

## **Guidelines for the Use of Non-Pharmaceutical-Grade Chemicals/Compounds in Laboratory Animals**

The use of pharmaceutical-grade chemicals/compounds in laboratory animals ensures that the chemicals/compounds administered meet the established documentable standards of purity (~97%) and composition established by the United States Pharmacopeia National Formulary (USP/NF) or the British Pharmacopoeia (BP). The indiscriminant 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. Although pharmaceutical grade chemicals/compounds should be used in experimental animals whenever possible, the use of non-pharmaceutical-grade chemicals/compounds in experimental animals is an acceptable practice under certain circumstances. 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 products 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 ACUC.<sup>1</sup> *Cost savings alone is not considered an adequate justification for the use of non-pharmaceutical-grade reagents in laboratory animals.*

Consideration should be given to the grade/purity of the chemical/compound being proposed, as well as the formulation of the final product. Issues such as sterility, pyrogenicity, stability, pH, osmolality, site/route of administration, pharmacokinetics, physiological compatibility, and quality control should be considered when proposing the use of a non-pharmaceutical-grade agent. When developing and reviewing a proposal to use non-pharmaceutical-grade agents the investigator and ACUC should also consider animal welfare and scientific issues related to the use of the agent, including potential for contamination, safety, efficacy, and the inadvertent introduction of confounding research variables. Whereas, many of the above issues have been addressed in the commercial manufacturing and formulation of pharmaceutical-grade products, the same cannot be said for non-commercial formulations using non-pharmaceutical-grade reagents or those manufactured in the laboratory. Although the possible implications of the use of non-pharmaceutical-grade chemicals/compounds in non-survival studies appears less evident, OLAW has stated that the scientific issues remain the same and professional judgment, as outlined above, must still apply.

The use of non-pharmaceutical-grade agents in laboratory animals should be clearly delineated and justified in the Animal Study Proposal (ASP). Where possible the description should include the chemical grade of the agent(s) being used (See definitions below), source of the reagents, as well as a description of the appropriateness of the agent, its formulation and vehicle. Formulations and vehicles may need to be adjusted depending on the route and site of administration, as well as the species under consideration. The NIH Veterinary Pharmacist can provide assistance in availability, procurement, and formulation of various agents, as well as consultation in the development of your ASP (<http://dvrnet.ors.od.nih.gov/internal/pharmacy.asp>).

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

## Definitions

1. USP/NF: United States Pharmacopeia/National Formulary
2. BP: British Pharmacopeia
3. Pharmaceutical grade chemical: ~97% purity; a chemical that states it meets the USP/NF or BP standard on the label. A certificate of analysis is *usually available* on request.
4. Analytical Standards: “Certificate of Analysis” a document that goes with each product run. This certificate lists the formula for the ingredients as well as the amount of each raw material/ingredient. The product name and lot number are listed to avoid confusion with other batches. The C of A also may contain results of tests for contaminants.
5. Analytical Grade: ~99% purity; Certificate of Analysis *usually available*; appropriate preparation is imperative.
6. Reagent ACS: This designates the highest quality commercial chemical. The “ACS” means the American Chemical Society. A Certificate of Analysis is available upon request.
7. Reagent Grade: The highest quality commercial chemical; HOWEVER, ACS has not set specifications for materials. A Certificate of Analysis is *usually not available*.

Approved – 12/03/08