EVMS
Eastern Virginia Medical School

OFFICE OF RESEARCH
USE OF CONTROLLED SUBSTANCES
IN ANIMAL RESEARCH

I. INTRODUCTION AND POLICY

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 are strictly regulated by the government because of their propensity for misuse. Accordingly, 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. In addition, EVMS desires to ensure the well-being of its animals and legal compliance by its researchers, employees, faculty, and staff when using Controlled Substances. This policy outlines the responsibility of researchers, and others who hold an existing Controlled Substance license, when Controlled Substances are being used for animal anesthesia, analgesia, restraint, or experimentation. The EVMS Office of Research maintains oversight for this policy and failure to abide by this policy, or any federal and state Controlled Substance regulations, may serve as a basis for suspension or termination of the affected animal research protocol by the IACUC, reporting to EVMS compliance officials, and referral to the state and federal licensing authorities.

II. DEFINITIONS

Animal Research: Any animal-related activity, regardless of funding source, including research, testing, teaching, and animal care or use procedures.

Authorized User: An EVMS employee or EVMS 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).

Controlled Substance Binder: The binder 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Disposal: The approved method of discarding Controlled Substances that is outdated, redundant, contaminated, waste, or no longer needed.

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.

CSRC: Controlled Substance Registration Certificate, issued by the Virginia State Board of Pharmacy.

Licensed Practitioner: Any individual that is licensed, registered or otherwise permitted by the DEA and the state of Virginia to dispense or use a Controlled Substance in the course of professional clinical practice.

Public Vendor: Any licensed company or pharmaceutical provided who has a Controlled Substance license for selling Controlled Substances.

Registration: The formal grant of specific authority by the DEA and the state of Virginia.

Registrant: The individual that holds DEA and CSRC 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. Licensed Practitioners must register to perform animal based research using Controlled Substances.

III. PROCEDURE

A. Obtaining a Registration. Individuals who will be working with Controlled Substances in Animal Research must have a CSRC and be licensed by the DEA for use of Controlled Substances in research. **Under no circumstances will Controlled Substances be provided for individuals performing Animal Research under a Licensed Practitioner license.** To obtain a license for research individuals must (should be completed in the order as listed):

1. *Obtain a CSRC.* Complete the Virginia Department of Pharmacy form located at http://www.dhp.virginia.gov/pharmacy/pharmacy_forms.htm.

2. *Obtain a Federal Permit.* You must wait for the Virginia CSRC License number before filing for a federal license. The DEA 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 well in advance of your need.

3. *Complete the Federal 225 Form*. This form can be filed either on-line or by hard copy. The DEA preferred option is to file on-line at http://www.deadiversion.usdoj.gov/drugreg/regapps/onlineforms_new.htm Please note that

Registration requires that federal agents conduct a physical inspection for all Schedule I agents. Physical inspections for Schedule II-V Controlled Substances may or may not be required.

B. Ordering and Receiving Controlled Substances**.**

1. *Ordering.*

a. In accordance with DEA regulations**,** only the Registrant or an individual authorized by the Registrant may order or receive Controlled Substances. A prescription is not required.

b. For compounded substances, Veterinary compounding pharmacies may only sell compounded Controlled Substances to licensed veterinarians or to persons with a legal veterinary prescription. The EVMS attending veterinarian must provide prescriptions to researchers using such compounds. Examples: Buprenorphine SR and Meloxicam SR sold by Zoopharm, Inc. The veterinarian's license number and DEA number will be used with the order. These controlled compounded drugs may only be used on EVMS research animals and the investigator is required to keep track of the drug usage as if it was under his/her DEA license.

c. All Controlled Substances (Schedule I-V) must be shipped directly from the vendor to the Registrant. EVMS Materials Management requires that, as part of the requisition order entry, Registrants must indicate when a product is a Controlled Substance. Such indication will allow EVMS buyers to know that the products need to be shipped directly to the license holder. To do this, select one of the notations below from the "BUYER NOTES" field in OneSource:

(i) "Controlled Substance - Schedule I, II" - For Schedule I and II Controlled Substances. DEA Form 222 is required to be provided by license holder/Registrant. License holder/Registrant must complete the form and send it directly to the vendor, not to Materials Management; or

(ii) "Controlled Substance - Schedule III, IV, V" **-** DEA certificate of license/Registration holder must be on file with the vendor.

2. *Receiving***.** Upon delivery, the receiving individual must:

a. Count and verify the contents of the order received.

b. Keep packing slip on file at the location in which the Controlled Substance is being handled and stored. Send a copy of the packing slip to materials management; and

c. Document and report discrepancies to the seller immediately. Rectify discrepancies prior to using the substances. A copy of the DEA Form 222 may be used to document initial quantities (or quantities added to the cabinet).

C. Use of Controlled Substances in Animal Research.

1. The EVMS Comparative Medicine animal program will assist researchers with advice and counsel on managing the purchase, storage, and use of Controlled Substances for Animal Research. All Controlled Substance use must be in accordance with the IACUC-approved animal research protocols, or under accepted clinical veterinary guidelines if prescribed by an EVMS veterinarian.

2. 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. Dispensing data must be kept in a Controlled Substance Binder, any written (paper) recording system may be used, but a bound book rather than loose leaf is recommended overall and, a bound book is required for Schedule I substances. Dispensing data must include:

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. Name of 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, and

m. Quantity remaining in the vial / bottle / box.

D. Labeling and Storage.

1. *Labeling***.** Controlled Substances shall be labeled as follows:

a. Each bottle (or box) of Controlled Substances must be individually identified by a unique (not re-used) number and must be placed on the product immediately upon receipt.

b. Original packaging showing the product information should be used when possible.

c. Controlled Substance 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 Substance, 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).

d. 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:

(i) the name of the Controlled Substances,

(ii) the lot number (or tracking number) of the product,

(iii)the date opened,

(iv)the final concentration,

(v) the amount per container, and

(vi)the expiration date (not more than 30 days after dilution date).

2. *Storage*. Controlled Substances must be stored:

a. In 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) or a locked inner cabinet in a locked cabinet; and

b. Using cipher locks (combination locks) or using key locks provided that the two key locks are keyed differently, the two keys are not stored together (i.e. not on the same key ring), both keys are safeguarded, and not in public sight and individuals with access to the keys may have to be approved by state and federal agencies.

E. Transfer of Controlled Substances 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.

F. Auditing Controlled Substances.

1. *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>"

2. *Federal or State Audits:* Federal and state audits may occur at random intervals determined by the state or federal agency. 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.

G. 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 Office of Research 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 Office of Research will assist the Registrant with reporting. The goal of this partnership is to protect the Registrant and assist is accurate and timely reporting of required information.

H. Disposal. Registrants must adhere to all federal, state and local regulations when disposing of Controlled Substances and shall follow the procedures below for disposal.

1. For all Controlled Substances:

   a. Empty Controlled Substance bottles should have the cap removed and be placed in a sharps container to prevent the illegal use of *de minimis* amounts in an empty bottle.

   b. To dispose of Controlled Substances (e.g. expired, waste, or contaminated):

      (i) the Registrant or his/her designee shall complete DEA Form 41. Form 41 is located at: http://www.deadiversion.usdoj.gov/21cfr_reports/surrend/index.html. You are not required to submit this form to DEA, unless requested to do so. This form must be kept as a record of destruction and be available by the registrant for at least two years in accordance with 21 U.S.C. 827.Contact EVMS Environmental Health and Safety to arrange for disposal of the Controlled Substance. An EH&S Safety Officer will contact EVMS Police and Public Safety to arrange for a Police Officer to be present to co-witness the disposal of the Controlled Substance into a marked and labeled waste container that contains at least one gallon of waste solvents. When the container is full, EVMS EH&S will arrange for the hazardous waste to be collected by a qualified waste management company for delivery to a licensed incineration facility for disposal.

c. For Controlled Substances that have been dispensed, but not used for the reason they were dispensed (e.g. 1 ml left over after the surgeries are complete:

(i) the Controlled Substance may be disposed of (or discarded) by any approved route, including denaturation, dissolution, or dispersion and the container of such substances should be placed in a sharps container.

(ii) the 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.