



CONTROLLED SUBSTANCE USE AND MANAGEMENT PROCEDURES

PERFORMANCE STANDARD: The Duke animal program will assist researchers with advice and counsel on managing their purchase, storage, and use of controlled substances.

BACKGROUND / PURPOSE: Biomedical research, testing, and teaching programs involving animals often require that controlled substances be administered to produce anesthesia, analgesia, tranquilization, sedation or hypnosis or to study the actions of specified drug regimens. Controlled substances have the potential for misuse. Accordingly, the federal and the state Drug Enforcement Agencies require individuals using controlled substances to hold a state and federal license and abide by the regulations and policies which pertain to the licensing, storage, distribution, and use of these agents. Licensure for use of controlled substances is an individual license, for which there are no federal regulatory provisions concerning institutional management of the individual's license. Even so, Duke has an interest in the well-being of its animals and legal performance by its researchers, employees, faculty, and staff. Therefore, this set of procedures describes an investigator assistance process which will be coordinated by the Office of Animal Welfare Assurance (OAWA), and performed by the Institutional Animal Care & Use Committee (IACUC) and the OAWA.

DEFINITIONS:

- **Authorized User:** A University (or Medical Center) employee or University (or Medical Center) scientific staff member authorized to use controlled substances under the authority of a Unit / Principal Investigator Registrant who serves as his/her direct supervisor.
- **Controlled Substance:** Any substance listed in the Controlled Substances Act, Code of Federal or Substance Regulations (21 CFR, part 1300 to end), or in the North Carolina Controlled Substances Act, Chapters 26 and 29.
- **Controlled Substance Folder:** The file or folder where transactions of controlled substances (e.g. receipt, use, disposal) are recorded. Recommended forms are provided as a part of this policy.
- **Disposal:** The approved method of discarding controlled substances that is outdated, redundant, contaminated, waste, or no longer needed.
- **Disposition Records:** An accurate, continuous, and current record used to track the acquisition, use and disposal of controlled substances.
- **Drug Enforcement Administration (DEA):** The unit within the United States Department of Justice that establishes and enforces the regulations for the handling and the use of controlled substances.
- **Institutional Animal Care and Use Committee (IACUC):** The Duke University Institutional Animal Care and Use Committee

- **Licensed Practitioner:** Any individual that is licensed, registered or otherwise permitted by the United States and the state of North Carolina to dispense or use a controlled substance in the course of professional practice. If a clinical practitioner wishes to do research, they will need to obtain a researcher license.
- **North Carolina Department of Health and Human Services (NCHHS):** Authorized by North Carolina statute, NCHHS is the agency that requires annual application for registration of any person engaging in animal-based research, teaching or educational projects involving the use, study or testing of controlled substances.
- **Public Vendor:** Any licensed company or pharmaceutical provider who has a controlled substance license for selling controlled substances.
- **Registration:** The formal grant of specific authority by the DEA and/or North Carolina Department of Health and Human Services (NCHHS)
- **Registrant:** The individual that holds DEA and NCHHS registrations and is responsible for ordering, storing, using, and disposing of controlled substances. This individual is obligated to ensure compliance with controlled substance regulations at the location where the controlled substances are held. Registrants are the only ones authorized to use controlled substances. Registrants may appoint a subordinate to manage the records; however, the registrant retains the obligation for recordkeeping, storage, and use of controlled substances. Deficiencies or discrepancies in recordkeeping are the responsibility of the registrant. Note: Clinical registrants may use up to 5% for research purposes, but this provision does not apply to animal based research activities. Clinicians holding a clinical license must obtain a research license to perform animal based research using controlled substances.
- **Research:** Any animal-related activity, regardless of funding source, including research, testing, teaching, and animal care or use procedures.
- **Unit or Location:** A Unit/Location is a department, investigator's laboratory, or other administrative structure where the controlled substances are maintained.

APPLICABILITY: These procedures only apply to those situations where controlled substances are being used for animal anesthesia, analgesia, restraint, or experimentation. Each section addresses specific aspects of controlled drug utilization. Failure to abide by federal and state controlled substance regulations may serve as a basis for suspension or termination of the affected animal research protocol by the Institutional Animal Care and Use Committee (IACUC), reporting to Duke compliance officials, and referral to the state and federal licensing authorities.

PROVISIONS OF CONTROLLED SUBSTANCE USE IN ANIMAL CARE OR USE ACTIVITIES:

- a. All controlled substance use must be in accordance with the IACUC-approved protocol, or under accepted clinical veterinary guidelines if prescribed by a Duke veterinarian.
- b. The registrant must hold North Carolina Health & Human Services (NCHHS) and federal Drug Enforcement Agency (DEA) registration(s) for ordering, storing, or using controlled substances.
- c. Schedule 1 controlled substances are not available through the DLAR Pharmacy. Schedule I controlled substances must be ordered directly from a national distributor.

PROCEDURES FOR CONTROLLED SUBSTANCE REGISTRATION, RECORDKEEPING, AND USE UN DUKE ANIMAL CARE OR USE ACTIVITIES:

1. **Filing for a controlled substance license:** Process for obtaining a license (should be completed in this order):

a. **Duke:** Complete the Duke Controlled Substance Database at

<http://www.safety.duke.edu/ControlledSubstances/ControlledSubstances/DefaultCS.aspx> This database is used to track locations of controlled drug storage so the IACUC and OAWA can provide assistance to the license holder.

b. **North Carolina:**

i. Complete North Carolina Department of Health and Human Services (NC DHS) form 225. Submit NC DHHS Form 225 to the address listed on the form. Questions concerning the state DEA application should be directed to Ms. Jo Baker (919.733.1765). This form is available for download from the Duke Animal Program

Web Site: http://vetmed.duhs.duke.edu/documents/controlled_substances/State_DEA_Form.pdf

ii. The licensing fee may be paid from departmental or personal funds. **You cannot use grant funds to pay for this license!** For specific questions, call 919.334.1218 and ask for Evelyn Johnson. Ms. Johnson handles the processing of license application fee payments. When paying by credit card, FAX a copy of the DHHS form 225 with the credit card information below to Ms. Evelyn Johnson (FAX number 919.334.1271):

1. Visa or Mastercard
2. Credit card number
3. Expiration date on the card
4. Name on the card
5. Phone number of the card holder (just in case there is a problem)

iii. An agent of the NC DHHS will contact the registrant and schedule an inspection of the proposed holding site. The registrant can call Duke OAWA (919.668.6720) prior to the scheduled physical inspection by the state agent and arrange a pre-visit by Duke OAWA staff. This will assist the registrant with location security or common DHHS concerns with controlled substance management. If there are concerns noted by the DHHS agent during the physical visit, you may request the agent accept photographs of the corrected item, rather than requiring a return physical inspection.

iv. Update the Duke registration database at the link above.

c. **Federal Permit:**

i. **Wait for the North Carolina State License number BEFORE filing for a federal license! The feds WILL NOT process a federal license until the state has granted a state license. It may take many weeks to schedule an inspection by the state agents, so PLEASE apply EARLY!**

ii. Complete the Federal 225 form. This form can be filed either on-line or hard copy. The DEA preferred option is to file on-line. The link for filing on-line is:

http://www.deadiversion.usdoj.gov/drugreg/reg_apps/onlineforms_new.htm

iii. The federal agents require a physical inspection for all Schedule I agents. Physical inspections for Schedule II-V controlled substances may or may not be required.

iv. Update the Duke registration database at the link above.

2. Fees: The cost of maintaining state and federal registrations is the responsibility of the researcher using the controlled substances. Fees are currently:

- a. NCHHS (state):
 - i. \$125.00 for the initial application
 - ii. \$125.00 for annual renewals
- b. DEA (federal):
 - i. \$160.00 for the initial application
 - ii. \$160.00 for annual renewals

3. Establishing Storage for Controlled Substances: Controlled substances must be maintained behind a minimum of two (2) locks.

- a. Options for storage of the controlled substances are:
 - i. A locked cabinet in a locked room. The 'locked room' must always be locked when it is not occupied by either the registrant or an authorized user.
 - ii. A locked inner cabinet in a locked cabinet.
- b. Locks may be cipher locks (combination locks) or key locks:
 - i. The two locks (if key locks are used) must be keyed differently.
 - ii. The two keys (if key locks are used) must not be stored together (not on the same key ring).
 - iii. Both keys must be safeguarded, and not in public sight.
- c. Individuals with access to the keys must be approved by the registrant, the state, and the federal agency.

4. Purchasing of Controlled Substances:

- a. **Schedule I:** These controlled substances are not available through DLAR. The Schedule I registrant will legally procure these substances through federally approved public vendors.
- b. **Schedule II:** These controlled substances may be purchased through DLAR or a public vendor. A DEA Form 222 is required to purchase these substances from either DLAR or licensed public vendors.
- c. **Schedule III – V:** Controlled substances for animal studies may be purchased from the DLAR Pharmacy or licensed public vendors.

5. Receiving of Controlled Substances:

- a. Only the registrant or registrant authorized person may receive controlled substances.
- b. The receiving individual must:
 - i. Count and verify the contents of the order received.
 - ii. Document and rectify discrepancies prior to using the substances. Report discrepancies to the seller immediately. A copy of the DEA Form 222 may be used to document initial quantities (or quantities added to the cabinet).

6. Transfer of controlled substance between registrants: If a laboratory wishes to use a controlled substance, is licensed for the controlled substance, but does not have the substance on hand, it may transfer the substance from another registrant. DEA Form 222 must be used for any transfer of Schedule II substances between researchers; the same form should be use for transfer of Schedule III – V substances.

7. Recording Dispensing of Controlled Substances: Any written (paper) recording system may be used for maintaining dispensing data, which includes:

- a. Name of the substance (may be in page header)
- b. Source of the substance (may be in page header)
- c. Date of expiration of the substance (may be in page header)
- d. Date of receipt (may be in page header)
- e. Unique identification number for the bottle (may be in page header)
- f. Starting quantity of controlled substance
- g. Date of use
- h. Protocol (or project) for which it is being used
- i. Animal (or group of animals) for which it is being used
- j. Person dispensing the medication from storage
- k. Person administering the medication to the animal (s)
- l. Quantity (cc / ml / grams) of agent dispensed
- m. Quantity remaining in the vial / bottle / box

NOTE: Schedule I substances require a bound book rather than a loose leaf. This is a good idea for all controlled substance use, but is required for Schedule I use.

8. Labeling of Controlled Substances: Each bottle (or box) of controlled substances must be individually identified by a unique (not re-used) number. For substances obtained from DLAR, this is performed by the DLAR Pharmacy. For substances purchased outside of DLAR, an individual unique identification (created by the registrant) must be placed on the product immediately upon receipt.

- a. Original packaging showing the product information should be used when possible. Controlled substances containers (vials, ampoules, or boxes) may be removed from the original packaging if the interior container(s) has been labeled to include: the name of the controlled substances, the lot number (or unique identifier), the date opened, the final concentration, the amount per container and the expiration date (not more than 30 days after dilution date).
- b. If syringes are filled and stored in the controlled substance cabinet; or if controlled substances are compounded, diluted or combined, each container must be labeled and tracked. The label must include the following:
 - the name of the controlled substances,
 - the lot number (or tracking number) of the product,
 - the date opened,
 - the final concentration,
 - the amount per container, and
 - the expiration date (not more than 30 days after dilution date).

9. Losses of Controlled Substances: Losses (whether identified by the internal audit or another method of discovery of the loss) should be reported by the registrant to the OAWA within 3 business days of discovering the loss. Losses may also require reporting to the state and federal DEA offices by the registrant. While the registrant is responsible for the reports to the DEA offices, the OAWA will assist the registrant with reporting. The goal of this partnership is to protect the registrant and assist in accurate and timely reporting of required information.

10. Disposing of 'Waste' Controlled Substances:

- a. **Reverse Distributors:** For quantities of controlled substance (bottles of expired agent or Schedule I substances), contact a DEA certified reverse distributor for disposal. In North Carolina, the approved reverse distributors are:
 - i. RxNet Services @ 336.273.5112
 - ii. BMWNC @ 704.821.4766
 - iii. Medicycle @ 336.510.4970
 - iv. Pharmaceutical Dimensions @ 336.664.5287
- b. **Schedule I:**
 - v. Empty bottles and expired drugs: The state and federal DEA are presently re-evaluating their position of proper methods of discarding these items. Until a new decision is reached, please continue discarding down the drain for liquid agent, mixing powders with liquid and then discarding, and discarding of bottles in the sharps container.
 - vi. Wastage/loss: The state and federal DEA are presently re-evaluating their position of proper methods of discarding these items. Until a new decision is reached, please continue discarding down the drain for liquid agent, mixing powders with liquid and then discarding, and discarding of bottles in the sharps container.
- c. **Schedule II-V:**
 - i. **Empty Bottles:** All bottles should be flushed with water to prevent illegal use of minimal amounts in an empty bottle.
 1. **When purchased from DLAR:** Empty bottles and a copy of the log tracking sheet should be returned to DLAR pharmacy.
 2. **When purchased from a licensed public vendor:** Empty Schedule I substance bottles will be disposed by the registrant according to federal DEA requirements. Empty Schedule II-V bottles may be disposed of via standard sharps/glass disposal systems.
 - ii. **Partial Filled Bottles (e.g. expired, waste, or contaminated):** The remaining material may be mixed with an absorbent (e.g. kitty litter) and then disposed in standard trash.
 - iii. **Terminal amount in a syringe:** For controlled substances dispensed but not used for the reason they were dispensed (e.g. 1 ml left over after the surgeries are complete), the controlled substance agent may be disposed of (or discarded) by any approved route, including denaturation, dissolution, or dispersion. Disposal of unused product must be witnessed by a second individual. The individual disposing of the substance and the witness must both sign the controlled substance log book. The log entry should include what was discarded, when it was discarded, how much was discarded, and who (printed name) discarded and who (printed name) witnessed the disposal.
 - iv. **Patches:** The state and federal DEA are presently re-evaluating their position of proper methods of discarding these items. Until a new decision is reached, please continue discarding patches in the sharps container.

11. Auditing of Controlled Substances:

- a. **Local (laboratory) Auditing of Controlled Substances:** At least quarterly, the registrant (or their designee) should audit the controlled substance cabinet and the records of dispensing. At the conclusion of the audit, the auditor will write in the next open line of the tracking log the following statement:
"Audited on <date> by <print name> and found to be accurate. <signed>
- b. **Institutional Audits:** While licensure is strictly between the registrant and the state and federal agencies, Duke University provides audits to assist the license holder with assuring compliance. The animal program will perform audits of controlled substances as a routine process of animal use oversight. The audits may be performed by members of the IACUC, DLAR, OAWA or other members of the institution's compliance program. These audits focus on accurate and appropriate documentation. The general framework for the program audits is a semi-annual audit at the time of the routine IACUC Semi-Annual inspections, and includes ALL schedules of controlled substances. Additional audits may be performed at more frequent time periods.
- c. **Federal or State Audits:** Effective management of controlled substances by controlling access, recording use, documenting disposal, and auditing the process, decreases the likelihood of a state or federal audit. Federal and state audits may occur at random intervals determined by the state or federal agency.

12. Annual License Renewal: Both the state and the federal agency requires an annual license renewal. Individuals should receive a notice from the state in September of each year reminding them to renew the state license (See appendix to this procedure document). October is the renewal month for all licenses in Durham county, regardless of when in the calendar year the license was initially granted. The federal license is also annual, but is based upon the calendar issuance of the original federal license, which generally will be a month or two after the date the state license was renewed. Procedures for applying for the annual renewal are the same as the original licenses (but a re-inspection of the holding location is not routinely performed).

13. Use of DLAR Technical Services Protocol: In certain cases, researchers may require the use of controlled substances but may not have their license (e.g. the application has been submitted but the license has not been received). It is possible to utilize the DLAR Technical Service Protocol for administration of controlled substances. To use the DLAR Technical Services protocol for controlled substance administration, the researcher must have included such a statement on their approved protocol, or submit an amendment to add DLAR Technical Services to their approved protocol. Contact DLAR for additional details concerning use of the DLAR Technical Services protocol for controlled substance administration to research animals.

APPENDIX A
Example of annual renewal letter



North Carolina Department of Health and Human Services
Division of Mental Health, Developmental Disabilities and Substance Abuse Services
3008 Mail Service Center • Raleigh, North Carolina 27699-3008
Tel 919-733-1765 • Fax 919-733-4665

September 15, 200_

Dear Controlled Substance Registrant:

In accordance with N.C.G.S. 90-101, "Every person who manufactures, distributes, dispenses, or conducts research with any controlled substance within this State or who proposes to engage in any of these activities shall annually, register with the North Carolina Department of Health and Human Services, in accordance with rules adopted by the Commission, and shall pay the registration fee set by the Commission for the category to which the applicant belongs."

Your current DHHS Controlled Substance Registration **expires October 31, 200_**. The enclosed application and your required fee must be received by our office **prior to October 31, 200_**, otherwise your existing DHHS Controlled Substance Registration will expire and the Drug Enforcement Administration (DEA) will be notified that you no longer have a North Carolina Controlled Substance Registration.

If your facility has undergone a physical change of address, please enclose a letter stating the name of your facility, the old address and the new address. You must request a new registration form and return it with the necessary fee to the address listed on the registration form.

If your facility has undergone a change of name only, please enclose a letter stating the old name, the new name and the effective date.

If your facility has undergone a change of ownership, you must request a new registration form and return it with the necessary fee to the address listed on the registration form.

All registrants possessing DEA Registrations must include their DEA Registration Number on the application. Should you have any questions regarding your DEA Registration, please contact the Drug Enforcement Administration in Greensboro at (336) 547-4219.

Should you have any questions concerning your DHHS Controlled Substance Registration or feel you have received this in error please contact the Drug Control Representative at (919) 733-1765.