Policy on the Use and Preparation of Non-Pharmaceutical Grade Substances and Compounds

OLAW (NIH) and USDA policy states that non-pharmaceutical grade substances and compounds in research animals under certain circumstances has been, and will continue to be, a necessary and acceptable component of biomedical research. Their use should be based upon:

- Scientific necessity
- Non-availability of acceptable veterinary or human pharmaceutical-grade compounds
- Specific review and approval by the IACUC

No reagent-grade chemicals may be used in research animals if a pharmaceutical-grade substance or compound is available through human or veterinary suppliers. Examples of available pharmaceutical-grade substances and compounds frequently used in research animals include (but are not limited to): ketamine, xylazine, diazepam, buprenorphine, cefazolin, isoflurane and (sometimes) pentobarbital. Cost savings alone do not justify the use of non-pharmaceutical grade compounds in animals. If a pharmaceutical-grade compound is not available through human or veterinary suppliers, the Principal Investigator or their staff may compound the drug in their laboratory. Examples of compounds not always available through suppliers include (but are not limited to): experimental test compounds and (sometimes) pentobarbital. For all species, any non-pharmaceutical chemical agents administered in survival and non-survival studies, and animal experimentation, must meet quality control and assurance standards.

The following are examples of procedures on how to prepare the compounds to insure sterility of the final product:

- All manipulations must occur in sterile vessels using sterile instruments (spatulas, syringes/needles, dosing vials, etc.). Work should be carried out in a biosafety cabinet or chemical fume hood to reduce contamination of the area.
- The drug must be reconstituted with sterile diluents (e.g., water, Phosphate Buffered Saline, DMSO, ethanol, oil) prepared by filtration through a 0.2 micron filter or by autoclaving according to the instructions provided by the manufacturer of the reagent-grade chemical.
- The final solution should be adjusted so that it has a pH value of between 4 and 9.5.
- After thorough mixing, the solution must be filtered into a sterile vial through a 0.2 micron filter to ensure removal of bacteria and other contaminants.
- The vial must be labeled with the drug name, concentration of the solution, the date of compounding and the expiration date (maximum of six months from the date of compounding).
- The solution must be handled in a manner to ensure continued sterility of the contents.
- The expiration date of the compounded solution is six months from the date of compounding at a maximum. Any solution remaining after six months must be discarded and not used in laboratory animals. *If the “shelf life” is not obtainable, it is recommended that the drug solution be freshly re-prepared each day it is used.
- Once prepared, proper storage of the compound must be maintained to necessitate its viability.
- Regardless of age, solutions should be discarded if changes in color and/or precipitation occur.
The following standards must be addressed in the IACUC Application for Use of Vertebrate Animals (AUVA), by providing a written standard operating procedure (SOP) for each non-pharmaceutical grade compound used in the research study. These standards are:

Substance Name:
Substance Obtained from:
Compounding/Recipe Instructions:
  - Ingredients:
  - Preparation:
  - Storage:
  - Dosing:
  - *Expiration Date/Shelf Life:
Cautions:
  - Side Effects or Adverse Reactions:

Note: Do not administer non-sterile solutions, outdated solutions, more concentrated solutions, or higher doses than recommended above.

References
John Hopkins University ACUC Policy on Use of Non-Pharmaceutical Grade Substances in Laboratory Animals

Washington College IACUC SOP Preparation of Sterile Non-Pharmaceutical Grade Compounds