



## Policy 365

### Non-Pharmaceutical Grade Substances

<b>Responsible Official:</b>	Research Administration
<b>Administering Division/Department:</b>	Research Compliance and Regulatory Affairs / IACUC
<b>Effective Date:</b>	11/16/2005
<b>Last Revision Date:</b>	02/02/2022

**365.1 Emory Policy:** In accordance with USDA<sup>1</sup> and OLAW<sup>2,3</sup> policy, Emory University requires that pharmaceutical grade substances (e.g., fluids, compounds, medications, drugs, vehicles, and diluents), as defined in section 365.2, be used in all cases in which they are available. This policy applies to all vertebrate species and includes survival as well as non-survival procedures. The Emory IACUC may approve the use of non-pharmaceutical grade (NPG) substances under certain circumstances, such as those cases in which pharmaceutical grade alternatives are not available, or not available in the required formulation or concentration, or do not exist in a form compatible with the intended route of administration. Approval in these cases is contingent on institutional review by the IACUC (see section 365.3).

#### 365.2 Definitions of Key Terms Specific to this Policy

**365.2.1** 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.

**365.2.2** Non-pharmaceutical grade agents refer to 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.

#### 365.3 Justification for Use of non-pharmaceutical Grade Substances



Both USDA and OLAW regulations indicate that “the IACUC should develop a consistent evaluation process that includes but is not limited to the scientific justification and the availability of an acceptable veterinary or human pharmaceutical-grade product. Cost savings alone is not sufficient justification for using a non-pharmaceutical-grade substance in regulated species. However, unavailability or shortages of pharmaceutical grade substances may lead to cost increases and the IACUC may determine that this justifies the use of the non-pharmaceutical grade substitution.”<sup>1</sup> A history of the use of a NPG substance alone is not a sufficient justification for continued use.

To secure approval for the use of non-pharmaceutical grade substances, the PI must (1) provide sound scientific justification for the use of the compound, (2) verify that the compound is not available as a pharmaceutical grade product in the required formulation or concentration (if available in higher concentrations than needed, identification of the diluent is necessary and dilution with a pharmaceutical grade diluent is generally required), and (3) justify use of the NPG product as an appropriate alternative. Required information for the latter includes description of the means to assure purity, sterility, and stability. In addition, information needed for review includes the site and route of administration, and potential side effects and adverse reactions. Other variables that investigators may wish to consider include information regarding the grade, acid-base balance, pyrogenicity, osmolality, compatibility of components, and pharmacokinetics of the NPG compound. Investigators may refer to sources of information such as QC data sheets from the manufacturer, references to previous publications using the substance, and/or documentation of independent testing for purity or sterility.

Note that the proper reconstitution and use of injectable agents is critical and is covered under the IACUC [Injectable Agents policy](#) (and see addendum below). For those instances in which it is not possible to use pharmaceutical grade compounds, the highest available reagent grade should be used instead.

#### **365.4 Identification and Assistance in Substance Identification.**

**365.4.1** A listing of pharmaceutical-grade drugs and biologics is available through the FDA Database

<http://www.fda.gov/Drugs/InformationOnDrugs/default.htm>

**365.4.2** The Orange book is the reference for FDA-approved human drugs

<http://www.accessdata.fda.gov/scripts/cder/ob/>

**365.4.3** The Green Book is the reference for FDA-approved veterinary drugs.

<http://www.fda.gov/animalveterinary/products/approvedanimaldrugproducts/default.htm>

#### **365.4.4 University Contacts**



Emory University Healthcare Investigational Drug Service, 404-712-7485

### 365.5 Applicability

This policy applies to all Emory research related animal activities that fall under the IACUC's jurisdiction.

### 365.6 References

- 1) [USDA-APHIS Animal Care Policy Manual, Policy #3](#) states that "Pharmaceutical-grade substances are expected to be used whenever they are available, even in acute procedures. This includes but is not limited to: compounds, medications, drugs, vehicles, and diluents. APHIS recognizes that some substances (e.g. test articles, novel compounds, and those resulting from a compounding process) are only available as a non-pharmaceutical grade product. Non-pharmaceutical-grade substances should only be used in regulated animals after specific review and approval by the IACUC."
- 2) On March 1, 2012, OLAW, with USDA and AAALAC, offered additional information through a webinar on the "[Use of Non-Pharmaceutical-Grade Chemicals and Other Compounds in Research with Animals](#)." Here you will find a recording of the webinar, a transcript that includes answers to numerous questions, plus examples of situations for the use of non-pharmaceutical-grade substances. OLAW indicates its agreement with the USDA that pharmaceutical-grade chemicals and other substances, when available, must be used to avoid toxicity or side effects that may threaten the health and welfare of vertebrate animals and /or interfere with the interpretation of research results but notes also that it is frequently necessary to use investigational compounds, veterinarian- or pharmacy-compounded<sup>1</sup> drugs, and /or Schedule I<sup>4</sup> controlled substances to meet scientific and research goals.
- 3) "Guide for the Care and Use of Laboratory Animals: Eight edition" National Research Council. The National Academic Press. 2011. Pg 31.
- 4) 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 [Compounding](#) for more information about federal regulations.



**Addendum**

**Reconstitution of Non-Pharmaceutical Grade Substances**

Injectable agents must be sterilized prior to administration. This may be accomplished by passing the reconstituted compound through a 0.2µm filter. Diluents and solvents used for reconstitution should be pharmaceutical grade if possible. Please refer to IACUC [Injectable Agents Policy](#) for comprehensive guidance.

- Compounds reconstituted for multi-use must be labeled identifying the compound, concentration or activity, the date of preparation, the initials of the person who prepared the solution/suspension and the expiration date.
- Reconstituted compounds should be discarded before degradation occurs. If degradation is unknown, prepare compound fresh for each use.
- Follow all manufacturer guidelines.

**Contact Information**

Subject	Contact	Phone	Email
Clarification of Policy	Office of Research Compliance and Regulatory Affairs - IACUC	404-712-0734	iacuc@emory.edu

**Revision History**

- 09/03/2014; 02/02/2022