



Additional Information for Investigators On the Use of Non-Pharmaceutical Grade Drugs

Why must I use pharmaceutical grade drugs?

The use of pharmaceutical-grade substances ensures that the substances meet established documentable standards of strength, quality, purity, and composition. This in turn helps ensure research animal health and welfare, as well as the validity of experimental results. The use of lower grade substances/compounds with undefined levels of impurities or poorly formulated preparations can introduce unwanted experimental variables or even toxic effects.

What factors will be taken into account by the IACUC when considering justifications for the use of non-pharmaceutical grade drugs?

- (1) If no equivalent veterinary or human drug is available, then 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.
- (2) 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.
- (3) Although an equivalent veterinary or human drug is available, dilution or change in formulation is required.
 - a. If adulteration by dilution, addition, or other change in formulation is required, there may be no additional advantage to be gained by using the USP formulation.
 - b. 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.
- (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.

NOTE: *Cost savings alone is not considered an adequate justification for the use of non-pharmaceutical grade substances in laboratory animals. However, as cited by OLAW, recent "exorbitant cost increases of pentobarbital have placed it logistically into the unavailable category." Thus, IACUC will consider use of pentobarbital from a reagent or analytical grade powder, when justified within the IACUC protocol.*

How can I assure sterility of my non-pharmaceutical grade compounds?

- (1) Perform preparations under a clean flow hood using only sterile diluents (e.g., sterile normal saline or phosphate buffered saline) and sterile instruments.
- (2) Filter substances through a 0.2 μ filter
- (3) Storage in sterile vials with rubber septum to maintain sterility

How can I determine an expiration or beyond use date?

- (1) The earliest expiration date of any agent/compound used in the preparation should be used as the expiration date for the prepared solution.



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- (2) Long-term storage of preparations (>30 days) is discouraged. Regardless of age, solutions should be discarded if changes occur in color and/or precipitation occurs.

Where can veterinary pharmaceutical-grade drugs be obtained?

The use of pharmaceutical-grade substances is always preferable; however investigators may be unsure how to obtain veterinary pharmaceutical drugs. Here are several options:

- (1) A select number of veterinary pharmaceutical drugs may be purchased through the Unit for Laboratory Animal Medicine (see [form](#)).
- (2) Veterinary pharmaceutical drugs may be purchased through MWI Veterinary Supply (www.mwivet.com). Your departmental purchasing administrator must contact Evie Toering (866-252-4069) at MWI Veterinary Supply to set up an account.
- (3) Veterinary pharmaceutical drugs may also be purchased through Butler Schein (www.henryschein.com); however you will need a medical or veterinary license or both a federal DEA registration and state of Michigan DEA license.

References

- (1) U.S. Department of Agriculture, Animal and Plant Health Inspection Service, Animal Care, Policy 3-Veterinary Care, March 25, 2011.
- (2) AAALAC Frequently asked questions about Non-Pharmaceutical Grade Compounds. http://www.aaalac.org/accreditation/faq_landing.cfm.
- (3) OLAW Position Statement- Non-Pharmaceutical Grade Substances. http://grants.nih.gov/grants/olaw/positionstatement_guide.htm#nonpharma.
- (4) Transcript of OLAW On-line Seminar broadcast on March 1, 2012 - Use of Non-Pharmaceutical Grade Chemicals and Other Substances in Research with Animals. http://grants.nih.gov/grants/olaw/120301_seminar_transcript.pdf.

Definitions

- **Pharmaceutical grade compound:** FDA-approved veterinary or human drug or biologic.
- **Active pharmaceutical ingredient (API):** Any substance that is represented for use in a drug and that, when used in the manufacturing, processing, or packaging of a drug, becomes an active ingredient or a finished dosage form of the drug (e.g., USP-grade).
- **Current Good Manufacturing Practice (CGMP):** Regulations that outline the expectations of the FDA in regard to the design, construction and operation of facilities intended for the manufacturing, processing, packing or holding of API's.
- **Analytical or reagent grade chemical:** Variable purity Non CGMP. Non-USP verified.
- **USP/NF:** United States Pharmacopeia/National Formulary (Official compendia for drugs marketed in the United States)
- **BP:** British Pharmacopeia



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- **FDA: Food and Drug Administration;** FDA approved compounds are manufactured in conformance with CGMP and USP standards.