

University of Louisville
Institutional Animal Care and Use Committee
Policies and Procedures

Use of Pharmaceutical-Grade Medications and Outdated Drugs or Supplies

Policy: Pharmaceutical grade medications must be used whenever they are available, including for non-survival procedures or euthanasia. The use of expired medical materials such as drugs, intravenous fluids, and supplies, including materials used for *in vitro* assays that might impact animal treatment or disposition, is prohibited unless specifically approved by the IACUC. Expiration dates on such materials must be monitored, and materials disposed of appropriately to avoid their accidental use. The IACUC recommends that each laboratory establish an inventory procedure to facilitate the identification and removal of expired drugs and materials utilized for research purposes involving animals.

Rationale: The use of expired medical materials in animal research is not considered to be acceptable veterinary practice as required by the PHS Policy and Animal Welfare regulations, because manufacturer's guarantees do not extend to expired materials. *The Guide for the Care and Use of Laboratory Animals* also states that "Agents that provide anesthesia and analgesia **must** be used before their expiration dates and should be acquired, stored, their use recorded, and disposed of legally and safely." Therefore, it should be considered a scientific as well as veterinary care imperative to use pharmaceutical-grade material and only while "in-date." Data obtained from *in vitro* assays are often used to determine treatment or humane endpoints; therefore, materials used in such assays should also be used while "in-date."

Definition: A *drug* is considered any substance or chemical, with the exemption of food items normally consumed by the applicable species, designed to be administered by injection, inhalation, topical application, ingestion, electroporation or suppository that is intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in research animals.

Procedures, Guidelines, and Exceptions:

I. Medications (Anesthetics, analgesics, therapeutic agents, drugs, etc.)

A. Pharmaceutical Grade

1. Pharmaceutical grade medications must be used whenever they are available, including for non-survival procedures and euthanasia.
2. Exceptions for use of non-pharmaceutical grade (*i.e.*, chemical-grade) medications may be allowed after review and approval by the IACUC. Requests for exceptions must be submitted in writing as a part of an approved *Proposal*.
 - a. All non-pharmaceutical-grade medications must be identified as such in the *Proposal*.
 - b. A justification for the use of each agent must be included. If a pharmaceutical grade equivalent is not available, then that is adequate justification, however if a pharmaceutical grade equivalent is available, then scientific justification for not using the pharmaceutical grade formulation must be provided in the *Proposal*. Cost-savings alone is not an adequate justification for using non-pharmaceutical grade medications.

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- c. For each of the non-pharmaceutical grade products consideration in writing should be given to the quality of the material (grade, purity, *etc.*), methods of ensuring sterility and physiological compatibility (pH, pyrogenicity, osmolality, *etc.*), expected shelf-life (stability, expiration date or discard timeframe that will be used), site and route of administration, and effectiveness (pharmacokinetics, *etc.*) of the chemical or substance to be administered, as well as any potential animal welfare and scientific issues relating to its use.

B. IACUC Approved Exceptions to the Use of Pharmaceutical Grade Medications

1. Due to limited or unavailability of some pharmaceutical grade (USP) drugs and medications in appropriate concentrations or formulations for various species the IACUC has approved the following drugs for use without the need to provide written consideration as described above. This improves animal welfare by decreasing the volume that needs to be administered and/or improving the palatability of the drug or medication. These specific drugs do not need to be listed or justified in the Non-Pharmaceutical grade drug section of individual IACUC proposals, but must still be listed in the “Anesthetics, Analgesics and Other Therapeutic Agents” section of an approved IACUC proposal.
 - a. **Injectable Drugs or Medications**

The following injectable drugs or medications in various concentrations from ZooPharm Compounding Pharmacy that provide concentrations more appropriate for the species to reduce the volume administered to the animal and are not available as USP in this concentration or are not available as USP.

 - i. Buprenorphine SR
 - ii. Ketamine
 - iii. Medetomidine
 - iv. Azaperone
 - b. **Oral Drugs or Medications**

The following oral drugs or medications in various concentrations from Wedgewood Compounding Pharmacy that are not available in an oral formulation as USP, or not available in an appropriate concentration for the species, or that are flavored to make the administration more palatable and less stressful for the animals.

 - i. Famotidine
 - ii. Prednisone
 - iii. Omeprazole
 - iv. Metronidazole
 - v. Folic acid
 - vi. Furosemide
 - c. **Medicated Feed Additives**
 - i. Neomycin Oxytetracycline for swine to prevent, control and/or treat diarrhea due to adventitious pathogens. This is not available as USP. If a Comparative Medicine Research Unit (CMRU) veterinarian has prescribed this for swine, it does not need to be listed in an approved IACUC proposal.
 - ii. Tylosin 40 for swine to prevent, control and/or treat diarrhea due to adventitious pathogens. This is not available as USP. If a CMRU veterinarian has prescribed this for swine, it does not need to be listed in an approved IACUC proposal.
 - iii. Carbodox type C medicated feed for swine to control/prevent vibronic dysentery and bacterial enteritis in young animals. Available as a commercial product Purina Ultracare

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CX50 which combines a complete starter ration for young animals with 50 grams/ton of carbadox. This is not available as USP. If a CMRU veterinarian has prescribed this for swine, it does not need to be listed in an approved IACUC proposal.

C. Expired Medications, Drugs, Biologics

1. The use of expired pharmaceuticals, drugs, biologics, and supplies is not consistent with acceptable veterinary practice or adequate veterinary care and is prohibited.
2. Euthanasia, anesthesia and analgesia agents **must not** be used beyond their expiration date, even if a procedure is terminal. Other expired materials **must not** be used unless the manufacturer verifies efficacy beyond the expiration date **and** the use of this material is approved by the IACUC in an IACUC *Proposal*.
3. Special precautions and procedures for disposal of expired DEA controlled substances must be followed as per Department of Environmental Health and Safety (DEHS) policies and **must be labeled as per Section III** prior to discarding.
4. All expired medications or chemicals must be discarded in compliance with DEHS standards. Items that are expired and have not yet been discarded **must be labeled as per Section III**. Expired medications will be discarded by the IACUC immediately if found during inspections or with assistance of DEHS in compliance with these standards.
5. All expired medications (**that are not clearly labeled as per Section III**) in animal research settings that are found by or reported to the IACUC will be reviewed at the subsequent IACUC meeting and will be handled in the following progressive manner:
 - a. After consideration of the circumstances and the drug(s), the committee will levy a fine of \$25 for the first incident and the Principal Investigator (PI) will be required to submit a laboratory corrective action plan to the IACUC, as well as undergo training with the Chair of the IACUC and Attending Veterinarian.
 - b. For a second incident within 3 years, the fine will be extended to \$50 per incident or \$25 per item as determined by the committee.
 - c. For a third incident within the same 3-year period, the fine will be extended to \$100 per item.
 - d. For a fourth incident within the same 3-year period, the committee will consider suspension of the approved protocol(s).
 - e. For all incidents involving **anesthetics, analgesics or euthanasia agents**, the IACUC will levy a fine of \$100 per item in addition to the above items.
 - f. For all incidents of expired medications, the IACUC will appoint representative(s) to visit the laboratory or area unannounced prior to the subsequent semi-annual IACUC inspection and any expired medications found then will be handled according to I. C. 5. a-e as listed above.
 - g. Fines will be issued to the PI and reported to all Investigators on the *Proposal(s)* and the Department Chair. All fines will be billed through CMRU.

II. Materials (fluids, sutures, catheters, diagnostic strips, etc.)

- A. The use of expired medical materials (fluids, sutures, catheters and other supplies) in animal research is not considered acceptable veterinary practice as defined by the Animal Welfare regulations and PHS Policy. Exceptions may be granted for use of such materials generally for *non-survival* procedures only, although re-sterilization may be deemed acceptable for survival procedures. Use of such materials must be approved by the IACUC in an IACUC *Proposal*. If such usage is approved by the IACUC, expired supplies must be conspicuously labeled with the appropriate IACUC

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number(s) and the terms “Expired,” and “for non-survival use only,” and stored in a physically separate location from non-expired materials to avoid accidental use in survival procedures.

- B. The use of expired materials employed in diagnostic assays (glucose test strips, blood collection tubes, *etc.*) is not considered acceptable veterinary practice as the information obtained from such assays is often used to determine treatment regimens or to identify humane endpoints. Use of expired materials for other reasons and the storage of expired materials within the CMRU Facilities is strongly discouraged. If such materials are kept, they should be conspicuously labeled with the appropriate IACUC number(s) and the term “Expired – Not for Animal Use” **and** stored in a physically separate location from non-expired materials to avoid accidental use in diagnostic assays that might impact animal health and well-being.
- C. Exceptions to the use of expired medical materials may be granted by the IACUC on a case-by-case basis. Requests for exceptions must be submitted in writing as a part of an approved *Proposal*.

III. Labeling of Expired Medications, Drugs, Chemicals, or Materials

- A. All expired medications, drugs, chemicals or materials should be immediately discarded unless they require special disposal methods such as chemicals or controlled substances.
- B. If items cannot be immediately discarded, they must be clearly labeled “Expired - Do Not Use” **and should be stored** physically separated from other “in date” medications, drugs, chemicals, or materials until they can be properly disposed of. This includes items that are approved by the IACUC for non-survival procedures.
- C. Expired controlled substances should be stored in a separate locked location than “in date” items.
- D. For expired medications, drugs, and chemicals disposal, the [Department of Environmental Health and Safety Waste Disposal](#) Guide, Section 6.6 for Non-DEA Controlled Expired Pharmaceuticals and Section 6.7 for DEA Controlled Substances, should be followed. To arrange for proper disposal of Non-DEA controlled pharmaceuticals (i.e. Isoflurane, Povidone-iodine, etc), lab personnel will submit for DEHS pick up via online Chemical and Hazardous Waste Pick Up request form at <https://louisville.edu/dehs/waste-disposal>. If user encounters any difficulty with online form access, call DEHS at 852-6670.

To schedule a DEA-controlled substance(s) on-site destruction, DEA registrant or DEA-registrant authorized agent shall call DEHS at 852-6670 or email dehsih@louisville.edu, subject line “DEA Controlled Substance Destruction Request”.

IV. Medications, Drugs, Chemicals or Materials Stored Within CMRU Vivaria (Animal Facilities)

- A. Medications and materials stored within CMRU vivaria must be appropriately labeled with PI name and according to IACUC Policy: [Use and Labeling of Drug Compounds, Dilutions, and Chronic-Use Fluids](#).
- B. Items that are not appropriately labeled will be discarded by CMRU staff.
- C. Items that are expired will be discarded by CMRU staff and reported to the IACUC.

References:

1. USDA APHIS Animal Care Resource Guide Policies, (https://www.aphis.usda.gov/animal_welfare/downloads/Animal%20Care%20Policy%20Manual.pdf)
2. USDA APHIS Animal Welfare Regulations, 9 CFR § 2.33 (2008).

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3. NIH OLAW FAQ F. 4, “May investigators use non-pharmaceutical-grade substances in animals?”
(<https://olaw.nih.gov/faqs#/guidance/faqs?anchor=50361>)
4. NIH OLAW FAQ F.5, “May investigators use expired pharmaceuticals, biologics and supplies in animals?”
(<https://olaw.nih.gov/faqs#/guidance/faqs?anchor=50361>)
5. Public Health Service Policy on the Humane Care and Use of Laboratory Animals, Section IV., OLAW.
6. National Research Council. Guide for the Care and Use of Laboratory Animals. 8th Ed. Washington, DC: National Academies Press, 2011. 6. Federal Food, Drug and Cosmetic Act, 21 USC § 321 (2013).

Additional Information:

1. NIH Guidelines for the Use of Non-Pharmaceutical Grade Compounds in Laboratory Animals. Approved 4/28/2021 (https://oacu.oir.nih.gov/system/files/media/file/2021-06/b14_pharmaceutical_compounds.pdf)
2. NIH Guidelines for the Select Use of Expired Medical Products. Approved 1/26/2022
(https://oacu.oir.nih.gov/system/files/media/file/2022-01/b15_expired_medical_products.pdf)