

University of Colorado at Boulder, Office of Research Integrity Institutional Animal Care and Use Committee

SOP #10

Title: Use of Drugs, Solution and Materials in Animals

Background and Purpose

This SOP describes requirements for using non-expired, pharmaceutical grade drugs and materials, and describes procedures for preparation, labeling, inventorying, and disposal of drugs with research animals in order to be in compliance with the Animal Welfare Act [1] and Regulations [2] and the USDA Policies, the PHS Policy [3], NIH Guidelines, and the 8th edition of the Guide for the Care and Use of Laboratory Animals.

Procedures

- A. Pharmaceutical-grade chemicals and other substances must be used to avoid toxicity or side effects that may threaten the health and welfare of vertebrate animals and / or interfere with the interpretation of research results [4].
 1. Procedures that may cause more than momentary or slight pain or distress to the animals must be performed with medications, sedation, analgesia, or anesthesia agents that are veterinary or human pharmaceutical-grade compounds, unless the use of an investigational chemical or formulation is scientifically necessary, appropriately justified, and approved by the IACUC. The use of a non-pharmaceutical-grade euthanasia agent must meet the same standards [5].
 2. Investigators must use pharmaceutical-grade medications whenever they are available, even in acute procedures. The use of the drug must be listed in the protocol or addendum and reviewed and approved by the IACUC before use.
- B. Exceptions allowing use of Non-Pharmaceutical-grade chemicals and other substances.
 1. Test compounds and experimental agents are used in research and generally classified as non-pharmaceutical grade compounds without an acceptable pharmaceutical grade alternative.
 2. Diluents do not need to be pharmaceutical grade
 3. Requests to use non-pharmaceutical grade chemical compounds must be explicitly approved by the IACUC, based on an evaluation of:
 - Scientific necessity;
 - Non-availability of acceptable veterinary or human pharmaceutical-grade compound(s); and
 - The PI must address any aspect of a non-pharmaceutical grade compound that may have adverse effects on the animal.
 - Principal investigators must use all available knowledge of the compounds to ensure that preparation, evaluation, storage, use, and disposal standards are maintained.
 4. Cost savings is not an adequate justification for using non-pharmaceutical grade compounds in animals.
 5. The IACUC is responsible for evaluating the potential adverse consequences of non-pharmaceutical grade compounds [6] based on criteria that include:
 - Safety and efficacy,
 - grade and purity,
 - Physiological compatibility (i.e. sterility, acid-base balance pyrogenicity,, osmolality, stability)
 - site and route of administration,

- compatibility of components,
 - side effects and adverse reactions,
 - storage,
 - pharmacokinetics, and
 - the inadvertent introduction of research-complicating variables
- C. Preparation and Labeling of All Drugs (pharmaceutical and non-pharmaceutical grade)
1. Preparation of drug mixtures used in live animals must be conducted under sterile conditions. Unused reagent **must** be discarded through the EH&S hazardous waste program (see EH&S guidance on disposal of controlled substances and other pharmaceuticals).
 2. All injected compounds and diluents must be sterile when used for animal procedures.
 3. All drugs, dilutions, and mixtures must be clearly labeled with compound names, concentrations, and date of opening or preparation.
 4. For common surgical suites, medical materials and supplies with expiration dates and used in live animals should be individually labeled with the investigator's name. If items are not individually labeled, they must be kept in a drawer, bin, cabinet or other container clearly labeled with the principal investigator's name.
 5. The animal facility manager for animal facility shared procedures rooms shall be authorized to discard materials which do not indicate the name of the owner whether or not they have reached their expiration date.
- D. Use of drugs within their expiration date and exceptions
1. The use of expired pharmaceuticals, biologics, and supplies (e.g. syringes with expiration dates) is not consistent with acceptable veterinary practice or adequate veterinary care [4, 7]. No euthanasia, anesthesia and analgesia agents, emergency drugs and medications for veterinary care (e.g. antibiotics for infection prophylaxis) can be used beyond their expiration date under any circumstances, even if a procedure is terminal; no exceptions will be allowed [8].
 2. For all other expired materials, exceptions must be reviewed and approved by the IACUC through a full committee review before the expired material can be used. The committee will consider the following during a review:
 - Species and procedures: For USDA-covered species, only acute terminal procedures will be considered for using expired materials where an animal is put under anesthesia and the animal is euthanized without ever waking up.
 - Justification: medical materials may be used beyond their expiration date if the manufacturer verifies efficacy beyond the expiration date, or the investigator is able to document to the satisfaction of the IACUC that such use does not adversely affect the animal's wellbeing or compromise the validity of the scientific study. For such justification, the investigator should be prepared to verify efficacy of the drug.
- E. Drug Inventory for ensuring use within the expiration date
1. All expired drugs, including anesthetics and analgesics, must be separated from other materials and properly discarded on or before their date of expiration.
 2. Establish an inventory system which minimizes the amount of drug or medical supplies on hand.
 3. Perform regular monthly checks of your inventory and discard all expired drugs or medical materials.
 4. Contact your suppliers to see if they will accept the return of some expired drugs or medical supplies for credit.
- F. Storage

1. As a recommendation, store all drugs in one location as practical (to make checking easier). Lock all controlled drugs in accordance with the UCB Policy on the use of Controlled Substances
<http://www.colorado.edu/VCResearch/integrity/substance.html>
2. Expired drugs and medical materials may be maintained in the laboratory for non-animal use provided they are:
 - **Clearly labeled “NOT FOR USE IN ANIMALS” if kept in the vicinity of drugs currently for animal use”**
 - Stored in an area physically separate from supplies intended for live-animal use. Whenever possible, expired materials should be stored in an area where live animals are never used.

G. Record-Keeping

1. Inventory procedures are **required** for DEA-controlled substances. See <http://www.colorado.edu/VCResearch/integrity/substance.html>
2. The IACUC **recommends** that each laboratory establish an inventory procedure for all drugs, regardless of whether they are DEA controlled, to facilitate the identification and discarding of expired drugs.
3. Consider assigning the inventory responsibilities to one specific individual, with another individual assigned as backup.

H. Disposal of Drugs

1. Regardless of age, solutions should be discarded if changes in color and/or precipitation occur.
2. Dilutions and mixtures of drugs may change their stability. All drug dilutions and mixtures must be discarded after one month from the date of preparation regardless of original drug expiration date. The only exceptions **are** if the preparations are done in accordance with drug manufacturer’s instructions, **or** the drug-specific manufacturer-supplied diluent is used. In both cases the drug must be used within the manufacturer’s expiration date.
3. Disposal of Expired drugs:
 - Place all expired drugs and medical materials (e.g. Syringes with expiration date) in a clearly labeled container while they await pickup for disposal or return to manufacturer. Proper disposal of expired drugs is the responsibility of the Lead Researcher. See “Disposal of Drugs below”.
 - **EXCEPTION:** Controlled Substances have specific requirements for locked storage; expired Controlled Substances should be discarded as soon as possible after the expiration date.
4. Disposal services:
 - Non-DEA-controlled drugs and solutions must be disposed through the EH&S hazardous waste program by completing a hazardous material/waste tag. If you have any questions, call: 303-492-7845
 - Controlled substances can be disposed at no cost to the investigator by calling the EH&S Hazardous Materials Program Manager Mark Lapham at 303-492-8531; mark.lapham@colorado.edu For more details see the EH&S guidance document on “Disposal of controlled substances and other pharmaceuticals”.

For questions about this standard operating procedure, call the Institutional Animal Care and Use Committee office at 303-492-8187.

References

1. Animal Welfare Act, 7 USC Chapter 54, Section 2143(a)(3)(A)
2. Animal Welfare Regulations, 9 CFR Chapter 1, Subchapter A, Part 2, Subpart C, Section 2.33(b)1-5
3. PHS Policy IV, C, 1, a-b.
4. OLAW FAQs, F. Animal Use and Management
http://grants.nih.gov/grants/olaw/faqs.htm#useandmgmt_5
5. NIH Position statement on non-pharmaceutical grade compounds, May 2012:
http://grants.nih.gov/grants/olaw/positionstatement_guide.htm
6. NIH Office of Laboratory Animal Welfare: <http://grants.nih.gov/grants/olaw/faqs.htm#f4>
7. USDA policy 3 Veterinary Care, issued March 25, 2011
http://www.aphis.usda.gov/animal_welfare/policy.php?policy=3
8. Guide for the Care and Use of Laboratory Animals Page 122, 8th edition:
<http://grants.nih.gov/grants/olaw/Guide-for-the-Care-and-Use-of-Laboratory-Animals.pdf>