

Version: 1.2 Effective Date: 4/1/2022	USE OF NON- PHARMACEUTICAL GRADE COMPOUNDS	Supersedes Document Dated: 10/15/2015
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I. Background

Federal regulations require the use of pharmaceutical grade compounds in animals used for research and teaching unless those compounds are not available or are otherwise inappropriate for the aims of the proposed animal use.

II. Policy

Non-pharmaceutical-grade compounds cannot be used in animals unless a) the compound is not available as veterinary-grade or pharmaceutical-grade and there are no suitable alternatives; or b) use of the non-pharmaceutical grade compounds is a scientific necessity. Use of non-pharmaceutical grade compounds, diluents, and reagents must be described in the Animal Use Protocol (AUP) and must be approved by the Animal Care and Use Committee (ACUC). Cost savings is not ordinarily adequate justification for using non-pharmaceutical grade compounds. However, the ACUC may determine that unavailability or shortages of pharmaceutical-grade substances justifies the use of the non-pharmaceutical-grade substitution.

III. Definitions

- A. Pharmaceutical-grade compound – Any active or inactive drug, biologic, reagent, etc., manufactured under Good Manufacturing Practices (GMP) which is approved, conditionally approved, or indexed by the Food and Drug Administration (FDA) or for which a chemical purity standard has been written or established by a recognized compendia (e.g., United States Pharmacopeia-National Formulary (USP-NF), British Pharmacopeia (BP).
- B. Compounding – The customized manipulation of an approved drug by a veterinarian, or by a pharmacist upon the prescription of a veterinarian, to meet the needs of a research study.
- C. Bulk Chemical Agents - An analytical grade bulk chemical agent that has not been formulated for the production of medicine. Compounds distributed by “chemical vendors” (e.g., Fisher Scientific, Sigma-Aldrich) are not pharmaceutical grade.

IV. Responsibilities

- A. ACUC and the Office for Laboratory Animal Care (OLAC) – As part of protocol review, the ACUC and OLAC veterinarians must consider the health and well-being of the animals while aiding the researcher in minimizing potentially confounding experimental variables and maximizing reproducibility of the research.

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- B. Office for the Environment, Health & Safety (EH&S) – EH&S must review the protocols and assess the human safety of chemicals and agents used in the research or instruction.
 - C. Principal Investigator (PI) – The PI is responsible for identifying any drug, biologic or reagent administered to animals. If these agents are not human or veterinary pharmaceutical-grade substances, the investigator must provide a scientific justification for their use and describe the methods that will be used to ensure appropriate preparation, administration, storage, and safety.
- V. Uses & Considerations
- A. Pharmaceutical-grade compounds must be used if available and suitable for the research purpose. If non-pharmaceutical-grade compounds are requested to be used, the ACUC must consider the following factors:
 - 1. An adequate scientific justification is provided;
 - 2. The pharmaceutical-grade compound is not available in the appropriate concentration or formulation, or the appropriate vehicle control is unavailable;
 - 3. The use of the compound is required to generate data that are part of an ongoing study or that is necessary to compare to previous work;
 - 4. The chemical properties of the compound are appropriate for the study and the route of administration, including: formulation, grade of compound (analytical, etc.), adverse reactions, side effects, and compatibility with other compounds, osmolality, pH, purity, pharmacokinetics, pyrogenicity, safety and efficacy of the compound, the method of preparation (i.e., sterility, preparation, shelf-life), labeling, routes of administration, and storage should be appropriately considered with the aim of maintaining the stability and quality (i.e., to prevent inadvertent co-administration of infectious agents or contaminants); and,
 - 5. Adequately trained and experienced personnel are responsible for the preparation, administration and experimental evaluation of compounds.
- VI. Compounding
- A. Compounding of investigational agents or the customized manipulation by dilution or addition of vehicles to pharmaceutical-grade substances by the investigator, veterinary staff, or licensed pharmacist for administration to animals must be described in the AUP.
 - B. Compounding pharmacies may be a useful resource to animal care and use programs and investigators seeking to acquire pharmaceutical-grade drugs in unique combinations or concentrations for therapeutic or research purposes.

VII. References

- A. Animal and Plant Health Inspection Service (APHIS). United States Department of Agriculture (USDA).
<https://www.nal.usda.gov/sites/default/files/Policy3.pdf>.
- B. Association for the Accreditation and Assessment of Laboratory Animal Care (AAALAC). Frequently Asked Questions: Institutional Policies – 9. Non-Pharmaceutical-Grade Compounds. Found at
https://www.aaalac.org/accreditation/faq_landing.cfm#B9
- C. United States Food and Drug Administration (FDA). Drug Approvals and Databases. (<https://www.fda.gov/Drugs/InformationOnDrugs/default.htm>).
- D. Health Ministers of the United Kingdom. Commission on Human Medicines. *British Pharmacopoeia*. (<https://www.pharmacopoeia.com/>).
- E. United States Food and Drug Administration (FDA). Green Book. (<https://www.fda.gov/AnimalVeterinary/Products/ApprovedAnimalDrugProducts/>)
- F. United States Food and Drug Administration (FDA). Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations (<https://www.accessdata.fda.gov/scripts/cder/ob/default.cfm>)
- G. United States Pharmacopoeia-National Formulary (<https://www.uspnf.com/>).
- H. Office of Laboratory Animal Welfare (OLAW). National Institutes of Health. Position Statements: OLAW Responds to Concerns Regarding Adoption of the Guide for the Care and Use of Laboratory Animals: Eighth Edition. Position Statement 3) Non-Pharmaceutical-Grade Substances. Found at https://grants.nih.gov/grants/olaw/positionstatement_guide.htm#nonpharma
- I. Office of Laboratory Animal Welfare (OLAW). National Institutes of Health. Public Health Service Policy on Humane Care and Use of Laboratory Animals – Frequently Asked Question #4. Found at <https://grants.nih.gov/grants/olaw/faqs.htm#662>