



## Policy: Use of Non-Pharmaceutical Grade Compounds and Expired Materials in Animals

<b>Objective:</b>	To describe use of non-pharmaceutical grade compounds and expired materials in animals
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<b>Date:</b>	January 24, 2022

### Scope

This policy provides a definitive position on the use of non-pharmaceutical grade compounds or expired materials in the UNC Charlotte animal care & use program. The policy is consistent with the guidance from the NIH/ILAR Guide for the Care and Use of Animals, the corresponding position statement from AAALAC International, and the NIH/Office of Laboratory Animal Welfare's position statement.

### Definitions

**Pharmaceutical Grade Compound:** 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<sup>4</sup> (e.g. the U.S. Pharmacopeia (USP), British Pharmacopeia (BP), National Formulary (NF), European Pharmacopeia (EP), 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. Pharmaceutical grade drugs are formulated to a standard compatible with the legal and ethical treatment of human or veterinary patients in a health care or practice setting by a pharmaceutical company or qualified compounding pharmacist.

**Non-pharmaceutical grade agents:** Chemical compounds that have not been formulated for production of medicine. Agents obtained from chemical supply companies and or prepared in a research laboratory are of reagent and not pharmaceutical grade.

### Policy

#### Non-Pharmaceutical Grade Compounds

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 consider that the use of non-pharmaceutical grade compounds should be based on:

- Scientific necessity;
- Lack of availability of an acceptable veterinary or human pharmaceutical-grade compound; and
- Specific review and approval by the IACUC.

Further, OLAW and USDA state: *“Investigators and IACUCs should consider relevant animal welfare and scientific issues including safety, efficacy, and the inadvertent introduction of new variables. In preparing and reviewing proposals to use non-pharmaceutical-grade products, investigators and IACUCs should consider a number of related animal welfare and scientific issues including safety, efficacy, and the inadvertent introduction of research-complicating variables. Although one can assume that issues such as*

*sterility, pyrogenicity, stability, pharmacokinetics, and quality control have been addressed during the course of producing pharmaceutical-grade drugs, one cannot say the same for substances produced in the research laboratory using non-pharmaceutical-grade chemical compounds. 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.”*

In keeping with this guidance, the UNC Charlotte IACUC expects Investigators to use pharmaceutical-grade medications whenever they are available, even in acute (non-survival) procedures. Use of non-pharmaceutical grade compounds must be approved in advance by the IACUC. The IACUC has established the following guidelines and policy for the use of non-pharmaceutical grade compounds:

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

- Must be prepared/maintained under sterile conditions
- Must be clearly labeled with compound names, concentrations, and date of preparation (expiration date shall be assumed to be 7 days after date of preparation).
- Should be compounded according to methods of successful use/efficacy in published scientific literature.

#### Non-Pharmaceutical Grade Agents

- Must be justified by scientific necessity and/or lack of availability of pharmaceutical-grade, commercially available preparations. (Cost alone is not valid justification for use). **Justification to be included in the protocol and approved in advance by the IACUC.**
- Should be documented regarding safety and efficacy consistent with methods of successful use/efficacy in published scientific literature if available.
- Must be prepared/maintained under sterile conditions.
- Must be evaluated by the investigator to assure physiological compatibility (pH, pyrogenicity, osmolarity, sterility, etc.)
- Must be clearly labeled with compound names, concentrations, and date of preparation. Since shelf life of such compounds is unknown, long-term storage (> 30 days) is strongly discouraged. Regardless of age, solutions should be discarded if changes in color and/or precipitation occur.

The NIH recommends that the following order of choice should be applied:

1. FDA approved veterinary or human pharmaceutical compounds;
2. FDA approved veterinary or human pharmaceutical compounds used to compound a needed dosage form;
3. USP/NF or BP pharmaceutical grade compound used in a needed dosage form;
4. Analytical grade bulk chemical used to compound a needed dosage form (requires justification in animal use protocol);
5. Other grades and sources of compounds (requires justification in animal use protocol).

#### Use of Expired Materials

OLAW states, “*The use of expired pharmaceuticals, biologics, and supplies is not consistent with acceptable veterinary practice or adequate veterinary care. Euthanasia, anesthesia and analgesia agents should not be used beyond their expiration date, even if a procedure is terminal. Other expired materials*

*should not be used unless the manufacturer verifies efficacy beyond the expiration date, or the investigator is able to document to the satisfaction of the IACUC that such use would not negatively impact animal welfare or compromise the validity of the study. The veterinarian and IACUC must maintain control over the use of expired medical materials in order to meet their responsibilities to avoid or minimize discomfort, pain or distress to animals.”*

The use of expired medical materials such as drugs, fluids, or sutures on animals is not considered to be acceptable veterinary practice and does not constitute adequate veterinary care as required by current animal care and use regulations. Medical materials (e.g. catheters, sterile gloves, sutures) are often imprinted with an expiration date, beyond which the manufacturer does not guarantee the safety or stability of the item. Because it is recognized that in some specific situations there may be a rationale to utilizing expired materials (e.g., the items would be difficult to replace and there is reason to believe they should be considered safe), the IACUC has established the following guidelines and policy for the conditional use of expired medical products.

- Expired analgesic or anesthetic drugs may NEVER be used, even in non-survival procedures.
- Expired euthanasia agents may only be used on anesthetized animals, however they may never be used in USDA covered species.
- Outdated materials may only be used in non-survival procedures if their use does not adversely affect the animal's well-being or compromise the validity of the study. Explicit IACUC justification and approval is required.
- Expired materials may not be used in survival procedures unless specifically approved by the IACUC. Such approval must be obtained prior to the use of expired materials in survival procedures.
- Medical materials (e.g. catheters, sterile gloves, sutures): in general, after the expiration date these materials should be used only in procedures involving anesthetized animals in non-survival studies. If needed for survival studies, outdated items (or any items that may no longer be sterile) should be re-packaged and re-sterilized using an appropriate method before use. Re-sterilized items should be labeled with a new expiration date that is appropriate for the packaging used. If an investigator obtains information from the manufacturer that provides documentation that a particular material or instrument has been shown to remain sterile beyond the date on the packaging, a request to use the item in survival studies will be considered by the IACUC.
- Expired/outdated items must be kept physically separated from other similar in-date items and clearly labeled “Outdated Materials – For Terminal Procedures Only” (or similarly).
- The UNC Charlotte IACUC recommends that each laboratory establish an inventory procedure to facilitate the identification and removal of expired drugs and materials utilized for research purposes involving animals.
- Expired materials should be maintained in sterile or clean condition.

## **References**

USDA/APHIS Animal Care Resource Guide Policies, AC, 3.1:

[https://www.aphis.usda.gov/animal\\_welfare/downloads/Animal%20Care%20Policy%20Manual.pdf](https://www.aphis.usda.gov/animal_welfare/downloads/Animal%20Care%20Policy%20Manual.pdf)

NIH OLAW FAQ F.5, May investigators use expired pharmaceuticals, biologics, and supplies in animals??: <http://grants.nih.gov/grants/olaw/faqs.htm#663>

Guidelines for the Use of Non-Pharmaceutical Grade Compounds in Animals. NIH Office of Animal Care and Use (OACU) Policy revised 04/10/2013:

[http://oacu.od.nih.gov/ARAC/documents/Pharmaceutical\\_Compounds.pdf](http://oacu.od.nih.gov/ARAC/documents/Pharmaceutical_Compounds.pdf)

National Research Council. *Guide for the Care and Use of Laboratory Animals: Eighth Edition.*

Office for Laboratory Animal Welfare (OLAW) Position Statements: <http://grants.nih.gov/grants/olaw/>

Association for the Assessment and Accreditation of Laboratory Animal Care International (AAALACi) Position Statements: <http://www.aaalac.org/accreditation/positionstatements.cfm>

Emory University Non-Pharmaceutical Grade Substances Policy (version 20140618 revised 09/2014): [http://www.iacuc.emory.edu/documents/365\\_Nonpharmaceutical\\_Grade\\_Drugs.pdf](http://www.iacuc.emory.edu/documents/365_Nonpharmaceutical_Grade_Drugs.pdf)

### **Revision History**

Approved August 27, 2012

Revised April 27, 2015; March 28, 2016

Re-approved March 25, 2019; January 24, 2022

Administrative changes October 1, 2022