

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

Definitions:

Pharmaceutical grade compound: Drug, biologic, reagent, etc. which is approved by the FDA or for which a chemical purity standard has been written/established by USP/NF, BP

Analytical grade bulk chemical: ~99% purity; Certificate of Analysis is usually available

Non-availability: Not commercially available from an active US vendor; includes formulations supplied as tablet, capsule, injectable, etc.

New investigational compound: Supplied by its manufacturer for testing in an experimental setting only and for this reason would not have chemical purity standards established; by default is considered a non-pharmaceutical grade compound

USP/NF: United States Pharmacopeia/National Formulary

BP: British Pharmacopeia

FDA: Food and Drug Administration; FDA approved compounds are manufactured using USP/NF compounds

Requirements:

The use of pharmaceutical-grade compounds in laboratory animals ensures that the compounds administered meet established documentable standards of purity and composition which in turn help ensure research animal health and welfare, as well as the validity of experimental results. The use of lower grade chemicals/compounds with higher levels of impurities or poorly formulated non-commercial preparations can introduce unwanted experimental variables or even toxic effects, and so should be avoided if at all possible. Although pharmaceutical grade compounds should be used in experimental animals whenever possible, the use of non-pharmaceutical-grade compounds in experimental animals is an acceptable practice under certain circumstances. For example, in the case of new investigational compounds, they would be the only grade and formulation available. The NIH Office of Laboratory Animal Welfare (OLAW) and the United States Department of Agriculture (USDA) both have determined that the use of non-pharmaceutical-grade compounds should be based on (1) scientific necessity, (2) non-availability of an acceptable veterinary or human pharmaceutical-grade compound, and (3) specific review and approval by the institutional ACUC.¹ *Cost savings alone is not considered an adequate justification for the use of non-pharmaceutical-grade compounds in laboratory animals.* OLAW has also stated that while the possible implications of the use of non-pharmaceutical grade compounds in non-survival studies appears less evident, the scientific issues remain the same and professional judgment, as outlined above, must still apply². It is important to understand that this guideline pertains to

all components, both active and inactive, contained in the preparation to be administered. Therefore, the vehicle used to facilitate administration of a compound is as important of a consideration as the active compound in the preparation.

The use of non-pharmaceutical-grade compounds in laboratory animals should be clearly delineated and justified in the Animal Study Proposal (ASP) and/or covered by an ACUC policy developed for their use. The NIH Veterinary Pharmacist can provide assistance in availability, procurement, and formulation of various pharmaceutical grade compounds. (<http://dvrnet.ors.od.nih.gov/internal/pharmacy.asp>).

Recommendations for use:

When developing and reviewing a proposal to use non-pharmaceutical grade compounds the investigator and ACUC should consider animal welfare and scientific issues related to the use of the compounds, including potential for contamination, safety, efficacy, and the inadvertent introduction of confounding research variables.

For all compound use, the ACUC should consider the grade/purity being proposed, the formulation of the final product, and issues such as sterility, pyrogenicity, stability, pH, osmolality, site/route of administration, pharmacokinetics, physiological compatibility, and quality control.

When selecting compounds the following order of choice should be applied:

1. FDA approved veterinary or human pharmaceutical compounds;
2. FDA approved veterinary or human pharmaceutical compounds used to compound a needed dosage form;
3. USP/NF or BP pharmaceutical grade compound used in a needed dosage form;
4. Analytical grade bulk chemical used to compound a needed dosage form (requires justification);
5. Other grades and sources of compounds (requires justification).

NOTE: For new investigational drugs the grade and formulation is not optional, but the investigator and ACUC can verify health and safety issues described above.

References:

¹ U.S. Department of Agriculture, Animal and Plant Health Inspection Service, Animal Care, Policy 3-Veterinary Care, April 14, 1997.

² [Frequently asked questions about the public health service policy on humane care and use of laboratory animals. Wolff A, Garnett N, Potkay S, Wigglesworth C, Doyle D, Thornton V. Lab Animal \(NY\). 2003 Oct;32\(9\):33-6.](#)

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