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, reagent, or adhesive/bonding agent which is approved by the FDA (e.g., Dermabond) or for which a chemical purity standard (e.g., Vetbond) 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 it can be assumed that issues such as sterility, pyrogenicity, stability, pharmacokinetics, and quality control have been addressed during the course of producing pharmaceutical grade compounds, this is not necessarily the case for substances produced in a research laboratory or core facility producing non-pharmaceutical grade 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 and documented as such 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 criteria are met:

1. Scientific necessity (includes preclinical testing of agents for potential human use).
2. The test article or compound is not available in the required concentration or formulation 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 must 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 0.2 µm filter unless administered orally, rectally, or topically and care taken with aseptic preparation to avoid contaminants that could result in an adverse event and/or negatively impact the research, or unless otherwise indicated in the approved IACUC protocol. If the product does not use a buffered and/or isotonic diluent or vehicle, a veterinary consultation must occur.

If the test article or compound has been prepared at the required level, and has a certificate of analysis indicating preparation under sterile conditions, testing for sterility, and assessed for contaminants (e.g., endotoxin, mycoplasma) then additional testing and sterilization may not be required.

Non-pharmaceutical grade adhesives/bonding agents that will be used directly on animals should be noted on IACUC proposals. While sterilization processes may not be appropriate for many materials, process for ensuring tissue compatibility and sterility/antimicrobial properties should be addressed.

Protocols approved for the use of saturated 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: “Use of Non-Pharmaceutical Grade Sodium Pentobarbital for Anesthesia of Laboratory Animals” and “Avertin Preparation and Use”
V. Resources

1. ILAR, Guide for the Care and Use of Laboratory Animals
   http://nap.edu/12910
2. Animal Welfare Act and Regulations
3. USDA Animal Care Resource Guide Policy #3
4. OLAW FAQ
   http://grants.nih.gov/grants/olaw/faqs.htm#useandmgmt_4
5. IACUC-44 “Use of Non-Pharmaceutical Grade Sodium Pentobarbital for Anesthesia of Laboratory Animals”
6. SC-40-405 “Avertin Preparation and Use”