PHARMACEUTICAL-GRADE COMPOUNDS IN RESEARCH

(USDA Policy #3)

Background:

To ensure humane care and proper use of laboratory animals in research, The University of Missouri – Kansas City (UMKC) Institutional Animal Care and Use Committee (IACUC) is obligated to provide policies that notify and train personnel concerning the appropriate techniques, equipment, and agents in agreement with the policies and procedures set forth by the United States Department of Agriculture (USDA) and the Office of Laboratory Animal Welfare (OLAW).

USDA Policy #3: Pharmaceutical-Grade Compounds in Research is as follows:

> *"Investigators are expected to use pharmaceutical-grade medications whenever they are available, even in acute procedures. Non-pharmaceutical-grade chemical compounds should only be used in animals after specific review and approval by the IACUC for reasons such as scientific necessity or non-availability of an acceptable veterinary or human pharmaceutical-grade product. Cost savings alone are not an adequate justification for using non-pharmaceutical-grade compounds in regulated animals."*

The 8th Edition of the Guide for the Care and Use of Laboratory Animals and the NIH Office of Laboratory Animal Welfare has issued the following guidance regarding the use of non-pharmaceutical grade agents:
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. Their use should be based on:

1. Scientific necessity,
2. Non-availability of an acceptable veterinary or human pharmaceutical grade product, and
3. Specific review and approval by the IACUC.

Definitions:

Non-pharmaceutical-grade compounds are chemicals not formulated or manufactured for use in human or veterinary medicine, including substances obtained from chemical supply companies and prepared in research laboratories. USP purity grade, analytical standards, analytical grade, and reagent grade compounds are all non-pharmaceutical grade compounds.

Pharmaceutical grade compound is any active or inactive drug, biologic, reagent, etc. which is approved by the Food and Drug Administration (FDA) or for which a chemical purity standard has been written/established by any recognized pharmacopeia (book/compendia) such as the US Pharmacopeia (USP) and the National Formulary (NF) and have an expiration date. Pharmaceutical grade chemicals or substances compounded with other non-pharmaceutical grade chemicals, substances, or diluents, such as saline or distilled water, are considered non-pharmaceutical grade.

Procedures:

1) Pharmaceutical Grade Compounds
   a) Define within the applicable animal use protocol whether all compounds being administered to research and teaching animals are pharmaceutical grade.
   b) Search FDA databases to determine if compounds are pharmaceutical grade,
      i. The "Orange Book" is a reference for FDA-approved human drugs.
      ii. The "Green Book" is a reference for FDA-approved veterinary drugs.
      iii. Pharmaceutical grade compounds occasionally may not be listed in the Orange or Green book. These compounds should be labeled with a New Animal Drug Application/Abbreviated New Animal Drug Application (NADA/ANADA) or with a

National Drug Code (NDC).

c) UMKC's IACUC considers dilutions and/or mixtures of compounds to be equivalent to pharmaceutical grade so long as all ingredients within the solution/mixture are pharmaceutical grade.

2) Non-pharmaceutical Grade Compounds
   a) The use of non-pharmaceutical-grade compounds in animals must be described and justified in an animal use protocol approved by the IACUC.
   b) Take precautions to ensure a reasonable degree of safety when preparing and using a non-pharmaceutical grade compound regarding:
      i. Grade
      ii. Purity
      iii. Sterility
      iv. Solute vehicle?
      v. pH
      vi. Pyrogenicity
      vii. Osmolality
      viii. Stability (in and out of solution)
      ix. Site/route of administration
      x. Compatibility of components
      xi. Adverse reactions
      xii. Pharmacokinetics
      xiii. Storage of drug & sterile containment?

All compounds used in animals must be labeled correctly with the following information: compound name, concentration, date of preparation, initials of preparer, and expiration date. The expiration date must be 30 days following mixture unless there is literature to demonstrate otherwise. If the expiration is more than 30 days this must be described in the approved IACUC protocol.

Applicable To:

All UMKC faculty, staff, employees, and students involved in the care or use of animals owned by the UMKC.

Revisions to the Policy:

This policy is intended to be flexible and readily adaptable to changes in regulatory requirements. It is reviewed as part of the semiannual program review to ensure regulatory compliance. The UMKC IACUC has the authority to amend this policy as needed. The UMKC Institutional Animal Care and Use Committee has reviewed and approved this policy.

References:

- FDA Orange Book, Approved Drug Products with Therapeutic Equivalence Evaluations: https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm
- FDA Green Book, Animal Drugs: https://www.fda.gov/animal-veterinary/products/approved-animal-drug-products-green-book
- OLAW, FAQs, PHS Policy on Humane Care and Use of Laboratory Animals: http://grants.nih.gov/grants/olaw/faqs.htm
- USDA Animal Care Resource Guide Policies, Policy #3, Veterinary Care, Pharmaceutical-Grade Compounds in Research; March 25, 2011
- United States Pharmacopeia-National Formulary (USP-NF): https://www.uspnf.com/
- Brown P, Clarke C, and Newcomer C. OLAW, Educational Resources, "Use of Non-Pharmaceutical-Grade Chemicals and Other Substances in Research with Animals – March 1, 2012