

<b>Iowa State University Institutional Animal Care and Use Committee</b>	
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## **Institutional Animal Care and Use Committee (IACUC) Standard Operating Procedure**

### **THE USE OF NON-PHARMACEUTICAL GRADE COMPOUNDS**

#### **1. Purpose**

These guidelines describe the use of compounds and other chemicals administered to animals used for research, teaching or testing at Iowa State University. The NIH Office of Laboratory Animal Welfare (OLAW) and the United States Department of Agriculture (USDA) have both 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 IACUC.

These guidelines apply to compounds used for experimental or for therapeutic purposes. Deviation from these guidelines must be described and justified in an IACUC approved Animal Protocol.

The use of non-pharmaceutical grade compounds in animals may be necessary and appropriate but must be scientifically justified in an IACUC-approved Animal Protocol.

#### **2. Scope**

This SOP is applicable to all ISU staff, research investigators, and technicians who are on an approved IACUC protocol and are responsible for administration of experimental and/or therapeutic compounds to animals.

#### **3. General Requirements**

All investigators, staff, veterinarians and others who will administer drugs to animals for an IACUC protocol must follow the procedure outlined in this SOP. FDA approved pharmaceutical-grade drugs must be used if available. When investigational test compounds are being used, it is understood that the compound is not yet FDA approved.

If FDA approved drugs are not available, non-FDA approved drugs may be used only after specific review and approval by the IACUC for reasons such as scientific necessity, non-availability, or excessively high cost.

## 4. Procedure

### A) Drugs Administered for Therapeutic Purposes

- Current standards for veterinary therapeutic care of research animals state that pharmaceutical grade medications should be used for routine treatment.
- Examples of therapeutic purposes include:
  - Sedation and anesthesia for surgery or other procedures
  - Relief or treatment of disease or injury
  - Pain control (analgesia)
  - Euthanasia
- Drugs used for veterinary care, either as part of an IACUC approved Animal Protocol or an ISU veterinarian **approved treatment plan, should be obtained from a veterinary supply vendor or from a pharmaceutical supplier licensed by the FDA.**

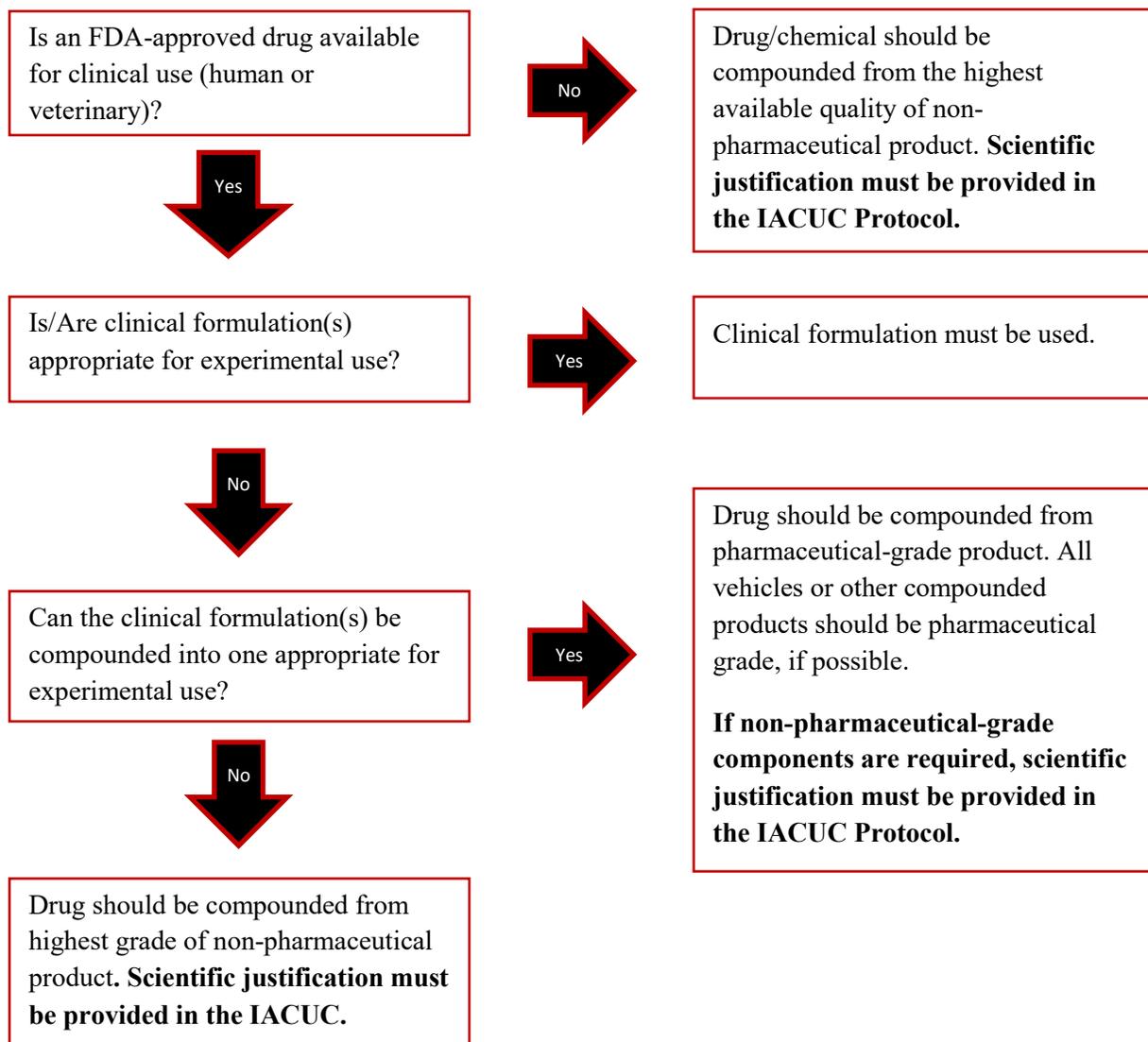
### B) Substances Administered for Experimental Purposes

When developing a protocol to administer a substance to an animal, the following factors should be considered:

- Purity/grade- the following order of choice should be applied:
  1. FDA approved veterinary or human pharmaceutical compound
  2. FDA approved pharmaceutical compound used to compound a needed dosage/formulation
  3. USP/NF or BP pharmaceutical grade compound used to compound a needed dosage/formulation
  4. Analytical grade bulk chemical used to compound a needed dosage/formulation
  5. Other grades and sources of compounds
- Safety
- Efficacy
- Sterility
- Pyrogenicity

- Stability
- pH/osmolality
- Site/route of administration
- Pharmacokinetics
- Physiological compatibility
- Quality control

The following questions should be considered when deciding what formulation(s) to use for your animal experiments:



### **C) Scientific Justification**

- In situations where use of a non-pharmaceutical grade substance is necessary and appropriate, the following sample text may be used and/or modified to illustrate scientific justification in your Animal Protocol:
  1. No pharmaceutical-grade human or veterinary drug is available
  2. A pharmaceutical-grade drug is available, but is not compatible with the concentration, formulation, delivery, or vehicle requirements of experimental administration
  3. A pharmaceutical-grade drug is available, but the use of a non-pharmaceutical grade product is required to replicate methods from previous studies because results must be directly compared to the results of replicated studies.

### **D) Anesthetic Agents for Aquatic Species**

The most commonly used anesthetic agent for fish and frogs is tricaine methane sulfonate, or MS-222. This agent is available as an FDA approved veterinary drug under the label Tricaine-S. Thus, ISU researchers should use this veterinary pharmaceutical-grade product according to the product label, which involves dilution in the appropriate aquatic habitat water from the housing facility, followed by buffering with sodium bicarbonate to an appropriate pH. Dosage and storage instructions contained in the IACUC Drug Formulary should be followed, unless otherwise described and justified in the IACUC Protocol.

### **E) Preparation and Handling of Drugs/Chemical Agents**

- Agents to be administered to animals must be handled and stored to maintain sterility and efficacy.
  - Appropriately closed sterile containers (e.g. injection vials, red-topped blood tubes) must be used, rather than snap-cap or screw-top containers.
  - The smallest amount of agent suspension/dilution/mixture should be used to minimize storage time prior to administration.
  - The rubber injection port/cap should be swabbed with alcohol prior to insertion of the needle.
  - Use a clean, sterile container for each preparation (do not reuse).
  - Use new sterile needles for each entry into a sterile container.
- Examine multiple-dose injection vials/tubes prior to use for evidence of physical or chemical contamination. Discard any substance meeting any of the following criteria:
  - Particulate matter visible

- Precipitation of solids
- Turbid or discolored appearance
- Mislabeled or unlabeled container
- Damage to the rubber stopper compromising integrity
- All containers must be labeled with:
  - Name of the drug(s)/chemical(s) contained
  - Concentration of the drug/chemical
  - Date of expiration (see below)

An example template is available [here](#).

#### F) Expiration of Drug Dilutions/Mixtures

- Sterile dilutions of mixtures of drugs may result in a shorter effective expiration date than the expiration date of the individual components, due to risk of contamination and dilution of preservatives.
- An expiration date of six (6) months from the date of preparation, or the earliest expiration date for any single component (if less than six months), is recommended as a general guideline; a shorter or longer time frame may be appropriate depending on the nature of the compound(s) and diluent(s), the frequency of vial entry, and the stability, efficacy, and safety of the compound(s) upon storage.

### 5. Roles and Responsibilities

<b>Roles</b>	<b>Responsibilities</b>
<b>Investigators, Staff and Students</b>	<ul style="list-style-type: none"> <li>● Must ensure that pharmaceutical-grade compounds are used if they are available.</li> <li>● If a pharmaceutical-grade compound is not available, must provide the IACUC specific details regarding the non-pharmaceutical compound proposed and give scientific justification for the use of it.</li> </ul>
<b>ISU IACUC</b>	<ul style="list-style-type: none"> <li>● Must evaluate the appropriateness of the proposed formulation of the final product and consider issues including grade/purity, sterility, pyrogenicity, stability, pH, osmolality, route of administration, pharmacokinetics, physiological compatibility with species under study, storage, and quality control.</li> </ul>
<b>ISU Attending Veterinarian</b>	<ul style="list-style-type: none"> <li>● The Attending Veterinarian is a consultant for the investigators and will help investigators make sure they are in compliance with this SOP.</li> </ul>

## 6. Definitions

Briefly define any job title, technique, equipment, or any other person/object described in the SOP that needs to be defined for clarification.

- FDA: Food and Drug Administration
- USP/NF: United States Pharmacopeia/National Formulary
- BP: British Pharmacopeia
- Pharmaceutical grade compound: Any substance which does not meet the above definition of pharmaceutical grade, including:
  - Analytical grade bulk chemical: ~99% purity chemical, Certificate of Analysis typically available
  - Pharmaceutical grade drug compounded with non-pharmaceutical grade vehicle or other substance

## 7. Health and Safety Information

n/a

## 8. Appendices

n/a

## 9. Forms and Templates

n/a

## 10. References

- University of Iowa SOP. Copied and used with permission. IACUC Guidelines: Use of Drugs and Chemicals in Laboratory Animals <https://animal.research.uiowa.edu/iacuc-guidelines-use-drugs-and-chemicals-laboratory-animals>
- PHS Policy on Humane Care and Use of Laboratory Animals <http://grants.nih.gov/grants/olaw/references/phspol.htm>
- *Guide for the Care and Use of Laboratory Animals*, Eighth Edition. Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council, National Academy Press, Washington, D.C., 2011.
- Office of Laboratory Animal Welfare: Educational Resources: Non-Pharm Use [http://grants.nih.gov/grants/olaw/educational\\_resources/webinar\\_06042015.htm](http://grants.nih.gov/grants/olaw/educational_resources/webinar_06042015.htm)
- [http://oacu.od.nih.gov/ARAC/documents/Pharmaceutical\\_Compounds.pdf](http://oacu.od.nih.gov/ARAC/documents/Pharmaceutical_Compounds.pdf)

## 11. Contact Information

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