO and RO. The signed INVOICE ORIGINAL will remain with pharmacy procurement, to be sent to Fiscal Service. The DENOTED COPY will be filed in the research pharmacy. The signed DENOTED COPY will then be processed by procurement personnel in the VistA Drug Accountability package as "Uploaded Prime Vendor Invoice Data." This action changes the status of the invoice in the Drug Accountability package to "Processed." The research pharmacist will reconcile the controlled substances received with the copy of the invoice detailing the controlled substances processed and complete the invoice verification process in the VistA Drug Accountability package. The research pharmacist will then perform and print an Invoice Review and sign it. The AO will also sign it to serve as verification that the receipt of the controlled substances has been posted to research pharmacy inventory in VistA. The signed copy of the Invoice Review will be kept in the research pharmacy for the Controlled Substance Coordinator to review as part of the monthly controlled

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substance inspection program. A copy of the signed invoice review will be provided to the AO.

2. In the instance of a non-prime vendor receipt, warehouse personnel will sign for the shipment and generate a receiving report documenting receipt of the drug shipment. Warehouse personnel will then notify or transfer the controlled substance shipment to pharmacy procurement. Pharmacy procurement personnel or designee will place the controlled substance in either the inpatient or outpatient vault. The research pharmacist will act as the receiving official (RO). The Accountable Officers (AO) and RO will reconcile the controlled substance shipment received with the controlled substance packing list and purchase order (PO) number. The packing list will be signed and dated by the AO and RO. The packing list will be attached to the original receiving report and will remain with the appropriate procurement department. A copy of the packing list will be filed in the research pharmacy. The Research Pharmacist will receive the Purchase Order Number in the Receipts into Pharmacy option of the Controlled Substance package in VistA. The Research Pharmacist will then perform and print a Purchase Order Review and sign it. The research pharmacist will also print the purchase order history and sign it. The AO will also sign both documents to serve as verification that the receipt of the controlled substances has been posted to research pharmacy inventory in VistA. The signed copy of the Purchase Order will be kept in the research pharmacy for the Controlled Substance Coordinator to review as part of the monthly controlled substance inspection program. Copies of the signed packing list, signed order review and signed order history will be provided to the AO.
3. In the instance of a controlled substance receipt directly from a Study Sponsor, the research pharmacist or designee will sign for the drug shipment documenting receipt. The research pharmacist will also maintain the controlled substance shipment securely within the research pharmacy until the AO has arrived. The research pharmacist will call the AO at the designated number to report onsite to reconcile the controlled substance shipment received. The research pharmacist will act as the receiving official (RO). The Accountable Officers (AO) and RO will reconcile the controlled substance shipment received with the controlled substance packing list. The packing list will be signed and dated by the AO and RO. The signed packing list will be filed in the research pharmacy. The research pharmacist will then perform a Balance Adjustment entry using the Supervisor menu in the Controlled Substances package in VistA. The balance adjustment will cite the source and the shipping list documentation number of the received items in the comments field. The Research Pharmacist will print the balance adjustment sheet and sign it. The AO will also sign it to serve as verification that the receipt of the controlled substances has been posted to research pharmacy inventory in VistA. The signed copy of the balance adjustment will be kept in the vault for the Controlled Substance Coordinator to review as part of the monthly controlled substance inspection program. Copies of the signed packing list and signed balance adjustment sheet will be provided to the AO.

(4) Veterinary Medical Unit (VMU) procedures

- (a) All controlled substances will be dispensed from the Research Pharmacy to the VMU via the VistA generated form 10-2321.

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- (b) When controlled substances must be compounded prior to administration to a research animal, the research pharmacist will compound all controlled substances prior to dispensing to the VMU. All procedures described in *Standard Operating Procedure for Balance Adjustment for Controlled Drugs* will be followed. The compounded controlled substances will be assigned the original source manufacturer expiration date or 6 months, whichever is sooner. When two or more medications are used in a preparation containing controlled substances, the earliest expiration date of any ingredient or 6 months, whichever is sooner will be assigned.
- (d) Controlled substances will be dispensed to the VMU ADS on a recurring basis at predetermined time intervals (i.e. every 30 days) or otherwise based on the needs of the animal protocols. The amount prepared and dispensed, however, may be subject to changes in study protocols.
- (e) All controlled substances issued by the VMU designated provider to laboratory technicians will be dispensed via VA Form 10-2638 (Attachment 2). All records for controlled substance dispensing activities will be maintained electronically in the Vista package and manually on VA Form 10-2638 signed by the principal investigator, laboratory technician, VMU designated provider and/or research pharmacist.
 - 1. The research pharmacist will dispense controlled substances to the VMU and physically load them into the VMU ADS in the respective drawer for that controlled substance. VA Form 10-2321 will document the quantities received, date, and serial number and will be signed by the research pharmacist and receiving VMU designated provider. VA Form 10-2321 will be filed in the research pharmacy.
 - 2. When laboratory technicians or PIs request controlled substances for administration to research animals, the VMU designated provider will remove the controlled substances from the ADS assigning it to patient – last name of the Principal Investigator and IACUC Protocol Number. The VMU designated provider will document on the header of VA Form 10-2638 (Attachment 1) the following information:
 - a. Under Pharmacy Dispensing number, enter sequential dispensing number
 - b. Enter the page number
 - c. Drug name, size, and strength
 - d. Drug Expiration Date
 - e. Drug dosage form and quantity
 - f. Lot number and manufacturer
 - g. Under ordered by, printed name of Principal Investigator
 - h. Under dispensed by, printed name of VMU designated provider and initials
 - i. Under ward number, lab number
 - j. Date dispensed
 - 3. The VMU designated provider will provide this VA Form 10-2638 to the principal investigator or laboratory technician to be utilized as a controlled substance administration record. The individual receiving the drug must date and sign at the bottom of the form confirming the drug has been received. The principal investigator or laboratory technician will maintain a secure record of drug accountability to include the following information on VA Form 10-2638:

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- a. Date and time administered
- b. Under Name of Patient, enter the Protocol number, Cage#
- c. Under dose, enter the quantity of drug administered
- d. Balance remaining after quantity administered
- e. Signature of individual administering drug
- f. If any wasting occurs, under Name of Patient, enter "Waste" and under dose, enter the amount wasted. The VMU designated provider must sign in addition to the individual wasting the drug as a witness to the wasting.

Note: The first line item entry will be the issuance of drug from the VMU designated provider to the principal investigator or laboratory technician. Therefore, the entry under name of patient will be "Issued to Lab", the dose will be "N/A" and the VMU designated provider will sign under administered by.

- 4. Expended VA Forms 10-2638 will be returned to the VMU designated provider. The individual returning the form must date and sign at the bottom of the form confirming all drug has been administered. The designated provider must review the completed form for errors, losses and/or waste upon receipt from the laboratory technician. After review, these forms will be returned to the research pharmacy. The research pharmacist will also review the completed form for errors, losses and/or waste and will date and sign at the bottom of the form confirming the review of entries. If any drug issued remains at the time of return of VA Form 10-2638, the drug will also be returned to the VMU designated provider and appropriately wasted as described in the final disposition section below.

(e) ADS/Omniceil Monitoring

- 1. All Omnicell Monitoring procedures described in *Controlled Substances and Automated Dispensing System Policy for Pharmacy Omnicell Machines* will be followed as written

(f) ADS/Omniceil Inventories and Discrepancies

- 1. The VMU designated provider will conduct weekly cycle counts and daily discrepancy resolution reports of the controlled substances within the ADS in the VMU as described in *Automated Dispensing System Policy for Pharmacy Automated Dispensing System Machines*.

(g) Final Disposition

- 1. Opened or breached containers or syringes will be disposed of by the VMU designated provider. Wasting of these medications will be documented using the automated dispensing system. In all cases, the wastage or disposal will be verified by a witness, to be reflected in the record. In order to reduce the risk of diversion, partially administered controlled substances and their residue will be destroyed as "Regulated Medical Waste" using the following procedures:
 - a. Injectable controlled substances will be drained into a locked sharps container and any associated empty vial and syringe placed into the locked sharps container.

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4. The Accountable Officer (AO) will be involved in the controlled substances turn-in to the destruction company. The AO will verify that the destruction company actually received the drugs identified for destruction.
4. **REFERENCES:** VHA Handbook 1108.01, VHA Handbook 1108.04, Hospital Policy Memorandum Drug Enforcement Agency (DEA) Registration, Research Service Standard Operating Procedure (SOP) Handling of Investigational Drugs and Devices, Pharmacy Service Policy Memorandums Automated Dispensing System Policy for Pharmacy Omnicell Machines, Controlled Substances, Standard Operating Procedures for Balance Adjustment for Controlled Drugs and Standard Operating Procedures for Procuring and Receiving Controlled Substances.
5. **RESPONSIBILITY:** Chief, Pharmacy Service (119)
6. **RESCISSIONS:** Research Service SOP for Controlled Substances Utilized in Animal Research, dated February 12, 2012
7. **RECERTIFICATION:** December of 2019



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Attachments (2)

STVHCS RESEARCH AND DEVELOPMENT
NON-HUMAN USE OF CONTROLLED SUBSTANCES
NON-PRACTITIONER EMPLOYEE SCREENING QUESTIONNAIRE

Instructions: A separate questionnaire must be filled out by the registrant and for each employee (non-practitioner) who is authorized by the registrant to handle DEA controlled substances under his or her direction.

The Drug Enforcement Agency requires that any non-practitioner who will have access to controlled substances under the direction of the registrant as a result of his or her status as an employee or agent of the University of Arkansas for Medical Sciences answer the following questions. Any false information or omission of information may jeopardize your position with respect to employment. Information revealed by this questionnaire will not necessarily preclude employment, but will be considered as part of an overall evaluation of your qualifications. The responses to this questionnaire will be held in strictest confidence.

1. In the past five years have you been convicted of a felony or within the past two years of any misdemeanor or are you presently charged with committing a criminal offense? (Do not include traffic violations, juvenile offenses or military convictions, except by general court-martial.) If the answer is yes, furnish details of conviction, offense, location, date, and sentence.

Yes _____ No _____

2. In the past three years, have you ever knowingly used any narcotics, amphetamines or barbiturates, other than those prescribed to you by a physician? If the answer is yes, furnish details.

Yes _____ No _____

Signature (Employee)

Name (Print)

Signature (Registrant - Principal Investigator)

Name (Print)

Date