



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

Document No.:	Edition No.:	Effective Date:	Page:
ACU-211	002	4/9/2024	Page 1 of 4

Table of Contents

**1. Overview..... 2**

1.1 Purpose.....2

**2. Definitions..... 2**

**3. Regulatory Background..... 2**

3.1 OLAW (NIH) and USDA Policy .....2

**4. Procedures ..... 3**

4.1 Pharmaceutical Mixtures (Cocktails, e.g., Ketamine/Xylazine) .....3

4.2 Non-Pharmaceutical Grade Agents .....3

4.3 Non-Drugs Administered to Animals by the Parenteral Route (recombinant DNA, infectious agents, tumor lines, experimental compounds, and biomaterials) .....3

**5. Responsibilities ..... 3**

5.1 Drexel University IACUC Responsibilities .....3

5.2 Principal Investigator Responsibilities .....4

**6. Revisions ..... 4**



Document No.:	Edition No.:	Effective Date:	Page:
ACU-211	002	4/9/2024	Page 2 of 4

## 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);  
and
- 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 substances produced in the research laboratory using non-pharmaceutical-grade chemical compounds. 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.



Document No.:	Edition No.:	Effective Date:	Page:
ACU-211	002	4/9/2024	Page 3 of 4

## 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)

- 1) Should be used for only **30 days** after preparation.
- 2) Must be prepared/maintained under sterile conditions.
- 3) **MUST** be clearly labeled with compound names, concentrations, date of preparation, and expiration date. (expiration date is 30 days after date of preparation).
- 4) Should be compounded according to methods of successful use/efficacy in published scientific literature.

### 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 assure 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. Regardless of age, solutions should be discarded if changes in color and/or precipitation occur.

### 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 assure 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. Regardless of age, solutions should be discarded if changes in color and/or precipitation occur.

## 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.



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

Document No.:	Edition No.:	Effective Date:	Page:
ACU-211	002	4/9/2024	Page 4 of 4

## 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 procedures.
- Addition of Drexel University IACUC responsibilities