



**Non-Pharmaceutical Grade Agents or Mixtures of
Pharmaceuticals (Cocktails) Use Procedures**

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1. Overview

1.1 Purpose

To ensure the use of non-pharmaceutical agents, mixtures of pharmaceuticals (cocktails) and non-drugs administered to animals by the parenteral route are of the appropriate chemical purity and quality and in the appropriate solution or compound, to ensure stability, safety, and efficacy.

2. Definitions

A **pharmaceutical-grade compound** is defined as any active or inactive drug, biologic or reagent, for which a chemical purity standard has been established by a recognized national or regional pharmacopeia (e.g., the U.S. Pharmacopeia (USP), British Pharmacopeia (BP), National Formulary (NF), European Pharmacopoeia (EP), Japanese Pharmacopeia (JP), etc.). These standards are used by manufacturers to help ensure the products are of the appropriate chemical purity and quality, in the appropriate solution or compound, to ensure stability, safety, and efficacy.

A listing of pharmaceutical-grade drugs and biologics is available through the [FDA database](#). The **Orange Book** is the reference for FDA-approved human drugs. The **Green Book** is the reference for FDA-approved veterinary drugs.

Veterinary compounding is 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. IACUCs considering the use of veterinary compounding for research purposes are advised to consult: <https://www.avma.org/KB/Resources/Reference/Pages/Compounding.aspx> for more information about federal regulations.

3. Regulatory Background

3.1 OLAW (NIH) and USDA Policy

The use of non-pharmaceutical grade chemical compounds in experimental animals under certain circumstances has been, and will continue to be, a necessary and acceptable component of biomedical research. OLAW and USDA have determined that their use should be based upon:

- a) scientific necessity;
- b) non-availability of acceptable veterinary or human pharmaceutical-grade compound(s);
- c) specific review and approval by the IACUC.

Although one can assume that issues such as sterility, pyrogenicity, stability, pharmacokinetics and quality control have been addressed during pharmaceutical-grade drug production, one cannot assume the same for non-pharmaceutical-grade chemical compounds ?? produced for use in a research laboratory. Many related animal welfare and scientific issues should be considered by investigators and by IACUCs when non-pharmaceutical-grade compounds are proposed. These issues include a) safety; b) efficacy; and c) the inadvertent introduction of research-complicating variables. Cost savings alone do not adequately justify the use of non-pharmaceutical-grade compounds in animals. Although the potential animal welfare consequences of complications are less evident in non-survival studies, the scientific issues remain the same, and the principles and need for professional judgment outlined above still apply.



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4. Procedures

Use of these compounds must be detailed in the IACUC protocol or amendment and approved by the IACUC.

4.1 Pharmaceutical Mixtures (Cocktails, e.g., Ketamine/Xylazine), Mixed-substance, and Secondary Containers

- 1) Should be used for only **30 days** after preparation, unless the manufacturer specifies an alternative expiration date or storage requirement. In such cases, the manufacturer's recommendations should be followed.
- 2) Must be prepared/maintained under sterile conditions.
- 3) ALL drugs to be mixed must be evaluated for expiration dates to ensure they are in date before they are compounded.
- 4) Must be clearly labeled with compound names, concentrations, date of preparation, and expiration date (Expiration date is 30 days after date of preparation or expiration of the drugs, whichever comes first).
- 5) Should be compounded per successful/effective use in published scientific literature.
- 6) Multi-dose containers must be labeled with date of first use/puncture.
 - a. Some compounds (e.g.- Rimadyl) have an abbreviated expiration once the vial is punctured and opened. This updated expiration date must be written on the vial.

4.2 Non-Pharmaceutical Grade Agents

- 1) Must be justified by scientific necessity and/or lack of availability of pharmaceutical-grade, commercially available preparations in the IACUC protocol. (Cost alone is not a valid justification for use).
- 2) Must be prepared and maintained under sterile conditions.
- 3) Must be evaluated to ensure physiological compatibility (pH, pyrogenicity, osmolarity, etc.)
- 4) Must be clearly labeled with compound names, concentrations, and date of preparation. Since the shelf-life of such compounds is unknown, these compounds should not be stored longer than 30 days after preparation, unless the manufacturer specifies an alternative expiration date or storage requirement. In such cases, the manufacturer's recommendations should be followed. Regardless of age, solutions should be discarded if they change color and/or precipitation occurs.

4.3 Non-Drugs Administered to Animals by the Parenteral Route (recombinant DNA, infectious agents, tumor lines, experimental compounds, and biomaterials)

- 1) Any agent administered to an animal must be described and justified in the protocol.
- 2) Must be prepared and maintained under sterile conditions.
- 3) Must be evaluated to ensure physiological compatibility (pH, pyrogenicity, osmolarity, etc.)
- 4) Must be clearly labeled with compound names, concentrations, and date of preparation. Since the shelf-life of such compounds is unknown, these compounds should not be stored longer than 30 days after preparation, unless the manufacturer specifies an alternative expiration date or storage requirement. In such cases, the manufacturer's recommendations should be



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followed. Regardless of age, solutions should be discarded if they change color and/or precipitation occurs.

5. Responsibilities

5.1 Drexel University IACUC Responsibilities

The Drexel University IACUC and the IACUC Office are responsible for maintaining this guidance document, training, and monitoring. All exceptions to this policy must be approved by the IACUC. For inquiries regarding these procedures, please contact the Director of Animal Welfare, a part of the Office for Research & Innovation (ORI), or the Attending Veterinarian.

5.2 Principal Investigator Responsibilities

The Investigator is responsible for ensuring that everyone working on an applicable protocol adheres to this policy.

6. Revisions

Edition 001/Effective Date: 12/12/2007 – Original Document

Edition 001/Review Date: 05/2017

Edition 002/Revision Date: 03/13/2024 and Effective Date: 04/09/2024 – Revised Document.

- Updated formatting to new template.
- Modified title to “Non-Pharmaceuticals Grade Agents or Mixtures of Pharmaceuticals (Cocktails) Use Procedures”
- Updated purpose to include safety and efficacy.
- Addition of non-drugs administered to animals by the parenteral route guidelines.
- Addition of Drexel University IACUC responsibilities

Edition 003/Revision Date: 06/10/2026 and Effective Date: 06/29/2026 – Revised Document.

- Guidance for secondary container use which aligns with current procedures for Pharmaceutical Mixtures
- Multi-dose containers must be labeled with the date of first puncture and the expiration date, based on the compounds abbreviated expiration date once punctured, as applicable.
- Addition of having the option for an expiration date outside of 30 days after preparation of the agent if "the manufacturer specifies an alternative expiration date or storage requirement. In such cases, the manufacturer's recommendations should be followed."