BACKGROUND

In accordance with the United States Department of Agriculture (USDA) and the National Institutes of Health Office of Laboratory Animal Welfare (OLAW) policy, the University of Rhode Island (URI) requires that pharmaceutical grade compounds (e.g., fluids, medications, drugs, vehicles, and diluents) be used in all cases in which they are available. This policy applies to all vertebrate species, and includes survival as well as non-survival procedures. The URI IACUC may approve the use of non-pharmaceutical grade (NPG) compounds under certain circumstances, such as those cases in which pharmaceutical grade alternatives are not available, or not available in the required formulation or concentration, or do not exist in a form compatible with the intended route of administration. Approval in these cases is contingent on institutional review by the IACUC (see below).

DEFINITIONS

A pharmaceutical grade compound is defined as any active or inactive drug, biologic or reagent, for which a chemical purity standard has been established by a recognized national or regional pharmacopeia (e.g. the U.S. Pharmacopeia (USP), British Pharmacopeia (BP), National Formulary (NF), 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 (NPG) agents refer to chemical compounds that have 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.

POLICY AND PROCEDURE

Justification for Use of non-pharmaceutical Grade Compounds:

Both USDA and OLAW regulations indicate that “the IACUC should develop a consistent evaluation process that includes but is not limited to the scientific justification and the availability of an acceptable veterinary or human pharmaceutical-grade product. Cost savings alone is not sufficient justification for using a non-pharmaceutical-grade substance in regulated species. However, unavailability or shortages of pharmaceutical grade substances may lead to cost increases and the IACUC may determine that this justifies the use of the non-pharmaceutical grade substitution.” A history of the use of a NPG substance alone is not a sufficient justification for continued use.
To secure approval for the use of non-pharmaceutical grade compounds, the PI must:

1. Provide sound scientific justification for the use of the compound
2. Verify that the compound is not available as a pharmaceutical grade product in the required formulation or concentration (if available in higher concentrations than needed, identification of the diluent is necessary and dilution with a pharmaceutical grade diluent is generally required),
3. Justify use of the NPG product as an appropriate alternative. Required information should include a description of the means to assure purity, sterility, and stability.

In addition, information needed for review includes the site and route of administration, and potential side effects and adverse reactions. Note that the proper reconstitution is critical. When necessary, plans must be described for documenting formulation preparation and storage conditions. For those instances in which it is not possible to use pharmaceutical grade compounds, the highest available reagent grade should be used instead.

REFERENCES

- USDA-APHIS Animal Care Policy Manual, Policy #3 states that “Pharmaceutical-grade substances are expected to be used whenever they are available, even in acute procedures. This includes but is not limited to: compounds, medications, drugs, vehicles, and diluents. APHIS recognizes that some substances (e.g. test articles, novel compounds, and those resulting from a compounding process) are only available as a non-pharmaceutical grade product. Non-pharmaceutical-grade substances should only be used in regulated animals after specific review and approval by the IACUC.”

RESOURCES

- A listing of pharmaceutical-grade drugs and biologics is available through the FDA Database [http://www.fda.gov/Drugs/InformationOnDrugs/default.htm](http://www.fda.gov/Drugs/InformationOnDrugs/default.htm)
- The Green Book is the reference for FDA-approved veterinary drugs. [http://www.fda.gov/animalveterinary/products/approvedanimaldrugproducts/default.htm](http://www.fda.gov/animalveterinary/products/approvedanimaldrugproducts/default.htm)