

Washington State University
Institutional Animal Care and Use Committee

Policy #29

“Use of Non-Pharmaceutical Grade Substances”

Approval Date: 2/6/2023 (Replacing Version 11/1/2019)

A. Purpose

This policy defines the Washington State University (WSU) Institutional Animal Care and Use Committee’s (IACUC) position on the use of non-pharmaceutical grade substances in research and teaching animals.

B. Background

The Office of Laboratory Animal Welfare (OLAW) and U.S. Department of Agriculture (USDA) agree that pharmaceutical-grade substances, when available, must be used to avoid toxicity or side effects that may threaten the health and welfare of vertebrate animals and / or interfere with the interpretation of research results. However, it is frequently necessary to use non-pharmaceutical-grade substances, such as investigational substances, veterinarian- or pharmacy-compounded substances, and / or Schedule I controlled substances to meet scientific and research goals.

OLAW and USDA have determined that the use of non-pharmaceutical grade substances should be based on:

1. Scientific necessity
2. Non-availability of an acceptable veterinary or human pharmaceutical-grade compound
3. Specific review and approval by the IACUC.

Cost savings alone is not considered an adequate justification for the use of non-pharmaceutical-grade substances in laboratory animals and determinants are to be applied to non-survival studies as well. This policy 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 must undergo the same evaluation as the active compound in the preparation.

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 or 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, this is considered a non-pharmaceutical grade compound
- **USP/NF:** United States Pharmacopeia/National Formulary. This is the official public standards-setting authority for all prescriptions, over-the-counter medications and other health care products manufactured and sold in the United States.
- **BP:** British Pharmacopeia. The BP provides a comprehensive collection of authoritative official standards for United Kingdom (UK) pharmaceutical substances and medicinal products.
- **FDA:** Food and Drug Administration. FDA-approved compounds are manufactured using USP/NF compounds
- **Compounding:** The combining, mixing, or altering of ingredients of a drug to create a medication tailored to the needs of an individual patient. Please view the [IACUC Guidelines on Compounding](#) for additional details for preparation and storage.

C. Policy

Pharmaceutical-grade substances must be used when available, including drugs used in non-survival studies, euthanasia, vehicles, etc. If proposing to use non-pharmaceutical grade substances, it must be described and justified within the Animal Subject Approval Form (ASAF). The IACUC will review each request and make a determination based on:

- 1) Scientific necessity
- 2) Non-availability of an acceptable veterinary or human pharmaceutical-grade compound.

The IACUC is responsible for evaluating the potential adverse consequences of non-pharmaceutical-grade substances when used for research. When developing and reviewing a proposal to use non-pharmaceutical grade substances, the investigator and IACUC should consider animal welfare and scientific issues related to the use of the substances. This includes potential for contamination, safety, efficacy, and the inadvertent introduction of confounding research variables. For all substance use, the WSU IACUC will consider the following factors:

- grade
- purity
- sterility
- acid-base balance
- pyrogenicity
- osmolality
- stability
- site and route of administration
- compatibility of components
- side effects and adverse reactions
- storage
- pharmacokinetics

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

1. FDA-approved veterinary or human pharmaceutical substances
2. FDA-approved veterinary or human pharmaceutical substances used to compound a needed dosage form
3. USP/NF or BP pharmaceutical grade substance used in a needed dosage form (also includes compounded products from any source)

4. Analytical grade bulk chemical used to compound a needed dosage form (requires justification)
5. Other grades and sources of substances (requires justification)

Most common substances used in laboratory animal research are available in pharmaceutical grade and should be used. Examples include:

- Saline
- DMSO (please view [SOP #1](#))
- Corn and sesame oil
- Tamoxifen
- Tetracycline
- Analgesics (e.g., Buprenorphine)
- Anesthetics (e.g., Ketamine, MS 222)
- Euthanasia agents (e.g., Pentobarbital and Phenytoin)

How to determine if your substance is pharmaceutical grade:

1. Presence of an NDC (National Drug Code) number on the box, bottle, or vial (this number is often in very fine print, and may be difficult to read; however, it is a reliable indicator of the substance grade); and
2. Presence of an expiration date; and
3. Presence of a lot number; and
4. Purchased from a USDA licensed vendor or pharmacy, or listed as “pharmaceutical grade” in the vendor catalog
5. Verbiage on box, bottle, or vial stating the product is FDA approved, or the presence of the USP insignia
6. The FDA has two reference books that can be used:
 - The “[Orange Book](#)” is for human FDA approved drugs
 - The “[Green Book](#)” is for veterinary FDA approved drugs

Specific IACUC SOPs for Non-Pharmaceutical Grade Substances

- [IACUC SOP #4](#) for Preparation of Sodium Pentobarbital Using Non-Pharm Grade Powder
- [IACUC SOP #6](#) for Euthanasia Using Saturated Potassium Chloride (KCl) Solution
- [IACUC SOP #1](#) for Preparation of Dimethyl Sulfoxide (DMSO)
- See [IACUC Guidelines on Compounding](#) for additional details on preparation and storage of compounds.

D. References

1. U.S. Department of Agriculture, Animal and Plant Health Inspection Service, Animal Care Policy 3
2. AAALAC Internationals Frequently Asked Question C9.
3. OLAW, Frequently asked questions, F. Animal Use and Management (4)
https://olaw.nih.gov/faqs#/guidance/faqs?anchor=questionuseandmgmt_4