

University of Southern California *Institutional Animal Care and Use Committee*

Non-Pharmaceutical Drugs and Compounds

A. Background

To define the expectation regarding the use of non-pharmaceutical grade drugs and compounds in research animals.

B. Definitions

Pharmaceutical Grade Compound Drug: any active or inactive drug, biologic or reagent which is approved, conditionally approved, or indexed by the Food and Drug Administration (FDA).

Non-Pharmaceutical Grade Compound Drug: anything that does not meet the above definition or criteria. An example is a **bulk chemical agent** such as those obtained from Fisher Scientific or Sigma-Aldrich which may be chemically identical to their pharmaceutical grade counterparts, but do not conform to recognized standards for purity.

Compound Drug: drugs that are combined, mixed, diluted, or otherwise altered from their original form to meet the needs of a particular animal. An example is Ketamine/Xylazine mixture for use in rodent anesthesia induction.

C. Applicability

The *Guide for the Care and Use of Laboratory Animals*, the Office of Laboratory Animal Welfare (OLAW), and the United States Department of Agriculture (USDA) all state that the use of pharmaceutical grade drugs, compounds, chemicals, and biologics must be used in laboratory animals. This ensures that toxic or unwanted side effects are not introduced into studies conducted with experimental animals. Since chemical grade compounds are not specially formulated for pharmaceutical use, they can compromise the health of the animals and validity of the study. These standards are used by manufacturers to help ensure the products are of the appropriate chemical purity and quality, in the appropriate solution or compound, to ensure stability, safety, and efficacy.

This includes anesthetics, analgesics, and any substances administered experimentally, and include non-survival or acute studies.

D. Policy

The use of non-pharmaceutical grade compounds is **not allowed**. If the use of non-pharmaceutical compound is required for experimental reasons, they must be described and scientifically justified in the animal use protocol and be approved by the IACUC. Examples of justification may include but are not limited to the following:

- No equivalent pharmaceutical grade veterinary or human drug is available.
- A pharmaceutical grade drug is available, but is not compatible with the formulation, concentration, delivery, or vehicle required for experimental research purposes.
- The non-pharmaceutical grade compound is needed to replicate or compare methods of previous studies or other peer reviewed research.

Cost savings is not ordinarily adequate justification for using non-pharmaceutical grade drugs or compounds in lieu of pharmaceutical grade.

Non-pharmaceutical grade compounds must be detailed and described for the method of preparation of the compound, grade, purity, sterility, pH, pyrogenicity, osmolality, and pharmacokinetics as applicable.

Compounds such as drugs that are combined, mixed, diluted, or otherwise altered from their original form must be prepared with pharmaceutical grade compound or drug. An example is Ketamine/Xylazine mixture or diluted ketoprofen or Carprofen mixtures.

- a. Preparation and handling
 - i. Single use sterile sealed containers such as multi-dose vials must be used. Non-sterile snap top, screw top, or conical tubes may not be used.
 - ii. Use a single use sterile needle to prepare vial and draw from vial.
- b. Labeling of vials
 - i. Name of all the drugs contained within
 - ii. Concentration of the drug (Mg/mL)
 - iii. Date of expiration (see below)
 - iv. Specific Controlled Substances Identifying Code (if applicable)
 - v. Date the dilution, compound, or mixture was prepared
- c. Expiration dates
 - i. An expiration date of **thirty (30) days** from the date of preparation or the earliest expiration date for any single component (if less than thirty days) is recommended unless scientifically justified otherwise.

B. References

1. ILAR, Guide for the Care and Use of Laboratory Animals
<http://nap.edu/12910>
2. Animal Welfare Act and Regulations
<https://www.nal.usda.gov/awic/animal-welfare-act>
3. USDA Animal Care Resource Guide Policy #3
<https://www.nal.usda.gov/sites/default/files/Policy3.pdf>
4. OLAW Use of Non-Pharmaceutical-Grade Chemicals
<https://olaw.nih.gov/guidance/topic-index/animal-use.htm#non-pharmaceuticalgradesubstances>
5. AAALAC Frequently asked questions about Non-Pharmaceutical Grade Compounds
http://www.aaalac.org/accreditation/faq_landing.cfm#B9
6. NIH (NIH OACU) Guidelines for the Use of Non-Pharmaceutical Grade Compounds
http://oacu.od.nih.gov/ARAC/documents/Pharmaceutical_Compounds.pdf
7. Taylor BJ, Orr SA, Chapman JL, Fisher DE. Beyond-use dating of extemporaneously compounded ketamine, acepromazine, and xylazine: safety, stability, and efficacy over time. *J Am Assoc Lab Anim Sci.* 2009;48(6):718-726.
8. Dodelet-Devillers A, Zullian C, Vachon P, Beaudry F. Assessment of stability of ketamine-xylazine preparations with or without acepromazine using high performance liquid chromatography-mass spectrometry. *Can J Vet Res.* 2016;80(1):86-89.