ANIMAL EYE CONSULTANTS OF IOWA

Animal Eye Consultants of Iowa *Instituti* *mittee*	
Policy #29	**"Use of Non-Pharmaceutical Grade Substances"**
Approval Date: 1/21/26 (Replacing Version 2/6/2023)	

A. Purpose

This policy defines the Animal Eye Consultants of Iowa (AEC) Institutional Animal Care and Use Committee's (IACUC) position on the use of non-pharmaceutical grade substances in vertebrate animals and cephalopods used for research and teaching.

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 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, including for non-survival studies. This policy pertains to *all* components, both active and inactive, contained in the preparation to be administered to the animal. 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 USP/NF or BP has established a chemical purity standard.
- **Analytical grade bulk chemical:** ~99% purity; Certificate of Analysis is generally available.
- **Non-availability:** Not commercially available from an active US vendor; it includes formulations supplied as a 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. The FDA is responsible for assuring the safety, efficacy, and security of human and veterinary drugs, food, cosmetics, and medical devices.
- **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 a principal investigator proposes to use a non-pharmaceutical grade substance, it must be clearly described and justified within the Animal Subject Approval Form (ASAF) with the following information included:

- Justification on why a non-pharmaceutical grade compound must be used instead of a pharmaceutical grade one. Examples of acceptable justifications for this are below, per OLAW guidance:
  - An equivalent non-pharmaceutical grade substance is not available; this includes new investigational compounds.
  - A non-pharmaceutical grade substance is not available in the appropriate concentration or formulation, or the appropriate vehicle control is unavailable.
  - A non-pharmaceutical grade substance is available but does not meet the non-toxic vehicle requirements for the specified route of injection.
  - The non-pharmaceutical grade substance is required to generate data that relates to an ongoing study or to generate data that is comparable to previous work.
- Information on whether the compound will be altered in any way prior to administration to the animal (diluted, dissolved, mixed, etc.). Please view the IACUC Guidelines on Compounding.
- Information on how sterility is ensured (sterile filter, autoclave, etc.). If the compound cannot be sterilized, then scientific justification must be provided describing why and what other techniques will be used to ensure the final product administered to the animal is free of unwanted pathogens or contaminants.
- Provide the pH and tonicity of the final product if it differs from neutral pH or does not use a buffered and/or isotonic diluent or vehicle.
- Dose (in mg/kg) or dose range to be administered.
- Route (e.g., intravenous, intraperitoneal, oral, etc.) and frequency of administration (e.g., twice per day for one month).
- A description of any potential outcomes, side effects, toxicities, etc.

The use of a non-pharmaceutical grade compound *must* be approved by the IACUC before being administered (please view IACUC Policy #2 and Policy #24). 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 also responsible for evaluating the potential adverse consequences of non-pharmaceutical-grade substances when used for research. This includes potential for

contamination, safety, efficacy, and the inadvertent introduction of confounding research variables. For all substance use, the AEC 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

If a non-pharmaceutical compound is considered hazardous, it may be subject to additional review by Biosafety and require a Safety SOP per IACUC Policy #41.

When selecting compounds to be used in animal research, the following order of choice should be applied:

1. FDA-approved veterinary or human pharmaceutical substances (including those used to compound a needed dosage form)
2. USP/NF or BP pharmaceutical grade substance used in a needed dosage form (also includes compounded products from any source)
3. Analytical grade bulk chemical used to compound a needed dosage form (requires justification)
4. 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 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)

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

4. OLAW, Guidelines for the Use of Non-Pharmaceutical Grade Compounds in Laboratory Animals https://oacu.oir.nih.gov/system/files/media/file/2023-05/b14_pharmaceutical_compounds.pdf