**DEPARTMENT OF VETERANS AFFAIRS**
**South Texas Veterans Health Care System**
**San Antonio, Texas 78229-4404**

**Research Service Policy Memorandum 13-63**

**January 29, 2013**

# RESEARCH STANDARD OPERATING PROCEDURES (SOP)
## Controlled Substances Utilized in Clinical Research

**1. PURPOSE**: To establish a standard operating procedure for the research pharmacy's handling of controlled substances utilized in clinical 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 clinical 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) **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 clinical 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.

(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 principal investigators are appropriately educated on this SOP.

(2) **The Research Pharmacist** is responsible for:

(a) 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 receiving nurse and research pharmacist and filed separately in the research pharmacy in a numerical file once completed.

(b) Reviewing expended VA Forms 10-2638 for errors, losses and/or waste upon receipt from the nurse.

(c) Ensuring all controlled substances returned to the research pharmacy are posted on the Controlled Substance Destruction menu in VistA and held for destruction.

(3) **The Principal Investigators** are responsible for:

(a) Ensuring compliance with Hospital Policy Memorandum Drug Enforcement Agency (DEA) Registration.

(b) Ensuring appropriate implementation of this policy and procedure on handling of controlled substances utilized in clinical research.

(c) Ensuring all study staff are in compliance with all local policies and procedures related to controlled substances.

(d) Notifying the Research Pharmacist of requests for controlled substances to be utilized in clinical research pursuant to a study protocol.

b. **Procedures**

(1) Ordering

(a) When investigational controlled substances are not supplied by the study sponsor, 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 clinical 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 clinical 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 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 with 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.

(3) Inventory

(a) Perpetual inventory of controlled substances stored and dispensed by the research pharmacist will be maintained and inspected monthly pursuant to VHA Handbook 1108.1.

(b) The research pharmacist will inventory the research vault with an accompanying pharmacist on Tuesdays and Fridays via the inventory sheet generated using the controlled substance menu in the VistA electronic system. This inventory sheet will be filed in the research pharmacy and provided to the appointed controlled substance inspecting officer monthly in accordance with VHA Handbook 1108.1.

(c) Although the research vault is a commercial Automated Dispensing System (ADS), the Research Vault is not subject to the same procedures and requirements of ADS on nursing units as detailed under *Pharmacy Service Policy Memorandum Automated Dispensing System Policy for Pharmacy Omnicell Machines* as its function is only as a vault.

(4) Preparation and Dispensing

(a) If controlled substances within the research vault require compounding prior to dispensing to an inpatient ward, patient, agent of a patient or study personnel, the following procedure will be followed:

1. An order or prescription for the compounded drug (dispensing item) must be received.

a. Schedule II substances to be provided for inpatient services will be electronically ordered in CPRS for a period not to exceed 7 days in accordance with local pharmacy policy.

b. All outpatient prescriptions for schedule II substances must also be written on VA Form 10-2577f. The form must be completed in accordance with local pharmacy policy.

c. Schedule III thru V prescriptions for both inpatient wards and outpatients will be electronically ordered in CPRS in accordance with local pharmacy policy.

2. At the time of compounding, the Research Pharmacist will remove the bulk drug (orderable drug) from the research vault assigning it to the compounded drug (dispensing drug) (i.e. zzINV-ABC-Compounded Drug A 10mg).

3. Balance adjustments from the bulk drug (orderable drug) will be made by the Research Pharmacist in the VistA controlled substances package as described below:

   a. The number of units of the bulk drug removed from the vault to be used to prepare the compounded drug should be deducted from the inventory balance in the form of a *balance adjustment* in the VistA controlled substances package.

   b. If there is any waste in production of the compounded drug, it is to be documented within the balance adjustment *comment* field citing the following for justification: patient identifying information (i.e. initial of patient's last name and last four of social security number), dose and units that were prepared, amount lost to waste, and initials of witnessing pharmacist or technician or technician to the waste.

   c. A balance adjustment sheet documenting the compounding and the waste will be generated in VistA and signed by the research pharmacist as well as a witnessing pharmacist or technician or technician. This balance adjustment sheet will be filed in the research pharmacy. These sheets and a balance adjustment report will be provided to the appointed controlled substance inspecting officer as well as a pharmacy designee on a monthly basis.

4. Balance adjustments to the compounded drug (dispensing drug) will be made in VistA as described below:

   a. The number of units of the compounded drug produced will be added to the inventory balance in the form of another *balance adjustment* using the VistA controlled substances package.

   b. The compounded drug must be stocked in the research vault using the compounded drug entry (dispensing drug) (i.e. zzINV-ABC-Compounded Drug A 10mg).

   c. When the compounded drug will be dispensed to the inpatient ward's Omnicell, the research pharmacist will remove the compounded drug from the research vault assigning it to the respective inpatient ward entry (i.e. zz_NAOU_7A).

   d. When the compounded drug will be dispensed to the patient as an outpatient prescription following a medication order entry in VistA, the research pharmacist will remove the compounded drug from the research vault assigning it to the specific patient.

   e. The compounded drug will be dispensed to the inpatient ward Omnicell or to the patient in the same number of units that were added into the inventory balance

for that compounded drug in VistA. The resulting inventory balance after dispensing will be zero.

f. A VistA generated balance adjustment report will be provided to the appointed controlled substance inspecting officer as well as to a pharmacy designee on a monthly basis.

5. INPATIENT DISPENSING AND ADMINISTRATION PROCEDURE

a. The procedure for dispensing the compounded drug to an inpatient ward is described below:

(1) The research pharmacist will dispense the product to the ward on VA Form 10-2321, prepared in duplicate, and physically stock this medication into the Omnicell in the appropriate drawer specified for that compounded drug. VA Form 10-2321 will document the quantities received, date, and serial number and will be signed by the research pharmacist and receiving nurse, charge nurse or nurse manager. All VA Form 10-2321 will be filed in the research pharmacy.

b. The procedure for administration of the drug dispensed to the ward is described below:

(1) The nurse will remove the compounded drug from the Omnicell, assigning it to the patient to which it will be given. Only in the case of computer failure will manual forms be utilized for dispensing to the patient. In such an instance, VA Form 10-2638 will be utilized as a controlled substance administration record. Expended VA Form 10-2638 will be returned to the research pharmacy, and the research pharmacist must review the completed form for errors, losses and/or waste upon receipt from the nurse prior to filing.

(2) If there is any waste during the administration process, the nurse will verify at the prompting of the Omnicell the amount of waste, by whom and the corresponding witness. Each nurse will provide an electronic signature upon verification.

6. OUTPATIENT DISPENSING PROCEDURE

a. The procedure for dispensing the compounded drug to a patient, agent of a patient or study personnel as an outpatient medication is described below:

(1) The compounded drug will be dispensed by the research pharmacist in accordance with local pharmacy policy.

(2) All persons picking up completed controlled substance prescriptions will sign the prescription pick-up label to be maintained in the research pharmacy.

(b) If the controlled substance within the research vault does not require compounding prior to dispensing, the following procedure will be followed:

1. An appropriate order or prescription must first be received prior to dispensing to an inpatient ward, patient, agent of patient or study personnel. All orders and prescriptions must be in accordance with local pharmacy policy.

2. When the drug will be dispensed to an inpatient ward Omnicell, the research pharmacist will remove the drug from the research vault assigning it to the respective inpatient ward (i.e. zz_NAOU_7A).

3. When the drug will be dispensed to the patient, agent of the patient or study personnel as an outpatient prescription, the research pharmacist will remove the drug from the research vault assigning it to the patient.

4. The procedure for dispensing to a ward Omnicell and administration of the drug detailed under INPATIENT DISPENSING AND ADMINISTRATION PROCEDURE (1.e.1.e) is applicable and will be followed accordingly.

5. The procedure for dispensing the drug to the patient as an outpatient prescription detailed under OUTPATIENT DISPENSING (1.e.1.f) is applicable and will be followed accordingly.

(5) Discrepancy Monitoring

(a) The research pharmacist will follow Pharmacy Service Policy for reconciliation of controlled substances when dispensing from the research vault to automated dispensing machines.

(6) Final Disposition

(a) Any unused controlled substances utilized in clinical research and stored within an inpatient ward's Omnicell that are determined to be unusable will be returned to the research pharmacy. They will be held for disposal in accordance with local pharmacy policy or for return to the study sponsor as described in the procedure below:

1. The research pharmacist will work with the charge nurse or nurse manager to initiate and complete the transfer no later than the next day, excluding weekends and holidays, after the patient will no longer receive the medication.

2. The research pharmacist will perform a destock of the medication in the Omnicell citing the reason for destock as *drug not administered to patient – held for disposal.* The Omnicell will prompt for an electronic signature from the individual performing the destock as well as a witness to the destock.

3. If the medications are to be disposed in accordance with the local pharmacy policy, an entry must be posted in the controlled substance destruction menu in VistA. The controlled substances will be placed in sealed bags and labeled in accordance with local policy. The appointed controlled substance inspecting officer must verify the "Drugs on Hold for Destruction" report in VistA and the accountability of the sealed

bags of the unusable controlled substances monthly. The contents will also be verified at the time of disposal. The unusable controlled substances ledger must be "cleared" of inventory accountability in VistA once the disposal of an item has been rendered.

4. The research pharmacist will utilize the local pharmacy policyfor guidance on appropriate disposition. Those items disposed of will be documented on a drug specific electronic drug accountability record to include: drug name, dosage form, strength, quantity, and date of disposal.

5. If the medications are to be held for pharmaceutical company disposition, the company will be notified of medications awaiting return, and the medications will be stored in the research pharmacy until the pharmaceutical company resumes custody. All inventory and storage policies described above are applicable and will be followed accordingly. Schedule II drugs will be returned to the study sponsor utilizing DEA Form 222 to be completed by the sponsor.

(b) Any unused controlled substances utilized in clinical research and stored in an inpatient ward Omnicell determined reusable will be returned to the research pharmacy. If determined reusable, the medications can be returned to the research pharmacy inventory as described in the procedure below:

1. The research pharmacist will work with the charge nurse or nurse manager to initiate and complete the transfer back no later than the next day, excluding weekends and holidays, after the patient will no longer receive the medication.

2. The research pharmacist will perform a Destock of the Omnicell citing the reason for destock as *drug not administered to patient - return to stock*. The Omnicell will prompt for an electronic signature from the individual performing the destock as well as a witness to the destock.

3. The research pharmacist will restock the research vault with the respective controlled substance. The research vault will prompt for an electronic signature from the individual performing the restock as well as a witness to the restock.

4. The research pharmacist will then balance adjust the inventory for that controlled substance in VistA to reflect the quantity to be returned to stock.

5. Within the balance adjustment *comment* field, the following should be cited as justification: date, patient identifying information (i.e. Initial of patient's last name and last four of patient's social security number), reason for return of the investigational controlled substance, serial number and the initials of the witnessing pharmacist or technician to return to stock. A balance adjustment sheet will be generated in VistA and signed by the research pharmacist as well as a witnessing pharmacist or technician. This balance adjustment sheet will be filed in the research pharmacy. These sheets and a balance adjustment report will be provided to the appointed controlled substance inspecting officer as well as a pharmacy designee on a monthly basis.

**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:** ACOS for Research and Development (151) and Chief, Pharmacy Service (119)

**6. RESCISSIONS:** Research Service SOP for Controlled Substances Utilized in Clinical Research, dated February 15, 2012

**7. RECERTIFICATION**: February 2017

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