Non-Pharmaceutical Grade Drugs IACUC Policy

The Guide for the Care and Use of Laboratory Animals (NRC, 2011), states that the use of pharmaceutical-grade drugs ensures that toxic or unwanted side effects are not introduced into studies conducted with experimental animals. Since chemical grade drugs are not specially formulated for pharmaceutical use, they can compromise the health of the animals and validity of the study.

**Definition of chemical/non-pharmaceutical grade drugs:** 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 Pharmacopoeia (EP), Japanese Pharmacopoeia (JP), 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.  

**Identify whether the drug is Pharmaceutical Grade:** The Food and Drug Administration (FDA) maintains a database listing of FDA approved commercial formulations for both FDA approved human drugs (the Orange Book) and veterinary drugs (the Green Book).

There are two scenarios when considering the use of non-pharmaceutical-grade compounds:

**Clinical Use** - compounds used for the clinical treatment of animals and to prevent or reduce/eliminate animal pain or distress (anesthesia, analgesia, and euthanasia). Whenever possible, pharmaceutical-grade compounds must be used.

**Research Use** - compounds used to accomplish the scientific aims of the study. If available, and suitable, pharmaceutical-grade compounds are preferred; but when non-pharmaceutical-grade preparations are used, investigators should consider the following factors: grade, purity, sterility, pH, pyrogenicity, osmolality, stability, site and route of administration, formulation, compatibility, and pharmacokinetics of the chemical to be administered, as well as animal welfare and scientific issues relating to its use.

The use of non-pharmaceutical –grade chemicals or substances must be described and justified in the animal use protocol and be approved by the IACUC (Wolff et al. 2003).

**Acceptable scientific justifications for the use of non-pharmaceutical-grade compounds:**

1. No equivalent veterinary or human drug is available for experimental use. The highest-grade equivalent chemical reagent should be used and formulated
aseptically, with a non-toxic vehicle, as appropriate for the route of administration.

2. Although an equivalent veterinary or human drug is available for experimental use, the chemical grade reagent might be required to replicate methods from previous studies if it is the only option to produce results that are directly comparable.

3. Although an equivalent veterinary or human drug is available, dilution or change in formulation is required.
   - If the formulation as provided must be diluted, altered by addition, or otherwise changed, there may be no additional advantage to be gained by using the USP formulation.
   - In this situation, use of the highest grade reagent may have the advantage of single-stage formulation and also result in purity that is equal to or higher than the human or veterinary drug.
   - Professional judgment should be used to determine the appropriate test material and to ensure use of an agent with the least likelihood for causing adverse effects.

4. The available human or veterinary drug is not concentrated enough to meet experimental requirements.

5. The available human or veterinary drug does not meet the non-toxic vehicle requirements for the specified route of administration.

With the exception of Pentobarbital\textsuperscript{4}, and presumably any other comparable situations, cost savings alone is not an adequate justification for the use of Non-Pharmaceuticals.\textsuperscript{1}

\begin{enumerate}
\item U.S. Department of Agriculture, Animal and Plant Health Inspection Service, Animal Care, Policy 3-Veterinary Care, March 25, 2011.
\item AAALAC Frequently asked questions about Non-Pharmaceutical Grade Compounds. \url{http://www.aaalac.org/accreditation/faq_landing.cfm#B9}.
\item The Guide for the Care and Use of Laboratory Animals, 2011.
\item Transcript of OLAW On-line Seminar broadcast on March 1, 2012 - Use of Non-Pharmaceutical-Grade Chemicals and Other Substances in Research with Animals.
\item \url{http://oacu.od.nih.gov/ARAC/documents/Pharmaceutical_Compounds.pdf}
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