Title: Use of Non-Pharmaceutical-Grade Compounds in Animals

I. Purpose:
To define the policy regarding the use of non-pharmaceutical-grade compounds in animals.

II. Definition:
A pharmaceutical grade compound/chemical is an active or inactive drug, biologic, or reagent which is approved by the FDA or for which a chemical purity standard has been established by any recognized pharmacopeia such as: US Pharmacopeia (USP), National Formulary (NF), British Pharmacopeia (BP), or Pharmacopoeia of the Council of Europe (EP). New investigational compounds are not considered pharmaceutical-grade because they are manufactured for research studies only and therefore do not have established chemical purity standards.

Pharmaceutical-grade products will include the recognized pharmacopeia on their label such as “USP” indicated on this Ketamine label:

III. Background:
The Office of Laboratory Animal Welfare (OLAW) and the U.S. Department of Agriculture (USDA) state that the use of non-pharmaceutical-grade compounds must be based on scientific necessity or non-availability of an acceptable veterinary or human pharmaceutical-grade compound. Non-pharmaceutical-grade chemical compounds may only be used in animals after specific review and approval by the IACUC.

Investigators and IACUCs should consider relevant animal welfare and scientific issues including safety, efficacy, and the inadvertent introduction of new variables. Although one can assume that issues such as sterility, pyrogenicity, stability, pharmacokinetics, and quality control have been addressed during the course of producing pharmaceutical-grade compounds, one cannot say the same for substances produced in the research laboratory using non-pharmaceutical-grade chemical compounds. Cost savings alone do not adequately justify the use of non-pharmaceutical-grade compounds in animals. Although the potential animal welfare consequences of complications are less evident in non-survival studies, the scientific issues remain the same and the principles and need for professional judgment outlined above still apply.

The use of non-pharmaceutical-grade chemical compounds in experimental animals under certain circumstances has been, and will continue to be, a necessary and acceptable component of biomedical research provided that the compounds are prepared under aseptic conditions prior to use. If there are reasons a compound cannot be purified or sterilized then justification and preparation methods must be presented to the IACUC for review.

IV. **Policy:**

It is the IACUC's policy to apply the above standards to all live, vertebrate animal research and teaching with animals covered under UC Davis Animal Care and Use Protocols. To further clarify, non-pharmaceutical-grade compounds **cannot be used** in research or teaching animals unless all of the following three criteria are met:

1. Scientific necessity.
2. The compound is not available or availability is unreliable as veterinary-grade or pharmaceutical-grade and there are no suitable alternatives.
3. The use is described in the animal care protocol and is approved by the IACUC.

Reconstituted compounds must be labeled with the name of the compound, the date the compound was prepared, concentration and the expiration date.

Non-pharmaceutical dry powder compounds that do not have an expiration date indicated on the container must be stored in accordance with manufacturer’s recommendations. For example Sigma-Aldrich suggests using products with no expiration date or retest dates within 5 years of opening. For compounds to be administered to animals, there
should be a method or procedure in place to validate effectiveness if they are stored for extended periods of time.

Non-pharmaceutical-grade compounds must go through a purification/sterilization process such as filter sterilization through a 0.2µm filter unless otherwise indicated in the approved IACUC protocol.

Protocols approved for the use of Potassium Chloride (KCl) for euthanasia in anesthetized animals can use non-pharmaceutical grade KCl because saturated KCl is not available as a pharmaceutical grade product. It is not necessary to filter sterilize KCl when used for euthanasia.

Researchers that propose to use non-pharmaceutical grade Sodium Pentobarbital or Avertin, in addition to the above requirements must also adhere to the following policies:

IACUC-44: “Use of Non-Pharmaceutical Grade Sodium Pentobarbital for Anesthesia of Laboratory Animals”
(http://safetyservices.ucdavis.edu/ps/a/IACUC/po/non-pharmaceutical-grade-sodium-pentobarbital)

AV-301: “Avertin Preparation and Use”

V. References:

1. USDA Policy #3
2. Guide for the Care and Use of Laboratory Animals, 8th edition, pg. 31
3. OLAW FAQ http://grants.nih.gov/grants/oaw/fqas.htm#useandmgmt_4