



Animal Facility SOP 23.2 Non-Pharmacological Grade Drugs SOP

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I. PURPOSE

To provide information for investigators on the use of non-pharmaceutical grade compounds in laboratory animals.

II. SCOPE

This SOP applies to all University Animal Users and support staff.

III. BACKGROUND

Regulation: USDA Policy 3 states the following regarding use of non-pharmaceutical grade compounds in animal experimentation:

Investigators are expected to use pharmaceutical-grade medications whenever they are available, even in acute procedures. Non-Pharmaceutical-grade chemical compounds should only be used in regulated animals after specific review and approval by the IACUC for reasons such as scientific necessity or non-availability of an acceptable veterinary or human pharmaceutical-grade product. Cost savings alone are not an adequate justification for using non-pharmaceutical-grade compounds in regulated animals.

OLAW: May investigators use non-pharmaceutical-grade compounds in animals?

OLAW and USDA agree that pharmaceutical-grade¹ 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. However, it is frequently necessary to use investigational compounds, veterinarian or pharmacy-compounded² drugs, and/or Schedule I

¹ A pharmaceutical grade compound is a drug, biologic, or reagent that is approved by the Food and Drug Administration (FDA) or for which a chemical purity standard has been established by the [United States Pharmacopeia-National Formulary \(USP-NF\)](#), or [British Pharmacopeia \(BP\)](#).

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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: http://www.avma.org/issues/drugs/compounding/veterinary_compounding_brochure.asp for more information about federal regulations.

³controlled substances to meet scientific and research goals.

Guide for the Care and Use of Laboratory Animals; Eighth edition:

“The use of pharmaceutical-grade chemicals and other substances ensures that toxic and unwanted side effects are not introduced into studies conducted with experimental animals. They should therefore be used, when available, for all animal-related procedures. The use of non-pharmaceutical-grade chemicals or substances should be described and justified in the animal use protocol and be approved by the IACUC; for example, the use of non-pharmaceutical-grade chemicals of substance may be necessary to meet the scientific goals of a project when a veterinary or human pharmaceutical-grade produce is unavailable.”

Please refer to the following documents for guidance when considering the use of Non-Pharmaceutical-Grade compounds in your experiments.

- [Use of Non-Pharmaceutical-Grade Chemicals and Other Substances in Research with Animals.](#)

Webinar slide presentation from OLAW, USDA, and AAALAC.

- [Examples for Use of Non-Pharmaceutical-Grade Substances](#)
- The FDA publishes the [Green Book](#) (veterinary) and the [Orange Book](#) (human) databases of approved drugs. Substances listed in these databases are recognized as pharmaceutical-grade. Please use the links to aid in your search. Also, you may determine whether a particular drug is available by consulting the [FDA database](#).

IV. PROCEDURES

The Morgan State University Institutional Animal Care and Use Committee (IACUC) requires that, for all vertebrate species, pharmaceutical grade medications ⁴be used for sedatives, analgesics, and anesthetics that are approved to be administered to prevent or alleviate pain and/or distress that may be caused by procedures carried out under an approved protocol.

If a Principal Investigator wishes to obtain approval to use a non-pharmaceutical grade compound instead, the procedures for the planned use (e.g., sterility of injected solutions) must be reviewed and approved by the IACUC in advance of use.

If the non-pharmaceutical grade compound is to be used in species regulated under the Animal Welfare Act ⁵a scientific justification must be provided or pharmaceutical grade formulations must be unavailable in order to obtain IACUC approval ⁶

³ United States Department of Justice Drug Enforcement Agency controlled substances Schedule I and II-IV drugs may be used in biomedical research according to the standards of the [Code of Federal Regulations 1301.13](#).

⁴ For the purposes of this policy, a pharmaceutical grade medication is one that has been formulated for clinical use in humans or in veterinary practice.

⁵ Species regulated under the AWA include all warm-blooded animals except that rats, mice, and birds that were bred for use in research are explicitly excluded from coverage by the Act (9 CFR, Part 1, Section 1.1.).

⁶ This requirement is consistent with USDA Policy #3, which provides guidance on interpretation of AWA regulations in 9 CFR, Part 2, Section 2.31, and 2.32.

What is a Pharmaceutical-Grade Compound?

Is any active or inactive drug, biologic, reagent, etc. which is approved by the FDA or for which a chemical purity standard has been written/established by any recognized pharmacopeia.

1. It is expected that all chemical compounds administered to any animal species be pharmaceutical grade, if that agent is available in pharmaceutical grade, even in acute procedures. It's expected that all PI's that propose to use chemical compounds to be administered conduct a search in any recognized pharmacopeia to find a pharmaceutical grade equivalent to be used. For all species, the IACUC requires that specific permission be obtained to use non-pharmaceutical agents for veterinary therapeutics or relief of pain or distress (including anesthetics, analgesics, sedatives, antibiotics, or paralytics). Justification for the use of non-pharmaceutical agents in these categories may include availability of suitable pharmaceutical grade drugs or scientific necessity.
 - a. The IACUC will follow all applicable guidelines for the use of non-pharmaceutical-grade compounds. There are two scenarios when considering the use of non-pharmaceutical-grade compounds:
 - i. **Clinical Use** - compounds used for the clinical treatment of animals and to prevent or reduce/eliminate animal pain or distress. Whenever possible, pharmaceutical-grade compounds must be used.
 - ii. **Research Use** - compounds used to accomplish the scientific aims of the study. If available, and suitable, pharmaceutical-grade compounds are preferred; but when non-pharmaceutical-grade preparations are used, the IACUC and investigators are expected to consider the following factors listed in #3 below.
2. For all species, permission must be obtained from the IACUC to administer any non-pharmaceutical chemical compounds. Justification for the use of non-pharmaceutical agents may include availability of suitable pharmaceutical grade drugs or scientific necessity. Cost in itself is not typically considered an adequate reason to employ non-pharmaceutical chemical compounds.
3. For all species, any non-pharmaceutical chemical agents administered in survival and non-survival studies, and animal experimentation must meet quality control and assurance standards, which must be addressed in the IACUC protocol form.

These factors would include:

- o Appropriate drug reconstitution, preparation and/or compounding
- o Drug purity, sterility, pH, osmolality, concentration, et cetera
- o Drug safety, efficacy, and shelf-life
- o Training, experience, and performance of personnel involved
- o Responsibility for monitoring preparation and use
- o Site and route of administration
- o Side effects and adverse reactions
- o Storage and pharmacokinetics

*Not all factors may be applicable.

*If the "shelf life" is not obtainable, it is recommended that the drug solution be re-prepared each day it is used.

In Accordance:

[Guide for the Care and Use of Laboratory Animals, 8th Edition, Page 31](#)

[USDA Policy #3, Veterinary Care](#)

[OLAW FAQ website on the use on Non-pharmaceutical grade compounds](#)

[9 CFR, Part 2, Sections 2.31, 2.32, 2.33, 2.40; 9 CFR, Part 3, Section 3.110](#)

[AAALAC FAQ #9 Non-Pharmaceutical-Grade Compounds](#)

[FDA Database](#)

[Orange Book:](#)

[Green Book:](#)