

 <p>Institutional Animal Care and Use Committee Guiding Principles and Procedures</p>	<p>Effective: 10/18/2018 Revised: 1/17/2019</p>
<p>Title: Pharmaceutical Management</p>	<p>Page 1 of 7</p>

Guiding Principle

The use of animals in research and teaching is a privilege granted to institutions, investigators, staff, and students that commit to meeting high ethical and regulatory standards. It is the responsibility of the NDSU IACUC to mandate proper pharmaceutical management for the use, documentation, and storage of all drugs and medical supplies used in live vertebrate animals. All drugs and medical supplies must be stored, labeled, and disposed of according to the procedures outlined in this Guiding Principle.

Requirements

DEA, This document which adheres to Title 2 United States Code (USC) Controlled Substance Act <http://www.deadiversion.usdoj.gov/21cfr/index.html> Title 21, CFR Section 1301.71(a), requires that all registrants provide effective controls and procedures to guard against theft and diversion of controlled substances.

USDA APHIS/AC Policy 3 the use of expired materials such as pharmaceuticals on regulated animals is not considered to be acceptable veterinary practice and is not consistent with adequate veterinary care as required by the regulations promulgated under the Animal Welfare Act.

PHS Policy, U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training:

V. Procedures with animals that may cause more than momentary or slight pain or distress should be performed with appropriate sedation, analgesia, or anesthesia.

IX. Where exceptions are required in relation to the provisions of these Principles, the decisions should not rest with the investigators directly concerned but should be made, with due regard to Principle II, by an appropriate review group, such as an institutional animal care and use committee. Such exceptions should not be made solely for the purposes of teaching or demonstration.

Guide for the Care and Use of Laboratory Animals, ILAR, NAS, Eighth Edition 2011, pg 31: The use of pharmaceutical-grade chemicals and other substances ensures that toxic or unwanted side effects are not introduced into studies conducted with experimental animals. They should therefore be used, when available, for all animal-related procedures (USDA 1997b). The use of non-pharmaceutical-grade chemicals or substances should be described and justified in the animal use protocol and be approved by the IACUC (Wolff et. al. 2003).

Procedures

1. Expired Drugs and Medical Supplies

1.1. The use of expired drugs and medical supplies is considered an unacceptable veterinary practice and therefore prohibited.

2. Pharmaceutical Grade Drugs/Reagents

2.1. Only pharmaceutical grade drugs (includes reagents, compounds, diluents, fluids) should be used on animals in research or instruction unless otherwise justified, reviewed, and approved by the IACUC.

2.1.1. Definition-Pharmaceutical grade compound: a drug, biologic, reagent, etc. which is approved by the Food and Drug Administration (FDA) or for which a chemical purity standard has been written/established by the United States Pharmacopeia (USP), National Formulary (NF), or British Pharmacopeia (BP).

2.1.2. When developing and reviewing a proposal to use non-pharmaceutical grade components and/or investigational drugs where the grade and formulation is not known the investigator and the IACUC should consider the following:

- Animal welfare and scientific issues related to the use of the compounds.
- Potential for contamination, safety, efficacy, and the introduction of research variables

2.1.3. For all compound use, the investigator and IACUC should consider the following:

- The grade/purity being proposed.
- The formulation of the final product.
- Issues related to sterility, pyrogenicity, stability, pH, osmolality, site/route of administration, pharmacokinetics, physiological compatibility, and quality control.

3. Labeling

3.1. Secondary Containers-at times it may be necessary to place drugs and other medical treatment products into a secondary container (e.g. iodine into a spray bottle, drug cocktail mixture)

3.1.1. All secondary containers must be labeled with the following information:

- Content(s) Name

- Concentration
- Date Constituted
- Expiration Date
- Lot number (if available)
- Initials of individual placing substances into secondary container

3.2. Drug Cocktails/Compounded Products-are products in which the drug dosage form is changed (e.g. mixing 2 drugs together). Drug cocktails must be labeled with the following information:

- Drug Names
- Concentrations
- Date Constituted
- Lot number (if available)
- Beyond Use Date (This date can only be determined by a compounding pharmacist)
- Name of Compounding Pharmacist

3.3. Medical supplies/products without expiration date

3.3.1. Medical supplies/products (shampoo, soap, etc.) without an expiration date must be labeled with the date received. The expiration date will be one (1) year from the date received.

3.3.2. Medical supplies/products considered to be a durable good (gauze squares, cotton balls, etc.) without an expiration date must be labeled with the date received. Durable goods without an expiration date should be discarded when the integrity of the item has become compromised (color change, etc.)

4. Storage and Inventory (Controlled Substances-See Section 6)

4.1. All drugs should be kept in a secure area.

4.1.1. Do not store controlled and uncontrolled drugs in the same primary storage container.

4.2. Limit the number of personnel who have access to secured drugs.

4.3. Establish a system for inventory control:

- Employ regular inventory schedule-recommend bi-monthly.
- Minimize the amount of drugs that are kept in inventory to avoid drugs expiring.
- Place all expired drugs and materials in a clearly labeled (e.g. EXPIRED-Do Not Use) container prior to disposal or pickup.

5. Discarding Expired Drugs (For Controlled Substances -See Section 6)

5.1. Dispose of remaining drug contents by expelling into an absorbable material such as blue absorbent pads, coffee grounds, kitten litter, or other chemical absorbent material and then place into covered waste container.

5.2. Black out the name of the drug on the container.

5.3. Place the empty bottle into a sharps container or a glass disposal container.

5.3.1. Do not pour drugs/chemicals/compounds down the sink or into any other drain that flows into the sewer.

5.3.2. For large amounts of drug disposal, chemicals, or other compounds, please contact the NDSU Safety Office for additional guidance and instructions.

6. Controlled Substances

6.1. A controlled (scheduled) substance is one whose use and distribution is tightly controlled because of its abuse potential or risk.

6.2. Controlled substances are rated in the order of their abuse risk and placed in [Schedules by the DEA](#) (Drug Enforcement Agency).

6.2.1. The substances with the highest abuse potential are placed in Schedule 1, and those with the lowest abuse potential are in Schedule V.

6.3. Registration-According to the [Drug Abuse Prevention and Control Act of 1970](#)-any person who will utilize a controlled substance in their research or practice, shall obtain annually a DEA registration. Therefore any researcher seeking to use a controlled substance in his/her research must obtain and maintain a DEA registration.

6.4. Registration procedures -follow federal regulations as indicated below.

6.4.1. New applicants, who do not currently possess a DEA license to conduct business with controlled substances in the following categories must apply for a DEA registrations using Form [225](#) and [225a](#) for renewal. DEA Registration Applicants must also have authorization from the [North Dakota State Board of Pharmacy](#).

6.4.1.1.1. North Dakota Requirements: Researchers are required to provide a Researcher Request for State Authorization to Obtain DEA Registration letter to the North Dakota State Board of Pharmacy. The letter must include the following:

- A copy of researcher protocols including IRB and IACUC approval if using human or animal subjects.
- A list of controlled substances that will be used and approximate quantities of each that will be used on an annual basis and the quantity that will be on inventory at one time.
- The address at which controlled substances will be stored.
- The security requirements that will be employed for storage.
- A list of individuals that will have access to the controlled substances and how usage will be recorded.

- A list of anticipated suppliers, their address and DEA Registration.

6.4.1.1.2. Exemption from DEA application fee applies to federal, state, or local government official or institution. The applicant's superior or agency officer must certify exempt status. The signature, authority title, and telephone number of the certifying official must be provided. The certifying official for NDSU is the VP for Research and Creative Activity.

6.4.1.1.3. Online application forms are available at:

<http://www.deadiversion.usdoj.gov/drugreg/index.html#1>

6.5. Controlled Drug Ordering

6.5.1. To order schedule I or II controlled substances [registrants](#) will need to submit a [DEA form 222](#) with the order.

6.5.1.1. The supplier will complete the packages shipped and date shipped columns on the 222 form.

6.5.1.2. When the shipment is received the registrant will complete the packages received and date received columns of the 222 form.

6.5.1.3. Individuals that have been identified as delegates may order schedule II controlled substances for a registrant ONLY if a [power of attorney](#) form is fully signed and in place.

6.5.2. To order schedule III-V controlled substances a 222 form is not required; Registrants should sign/initial and date the invoice. The invoice will need to be maintained and available for inspection and copying for at least 2 years.

6.6. Audits: registrants or delegates are encouraged to perform weekly to monthly audits of controlled substance inventories to accurately track inventory and avoid discrepancies. Inventory records must also be maintained and available for inspection and copying for at least 2 years.

6.6.1.1. Audits must be dated and include the signatures of the registrant/delegate and a witness.

6.7. Drug Receipt/Disposition Records/Usage Logs must be maintained for all controlled substances.

6.7.1. All controlled substance records must be retained for a minimum of two years according to [DEA 21CFR](#).

6.7.1.1. Records include: inventory forms, DEA form 222s, invoices, usage logs, DEA form 106 (Drug Theft/Loss), DEA form 41 (Record of Controlled substances Destroyed)

6.7.1.2. Records management is the responsibility of the DEA registrant.

6.7.2. DEA Regulations require a biennial inventory. Perpetual inventory records can be labeled with the biennial inventory date and attached to the biennial inventory form.

6.7.3. A Drug Disposition Record is required for each controlled substance on hand and must document the **receipt, administration, and disposal** of each of those drugs.

6.7.3.1. For each drug, the disposition record must reflect the **total volume of drug on hand.** (e.g. 10-10ml. bottles of Ketamine=100 ml) For each use deduct from the total volume on hand.

6.7.3.2. A witness must be present and initial the log to attest that the drug was legitimately disposed of.

6.8. Proper Storage of Controlled Substances

6.8.1. Controlled Substances should be stored under double lock and key separate from other (uncontrolled/unscheduled) drugs.

6.8.2. Store in **double lock safe** constructed of tamper proof material. Options include:

6.8.2.1. Store in a **locked box** in a **locked drawer**, with the keys stored in a secondary location.

6.8.2.2. Store in a **locked drawer** in a **lab or office that remains locked** at all times when not occupied, with keys stored in a secondary location. (The “locked room” must always be locked when it is not occupied by either the registrant or authorized user.)

6.8.3. Controlled substances must be stored in the physical location registered with the DEA (i.e. address on the DEA registration must match the address of the location where controlled substances are stored).

- Drugs may be removed for up to 24 hours from the registered storage location for use in facilities and treatment rooms. (For more information about the registered storage locations on file please contact the IACUC Office or DEA).
- Schedule I and II controlled substances must be stored separately from Schedule III-V substances. The separation may be a divider in a drawer or different shelf within a storage unit.
- Compounded solutions containing controlled substances prepared within the laboratory should be labeled with: name of controlled substance(s), lot number(s), date vial was opened/prepared, final concentration(s) and amount(s) per container, and expiration date of <7 days unless product stability data suggests otherwise.

6.9. Disposal of expired or unused stock of controlled substances

6.9.1. Smaller Amounts:

6.9.1.1. In the presence of a witness expel the remaining contents of the drug into an absorbent disposable paper or cloth and place into a garbage container.

- 6.9.1.2.** Record the amount of drug disposed of in the controlled drug log including the signatures of the person disposing of the drug and the witness.
 - 6.9.1.3.** Complete DEA form 41.
 - 6.9.1.4.** Black out the name of the drug on the label.
 - 6.9.1.5.** Place the empty bottle into a sharps container or a glass disposal container.
- 6.9.2.** Larger Amounts:
- 6.9.2.1.** To dispose of larger amounts of expired or unused controlled drugs contact the IACUC Office.

6.10. For information on obtaining forms and assistance please contact the following field office for North Dakota:

Minneapolis Diversion Control Office
100 Washington Ave. S.
Suite 800
Minneapolis, MN 55401
Phone (612)-344-4136