FSU
ANIMAL CARE & USE COMMITTEE
DIVISION OF RESEARCH

Guidelines for the Use of Non-Pharmaceutical Grade Compounds in Research Animals

Purpose: In accordance with the *Guide for the Care and Use of Laboratory Animals (Guide)*, USDA Animal Care Resource Guide Policies, and OLAW guidance, pharmaceutical-grade chemicals and other substances, when available, must be used to avoid toxicity or side effects that may threaten the health and welfare of vertebrate animals and/or interfere with the interpretation of research results. These guidelines describe ACUC expectations regarding the use of non-pharmaceutical grade compounds in research animals at Florida State University

Applicability: These guidelines apply to all chemical agents and compounds, including analgesics, anesthetics, investigational drugs, fluids and diluents/vehicles administered to research animals for research, teaching, or testing purposes.

Definitions:
Pharmaceutical grade compound: any active or inactive drug, biologic or reagent, for which a chemical purity standard has been established by a recognized national or regional pharmacopeia4 (e.g. the U.S. Pharmacopeia/National Formulary (USP/NF), British Pharmacopeia (BP), European Pharmacopeia (EP), etc.). 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. Pharmaceutical grade drugs are formulated to a standard compatible with the legal and ethical treatment of human or veterinary patients in a health care or practice setting by a pharmaceutical company or qualified compounding pharmacist.

Non-pharmaceutical grade compound**:** any chemical compound that has not been formulated for production of medicine. Agents obtained from chemical supply companies and or prepared in a research laboratory are of reagent and not pharmaceutical grade.

Guidelines:

- **A.** Investigators are expected to use pharmaceutical-grade compounds whenever they are available, even in non-survival procedures.
- **B.** When selecting compounds the following order of choice should be applied:
  - **a.** FDA approved veterinary or human pharmaceutical compounds—used without modification;
  - **b.** FDA approved veterinary or human pharmaceutical compounds used to compound a needed dosage form;
  - **c.** USP/NF, BP, or other pharmacopeia recognized pharmaceutical grade compounds used in a needed dosage form;
  - **d.** Analytical grade bulk chemical used to compound a needed dosage form (requires justification);
  - **e.** Other grades and sources of compounds (requires justification).
- **C.** The use of non-pharmaceutical-grade compounds in experimental animals may be acceptable under certain circumstances, based on:
  - **a.** Scientific necessity;
  - **b.** Non-availability of an acceptable veterinary or human pharmaceutical-grade compound.

c. Non-availability of an acceptable alternative pharmaceutical-grade compound.
d. Specific review and approval by the IACUC.

D. Cost savings alone is not justification for use of non-pharmaceutical grade compounds in research animals. However, unavailability or shortages of pharmaceutical grade substances may lead to cost increases and the ACUC may determine that this justifies the use of the non-pharmaceutical grade substitution.

E. The use of investigational compounds to meet research goals is permissible with ACUC approval.

F. When developing and reviewing an Animal Use Protocol proposing use of non-pharmaceutical grade compounds, the investigator and IACUC should consider grade, purity, sterility, pH, pyrogenicity, osmolality, stability, site and route of administration, formulation, compatibility, and pharmacokinetics of the compound to be administered, as well as animal welfare and scientific issues related to use.

G. The ACUC may approve use of non-pharmaceutical-grade compounds in the following situations:
a. No equivalent veterinary or human drug is available for experimental use. In such cases the highest grade equivalent chemical reagent should be used and formulated aseptically and with a non-toxic vehicle as appropriate for the route of administration.
b. Although an equivalent veterinary or human drug is available for experimental use, the chemical-grade reagent is required to replicate methods from previous studies because results are directly compared to those of replicated studies.
c. Although an equivalent veterinary or human drug is available, dilution or change in formulation is required.
d. The available human or veterinary drug is not concentrated enough to meet experimental needs.
e. The available human or veterinary drug does not meet the non-toxic vehicle requirements for the specified route of administration.
f. The pharmaceutical grade drug is effectively unavailable.

Notes:
A listing of pharmaceutical-grade drugs and biologics is available through the FDA database. The Orange Book is the reference for FDA-approved human drugs. The Green Book is the reference for FDA-for approved veterinary drugs.

References
Institute for Laboratory Animal Research. 2011. Guide for the care and use of laboratory animals, 8th ed. Washington (DC): National Academies Press.
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