

**Subject: Use of Non-Pharmaceutical Grade
Chemicals and Compounding Pharmaceutical Grade Drugs**

Source: Institutional Animal Care and Use Committee (IACUC)
Effective Date: 04/08/2024
Replaces: 11/13/2023
Applies to: Research or teaching studies involving animals
Reference: AWA; PHS Policy on Humane Care & Use of Laboratory Animals; Guide for the
Care & Use of Laboratory Animals

Introduction

The Institutional Animal Care and Use Committee (IACUC) maintains oversight review for federally mandated rules and regulations with regard to animal research, ethics, misconduct and biomedical research for the University of Colorado Denver | Anschutz Medical Campus (CU Denver | Anschutz).

Policy Statement

This policy provides information on non-pharmaceutical-grade chemical/compound use and compounding of pharmaceutical grade drugs in laboratory animals.

- The policy is based upon the Guide for the Care and Use of Laboratory Animals (8th edition, 2011) and the OLAW webinar “The Use of Non-Pharmaceutical-Grade Chemicals and Other Substances in Research with Animals” (Mar 1, 2012). Pharmaceutical grade materials should be used whenever available, including acute procedures. However, the use of non-pharmaceutical grade materials has been, and will continue to be, a necessary and acceptable component of biomedical research. Use of such compounds at CU Denver | Anschutz will be based upon:
 - non-availability of acceptable veterinary or human pharmaceutical-grade compound(s), including in the correct formulation or concentration.
 - scientific necessity
- Pharmaceutical Grade compounds are defined as substances that are available for use in human or veterinary clinical practice and are created using Good Manufacturing Practices (GMP) or obtained from a licensed compounding pharmacy.
- Substances purchased from a chemical company (such as Sigma, Fischer Scientific, etc.) are generally considered non-pharmaceutical grade, even if the powder is labeled as USP or pharmaceutical grade.
 - Use of these agents must be indicated in the protocols as non-pharmaceutical grade and have a scientific justification for their use. There must also be a description of the preparation and how the drug will be evaluated to assure physiologic compatibility with the criteria described in the section below.

Criteria for the Use of Non-Pharma-Grade Chemicals/Compounds in Laboratory Animals

- All non-pharmaceutical grade substances must be described and justified in the animal use protocol and be approved by the IACUC. In the review of non-pharmaceutical grade compounds, the CU Denver | Anschutz IACUC will consider:
 - safety;
 - efficacy; and
 - the inadvertent introduction of research-complicating variables.
- Cost savings alone is not sufficient justification to use non-pharmaceutical-grade compounds in animals. However, unavailability or shortages of pharmaceutical grade substances can lead to cost increases and allow the IACUC to determine if this justifies the use of non-pharmaceutical grade substitution.

- Contingent upon review and approval by the IACUC, non-pharmaceutical grade agents:
 - Should be prepared and maintained under sterile conditions, depending on use and route of administration.
 - Should be evaluated to assure physiological compatibility (e.g., pH, pyrogenicity, osmolarity, etc.)
 - Must be clearly labeled with compound names, concentrations, and date of preparation.
 - The beyond use date of non-pharmaceutical grade substances must not exceed 30 days after mixing unless exception criteria below are met.
 - Regardless of age, solutions with color changes and/or precipitation should be discarded.
 - Should be documented regarding safety and efficacy consistent with methods of successful use and efficacy in published scientific literature, if available.
 - Unused reagent must be discarded in accordance with standard EH&S practices.
- The CU Denver | Anschutz IACUC realizes that many test articles and novel compounds are only available as non-pharmaceutical grade products. However, PIs should use all available knowledge of the compounds to ensure the aforementioned appropriate preparation, evaluation, storage, use, and disposal and provide information on how this will be accomplished in the applicable section of the protocol.
 - The justification for the use of these novel items is that it does not exist as a pharmaceutical grade compound.

Beyond Use Dating of Compounded Pharmaceutical Grade Drugs

- Pharmaceutical grade drugs are often not manufactured at concentrations appropriate for accurate dosing in laboratory animal species. Changing a pharmaceutical grade drug's concentration, using different diluents than originally manufactured, changing the primary container for dilution, or mixing of two or more pharmaceutical grade drugs is termed "compounding." Once compounded a "beyond use date" serves as the new expiration date for the compounded drug(s).
 - The beyond use date of compounded drugs must not exceed 30 days unless exception criteria below have been met.
 - The beyond use date cannot exceed the original manufacturer's expiration date.
- Compounded drugs that originally were pharmaceutical grade:
 - Must be prepared and maintained under sterile conditions.
 - Must be clearly labeled with the drugs name (in English), concentration, and date of preparation.
 - Must be discarded in accordance with standard EH&S practices.
- Dilution does not exempt controlled substances from DEA requirements on record keeping.

Exceptions to 30 Day Beyond Use Dates

Beyond use dates that exceed 30 days are contingent upon review and approval by the IACUC with consideration of the following:

- Scientific justification.
- Sterility testing or published sterility information when formulated and stored in a similar manner.
- Stability testing or published stability information when formulated and stored in a similar manner.

Per regulatory requirements, failure to comply with this policy may result in notification of your funding agency (e.g. NIH) and regulatory agencies (e.g. USDA) that your research has violated federal and/or local policies regarding the humane use of animals. This notification may affect continuous funding of your animal-related research. Further, depending on the violation, you may be required to take additional training and/or your privilege to conduct animal research at CU Denver | Anschutz might be temporarily suspended or even completely revoked.