NIH Policy Manual

1345 - Handling and Safeguarding of Controlled Substances for Nonhuman Use

Issuing Office: OD/OM/ORS/SR/DVR **Phone:** (301) 435-2780

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Transmittal Notice

1. **Explanation of Material Transmitted:** This chapter describes the National Institutes of Health (NIH) policies and procedures for handling and safeguarding controlled substances for nonhuman use, and covers acquisition, storage, use, and disposal. This chapter is being partially revised to add the National Institute on Drug Abuse (NIDA) and the National Center for Advancing Translational Sciences (NCATS), both in Rockville, MD, to the list of exceptions from following this NIH Policy Manual (i.e.; MC – 1345 Handling and Safeguarding of Controlled Substances for Nonhuman Use) issued by the Division of Veterinary Services (DVR) which is organizationally located in the Office of Research Services (ORS), Office of Scientific Resources (SR).
2. **Filing Instructions:**

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A. Purpose

This chapter describes policies and procedures for handling and safeguarding controlled substances for nonhuman use including, but not limited to those to be administered to animals or used for*in vitro* research at the National Institutes of Health (NIH) covering acquisition, storage, use, and disposal, as required by the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended.

B. Background

The Veterinary Medicine Branch contributes to the Division of Veterinary Resources (DVR) mission of advancing NIH research through the application of laboratory animal science by managing and maintaining centralized surgical, intensive care, radiology, and pharmacy services to support NIH intramural animal protocols. Except as noted below under "Exceptions," the DVR Pharmacy is the **only** organization authorized to acquire controlled substances and Drug Enforcement Agency (DEA) regulated chemicals for nonhuman use for the NIH Institutes and Centers (ICs).

C. Policy

It is NIH policy that controlled substances will be used solely for research and patient care, and that adequate controls will be established to prevent unauthorized use. All controlled substances, including vendor samples and those supplied by other ICs, shall come through the DVR Pharmacy. All Intramural NIH personnel and organizations involved in the nonhuman use of controlled substances and DEA regulated chemicals are subject to the provisions of this policy.

Exceptions:

The National Institute on Drug Abuse (NIDA) and the National Center for Advancing Translational Sciences (NCATS) in Rockville, MD; the National Institute of Environmental Health Sciences (NIEHS) in Research Triangle Park, NC; the National Institute on Aging (NIA) and the National Institute on Drug Abuse (NIDA) Intramural Programs in Baltimore, MD; the National Institute of Allergy and Infectious Diseases (NIAID), Rocky Mountain Laboratories in Hamilton, MT; the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) in Phoenix, AZ; and the National Cancer Institute (NCI) and NIAID/Division of Clinical Research, Fort Detrick in Frederick, MD are authorized to procure controlled substances and DEA regulated chemicals for nonhuman use under research licenses granted to those organizations by the DEA. The above organizations shall develop internal policies and procedures governing controlled substances which are consistent with the policies and procedures contained herein.

D. References

1. NIH Delegations of Authority, Property: Personal - No. 04B, Controlled Substance for Nonhuman Use
2. NIH Delegations of Authority, Property: Personal - No. 04B1, Controlled Substance for Nonhuman Use-ORS Internal Delegation
3. Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended, 21 United States Code (U.S.C.) Chapter13,
4. 21 CFR 1300-1399,

E. Definitions

1. **Controlled Substances (CS)/Schedule I -V substances -** Drugs and other materials by whatever name (common or unusual name, chemical name, or brand name) designated and categorized under one of five schedules by the Controlled Substances Act of 1970, as amended (21 U.S.C. 812 et seq.). Controlled substances are those items listed in 21 U.S.C. 812 and21 CFR Part 1308.11-1308.15.
2. **DEA Regulated Chemicals -** Chemical precursors, reagents and solvents required for the manufacture of controlled substances, which appear on List I and List II in 21 CFR Part 1310.02.
3. **NIH Controlled Substance Officer (NIH CSO)** (or designee) - A senior level, permanent government employee, appointed by the Director of the Office of Research Services (ORS) to administer the NIH Controlled Substance Program for Nonhuman Use and directs the DVR Pharmacy.
4. **Alternate NIH Controlled Substance Officer -** A senior level permanent government employee who is designated in writing by the Director, ORS. The alternate performs the duties of the NIH CSO in the absence of the NIH CSO.
5. **IC Controlled Substance Program Coordinator (IC CSPC) -** A senior level permanent government employee who is designated by completion of an IC CSPC Signature Card (Form NIH 2765-4, obtained from DVR Pharmacy) by the IC's Scientific Director to oversee the IC's Controlled Substance Program.
6. **Alternate IC Controlled Substance Program Coordinator (IC CSPC) -** A senior level permanent government employee who is designated by completion of an IC CSPC Signature Card (Form NIH 2765-4 – obtained from DVR Pharmacy) by the IC's Scientific Director. The alternate performs the duties of the IC CSPC in the absence of the IC CSPC. There may be no more than two alternates in each IC.
7. **Controlled Substance Custodian (CS Custodian**) - A government employee designated by completion of a CS Custodian Signature Card (Form NIH 2765-5 - obtained from DVR Pharmacy) by the IC CSPC to be responsible for the oversight and use of controlled substances in his/her area of responsibility, including but not limited to an investigator, physician, veterinarian, facility manager, or technician.
8. **Controlled Substance Lock Box Number -** A number assigned by the NIH CSO to a specific CS Custodian for a specific lock box location. The assigned number will be affixed to the inside of the controlled substance lock box or safe.
9. **Controlled Substance Record File -** An organized and neat method of storing the Controlled Substance Record for Nonhuman Use, Form NIH-2765-2, that is in use. Examples: a three ring binder, a file folder, a Ziploc bag, a plastic page protector, a pocket page or folder (paper or plastic). Do not put more than two folds in a record page. Do not attach them by rubber band to the controlled substance. Instead, place both in the same Ziploc bag or page protector.

F. Responsibilities

1. NIH Controlled Substance Officer (CSO) and Alternate NIH CSO are responsible for:

a. Ensuring NIH complies with all DEA requirements (21 CFR Part 1300 to end), i.e., acquisition, receipt, delivery, security, reporting (inventory), and disposal of controlled substances for nonhuman use.
b. Ensuring renewal of the DEA registration certificate every year, obtaining preprinted DEA-222 order forms (See Section G.1. for ordering information) and securing them in a lock box; coordinating the biennial inventory and maintaining a separate file for controlled substance orders.
c. Maintaining a database of all controlled substances issued to CS Custodians. The database will contain a record for each substance dispensed. The record will include the name of the substance, quantity dispensed, lock box number, and CS Custodian responsible. The database will also contain the inventory of substances in the DVR Pharmacy; and will include a record for each item received.
d. Conducting the training course "Acquiring and Safeguarding Controlled Substances, Nonhuman Use" for IC CSPCs, IC CSPC Alternates, and CS Custodians on a monthly basis. The NIH CSO checks that training has been completed prior to the appointment of a new CS Custodian.
e. Maintaining an up to date list of CS Custodians as an on-going process. At the time of the annual inventory the list of CS Custodians is checked against the data base maintained in the pharmacy.
f. Maintaining a file containing a copy of current Schedule 1 DEA registrations.

2. IC Scientific Director is responsible for:

a. Ensuring the IC's compliance with this policy.
b. Appointing an IC CSPC and not more than two alternates, and providing this information in writing to the NIH CSO by completion of an IC CSPC Signature Card (Form NIH 2765-4 – obtained through DVR Pharmacy).
c. Ensuring the IC CSPC and alternate(s) attend the training course "Acquiring and Safeguarding Controlled Substances, Nonhuman Use" (contact the NIH CSO for course schedule) and receive a copy of the most recent version of this policy.

3. IC Controlled Substance Program Coordinator (IC CSPC) and alternate(s) are responsible for:

a. Attending the training course "Acquiring and Safeguarding Controlled Substances, Nonhuman Use" (contact the NIH CSO for class schedule); and providing training to CS Custodians in their IC, or referring them to the NIH CSO for training.
b. Appointing their IC's CS Custodians by completion of a Controlled Substance Custodian Signature Card (Form NIH 2765-5) and submitting it to the NIH CSO. By signing the Form NIH 2765-5 the IC CSPC validates the CS Custodian has completed mandatory training and that appropriate lock box(es)/security cabinet(s) or safe(s) are available in each CS Custodian's area of responsibility to secure all controlled substances and DEA regulated chemicals.

c. Reviewing and approving requests submitted by the IC's CS Custodians for acquiring controlled substances or DEA regulated chemicals. The IC CSPC reviews the request and justification of need to ensure its validity. The IC CSPC may require documentation of need, which can include, but is not limited to, a copy of the Animal Study Proposal, a brief outline of the study in which the controlled substance(s) are used, a copy of the research protocol and/or a progress report.
d. Having delegated authority for their IC's CS Custodian(s) in their absence.
e. Conducting a physical inventory of controlled substances stored by each of their IC's CS Custodian annually in the month of May. Assisting the NIH CSO in conducting the inventory sooner, if there is an issue.

4. Controlled Substance Custodian (CS Custodian) is responsible for:

a. Completing applicable controlled substance handling training required by their IC CSPC prior to ordering controlled substances.
b. Initiating requests for acquiring controlled substances and DEA regulated chemicals used within his/her area of responsibility.
c. Maintaining current records identified in this manual chapter for all controlled substances used within his/her area of responsibility. The use and disposal of all substances issued to his/her lock box shall be tracked on Form NIH 2765-2 "Controlled Substance Record for Nonhuman Use" provided by the DVR Pharmacy with each controlled substance received.
d. Ensuring that all controlled substances and DEA regulated chemicals used within his/her area of responsibility are kept secured in a lock box or double locked steel cabinet which has been previously registered with both the IC CSPC and NIH CSO.
e. Ensuring that all individuals utilizing controlled substances and DEA chemicals within his/her area of responsibility have been trained in the appropriate handling, record keeping and security procedures prior to being granted access to these substances.
f. Conducting periodic physical inventories of controlled substances within his/her area of responsibility to ensure that all records accurately reflect the current balance of each item. Physical inventories shall be conducted a minimum of every 3 months. In high volume areas more frequent physical inventories may be necessary.
g. The following additional responsibilities are required of all CS Custodians ordering controlled substances designated by the DEA as Schedule 1:

    1. The CS Custodian or investigator must apply to the DEA for a Schedule 1 Researcher Registration.
    2. Once the DEA has issued a Schedule 1 Researcher Registration to the CS Custodian or investigator, it is the CS Custodian's responsibility to submit a copy of the completed application form (listing the controlled substance(s) the registrant is permitted to procure), along with a copy of the Researcher Registration provided by DEA, to the NIH CSO prior to the

procurement of a Schedule 1 substance.

3. All Schedule 1 substances are subsequently ordered as outlined below in Section G., Items 1-3. Once the CS Custodian takes possession of a Schedule 1 controlled substance, his/her DEA Registration must be maintained as current until the substance is completely used or the remainder of the substance properly destroyed and the destruction of the remaining substance properly documented.

5. IC Principal Administrative Officer for Intramural Research is responsible for providing a current list of individuals who can certify funds availability for the purchase of controlled substances or DEA regulated chemicals.
6. The DVR Pharmacy, under the authority of the DVR Business Management Office and in accordance with DEA and other pertinent acquisition regulations and policies, is responsible for the acquisition of controlled substances and DEA regulated chemicals for nonhuman use in support of the NIH Intramural Research Program.

G. Procedures

1. Acquiring Controlled Substances for Nonhuman Use:

   Utilizing Form NIH 2765-1 "Request for Controlled Substances for Nonhuman Use", CS Custodians initiate requests for the acquisition of controlled substances and DEA regulated chemicals used within their area of responsibility. CS Custodians shall review the completed form for accuracy and obtain funding and approval signatures prior to submitting the form to the IC CSPC. **Note:** If the item(s) under procurement are not stocked by the DVR Pharmacy, possible sources must be included in the appropriate areas of the form.

   If the item requested is a DEA Schedule 1 substance, the CS Custodian or an investigator in his/her area of responsibility must hold a DEA Schedule 1 registration for the substance being procured (see Section F.4.g). When procuring DEA Schedule 1 substances, the "Request for Controlled Substances for Nonhuman Use" sent to the DVR Pharmacy must be accompanied by a completed DEA Form 222, which can be ordered on the following website.

2. Purchase Order/Contract Placement by DVR:

   The DVR shall designate, in writing, Purchasing Agents and Contracting Officers responsible for the placement of orders and approval of contracts for all controlled substances and DEA regulated chemicals. Only these individuals will be authorized to place and approve such orders and contracts.

3. Delivery and Receipt:

   With the exception of DEA Schedule 1 substances, the DVR Pharmacy is the only location for the receipt of controlled substances and DEA regulated chemicals from

outside vendors. Officials who order controlled substances may not receive delivery of those controlled substances.

The CS Custodian will arrange for pickup of the ordered substances from the DVR Pharmacy. The CS Custodian or, in his/her absence, the IC CSPC, will sign for and receive all controlled substances and DEA regulated chemicals. The CS Custodian must present an NIH identification (ID) card and record its number when signing his/her name. The DVR Pharmacy will issue a corresponding Form NIH 2765-2 "Controlled Substance Record for Nonhuman Use", with each controlled substance.

DEA Schedule 1 controlled substances will be delivered directly to the address printed on the DEA registration form. Upon receipt of a Schedule 1 controlled substance, the CS Custodian shall notify the DVR Pharmacy/NIH CSO immediately via fax (301) 480-0088 and provide the receiving information. Arrangements will be made by the DVR Pharmacy/NIH CSO for the CS Custodian to obtain Form NIH 2765-2 "Controlled Substance Record for Nonhuman Use" to record the use and disposal of the controlled substance.

4. Use and Security of Controlled Substances and DEA Regulated Chemicals:

    a. Controlled Substances

        1. Physical Security of Inventory - Each CS Custodian is responsible for the proper use and security of controlled substances in his/her area of responsibility. The CS Custodian shall ensure that all controlled substances are maintained in the appropriately numbered and registered lock box(es) and/or safe(s) assigned to him/her. The CS Custodian is responsible for control of the combination and/or key(s) for their safe(s) or lock box(es). Random, unannounced visits by the NIH CSO, IC CSPC or designees will be conducted to monitor compliance with these security requirements.
        2. Record-Keeping Requirements - A completed Controlled Substance Record File containing the NIH Form 2765-2 "Controlled Substance Record for Nonhuman Use" issued with each controlled substance, must be locked up in the same room where the controlled substances are stored. The forms must be accessible for review and recording at all times. When recording the use of a controlled substance, a line entry is made on the form, using one line per procedure or animal treated. Entries on the NIH Form 2765-2 "Controlled Substance Record for Nonhuman Use" shall be made by the individual withdrawing the drug from the lock box or safe at the time the item is withdrawn. Each line entry will include the date, name of the principal investigator or veterinarian authorizing the administration (as required by the DEA), the signature of the individual removing the drug from the lock box or safe, the quantity withdrawn, the balance remaining/current balance, and the purpose for administration. Units of measure must remain constant on an individual CS Record and accurately reflect the amount of controlled substance in stock (example- mg, ml,

tablet count, or gm).

There are three different formats for documenting the "purpose": 1) For an animal with an individual chart and ID number, record the animal ID number and species; 2) For an animal without an individual chart and ID number, record the species, the Animal Study Program (ASP) or protocol number and the reason why the controlled substance is being administered. When a group of animals of the same species without individual charts or identification numbers are treated at the same time, with the same dose, for the same purpose, a one-line entry can be made for the entire group, and; 3) when no animal is involved, describe the *in vitro* use of the substance.

3. On-site Destruction of Controlled Substances

    a. Accidental Destruction, Damage or Contamination - When a controlled substance is accidentally destroyed, damaged, or contaminated, a line entry is made on the NIH Form 2765-2 "Controlled Substance Record for Nonhuman Use". Each line entry shall include the date, description of the circumstances, the signatures of two individuals witnessing the destruction of the substance, the quantity involved and the current balance. When a dose is withdrawn from the lock box and recorded on the NIH Form 2765-2 "Controlled Substance Record for Nonhuman Use" and only partially administered to an animal, any remaining excess should be destroyed and logged as such, in either the animal's permanent medical record, (See Section H. Records Retention and Disposal), or on the NIH Form 2765-2 "Controlled Substance Record for Nonhuman Use". The entry should be witnessed and signed by both parties.
    b. Expired Controlled Substance Destruction - Only liquid controlled substances less than 5 ml can be destroyed on site. Draw up the balance of solution and spray it in a sharps container (MPW box, burn box). Then on the corresponding record page, record what happened and have two people who witnessed the destruction sign the notation. Send the record page to the pharmacy when the balance is zero. Powdered controlled substances need to be returned to the DVR Pharmacy along with the corresponding record page.

4. Powdered Controlled Substances - The following procedure shall be used to keep an accurate inventory of bulk powdered controlled substances. In general, these substances are provided in jars with removable and replaceable lids.

    a. Inventory - Following removal of the tamper-proof seal and prior to opening the jar, determine the total weight of the jar, lid and contents. On the first line of the NIH Form 2765-2 "Controlled

Substance Record for Nonhuman Use", make an entry that states: 1) the date; 2) the total weight of jar, lid and contents in mg; 3) the signature of person making the entry; and 4) in the balance column, record the weight of the controlled substance contained in the full jar as stated on the manufacturer's label.

b. When technically possible, the following is the recommended method to dispense powdered controlled substances:

- Prior to opening the jar, weigh the jar, lid and contents and verify the weight with that previously recorded on the NIH Form 2765-2 "Controlled Substance Record for Nonhuman Use";
- Remove the lid from the jar and place the jar containing the powder on an electronic balance and tare the balance;
- Remove the powder until the electronic balance indicates that the required amount has been removed;
- Make a line entry on the Controlled Substance Record as described above [Section G. Item 4.a.(2)], entering the "quantity withdrawn";
- Replace the lid and verify the weight of the jar, lid, and contents, which should be minus the amount removed;
- Reconstitution - When a vial of a powdered drug is reconstituted, record the following information on the NIH Form 2765-2 "Controlled Substance Record for Nonhuman Use": the date reconstituted, the final concentration of solution that was made, the name of individual who made the solution, and the final volume of solution in ml's.

5. Transfer of Controlled Substances - Transfer of controlled substances from one CS Custodian to another is only permitted within the same IC and must be arranged through the IC CSPC. All items transferred must be accompanied by the item's original NIH Form 2765-2 "Controlled Substance Record for Nonhuman Use". Following transfer of an item, the IC CSPC must submit a completed Form NIH 2765-3, "Intra-Institute Controlled Substance Transfer Notification" to the DVR Pharmacy/NIH CSO the day of the transfer or the next business day if transfer occurs on a weekend or holiday. Transfers between ICs are not permitted without the authorization of the NIH CSO. **Items listed as DEA Schedule 1 cannot be transferred.**
6. Project Completion and Records Retention. Upon completion of each NIH Form 2765-2 "Controlled Substance Record for Nonhuman Use", the balance of the controlled substance remaining should be zero. Prior to returning the completed form to the DVR Pharmacy, the CS Custodian shall retain a photocopy for his/her records. Copies shall be filed by drug and are required to be kept for a period of two years by the CS Custodian.

If at any time all entry lines are filled in on a given NIH Form 2765-2 "Controlled Substance Record for Nonhuman Use" and there is still a quantity of the drug remaining, the CS Custodian shall use a copy of a blank back page of NIH Form 2765-2 "Controlled Substance Record for Nonhuman Use" available on the NIH Electronic Forms website. The CS Custodian can also contact the DVR Pharmacy for a continuation page. Staple the first page and the continuation page together.

b. DEA Regulated Chemicals

The CS Custodian must ensure proper security of DEA regulated chemicals to prevent theft of these chemicals. Logging each use and keeping balances are not required for these items. Therefore, no Controlled Substance Records will be issued to the CS Custodian when they sign for and receive DEA regulated chemicals. Acquiring or procuring DEA regulated chemicals requires completion of the Form NIH 2765-1 "Request for Controlled Substances for Nonhuman Use".

5. Physical Inventory and Reporting:

a. Annual Inventory

The DEA requires registrants to conduct a physical inventory of all controlled substances a minimum of every 2 years. To meet this biennial inventory requirement, NIH will conduct a physical inventory annually in the month of May. The NIH CSO will notify, in writing, each IC CSPC when the annual inventory is to be conducted. Attached to the memo will be reports entitled "Outstanding Sheets by Lock Box" listing the outstanding NIH Form 2765-2 "Controlled Substance Record for Nonhuman Use" for each CS Custodian in the IC. The report will contain the Control number of each record and the corresponding controlled substance issued to each CS Custodian that has not been returned to the DVR Pharmacy. A physical inventory will be taken by comparing the report with the contents of the controlled substances lock box and the balance on each NIH Form 2765-2 "Controlled Substance Record for Nonhuman Use" in the CS Custodian's Controlled Substance Record File. Record the current balance on the same line as the corresponding control number and the controlled substance description on the "Outstanding Sheets by Lock Box" report. The controlled substances physical inventory list (contained on the "Outstanding Sheets by Lock Box" form) will reflect all controlled substances in stock at the time the inventory is taken. If there are items in stock that are not on the report, the IC CSPC should add them to the list. The CS Custodian and the IC CSPC (or designee) will sign and date the bottom of the report. The IC CSPC will compile the IC's response to the annual inventory, forward the original to the NIH CSO and keep a copy in his/her file for two (2) years.

b. Periodic Inventory

The CS Custodian can call the DVR Pharmacy to obtain an "Outstanding Sheets by Lock Box" report for their lock box prior to conducting the periodic inventory mentioned in section F. 4. f.

6. Surplus and Disposal:

   Controlled substances must be transferred to the DVR Pharmacy when they are no longer required by the CS Custodian. Contact the DVR Pharmacy to arrange the transfer of the controlled substance and the corresponding NIH Form 2765-2 "Controlled Substance Record for Nonhuman Use". The NIH CSO is responsible for arranging the disposal of controlled substances that are expired or no longer required. The DVR Pharmacy uses a reverse distributor to dispose of controlled substances. Quantities of DEA regulated chemicals below the threshold levels (SeeCFR 21 part 1310.04(f) (1)) can be disposed of through NIH's chemical waste contractor. For on-site disposal, see section G. 4. a. (3) (b).

H. Records Retention and Disposal

All records pertaining to this chapter must be retained and disposed of under the authority of 21 CFR 1300-1399.

I. Internal Controls

1. **Office Responsible for Reviewing Internal Controls Relative to this Chapter:** Through this manual issuance, the Division of Veterinary Resources (DVR), ORS is responsible for ensuring that internal controls are implemented and working.
2. **Frequency of Review:** Ongoing review.
3. **Method of Review:** The DVR will maintain oversight and ensure effective implementation and compliance with this policy through review of a number of resources. DVR will conduct annual physical inventories and random unannounced checks of the IC-controlled lock boxes by the NIH CSO or designee, and other issues or trends that may arise that require monitoring.
4. **Review reports are sent to:** The Director, Office of Research Services (ORS), NIH. Issues of special concern will be brought to the immediate attention of the Director, ORS; and the Deputy Director for Intramural Research (DDIR) as requested.