MASSACHUSETTS GENERAL HOSPITAL

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

POLICY ON THE USE OF NON-PHARMACEUTICAL GRADE SUBSTANCES IN LABORATORY ANIMALS

GENERAL POLICY

Both OLAW and AAALACi provide guidance regarding the use of non-pharmaceutical grade compounds in laboratory animals. Pharmaceutical-grade 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 non-pharmaceutical-grade substances such as investigational substances, compounded substances, and/or Schedule I controlled substances to meet scientific and research goals.

DEFINITIONS

Pharmaceutical-grade compound: A pharmaceutical-grade compound (PGC) 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. The Food and Drug Administration (FDA) maintains a database listing of FDA approved commercial formulations for both FDA approved drugs (the Orange Book) and veterinary drugs (the Green Book).

The following are considered **pharmaceutical grade**:

- FDA-approved, commercially available human or veterinary formulations
- Compounded product prepared by a registered pharmacist using USP standards
- Dilutions or combinations of FDA-approved, commercially available human or veterinary formulations used to compound a needed dosage. Examples: Buprenex (buprenorphine) diluted with sodium chloride (0.9%) injection solution or Ketaset (ketamine) and xylazine diluted with sodium chloride (0.9%) injection

solution for administration to rodents. *Note*: all constituents of the dosage **must** be pharmaceutical grade.

USP grade: USP grade refers to the chemical purity of a material. USP grade material is of sufficient purity to be used in the manufacture of food, drugs, or medications. The bulk drug or chemical is considered **non-pharmaceutical grade**. Example: USP grade tamoxifen purchased as a powder from Sigma.

New investigational substances: substances that are supplied by the manufacturer for testing in an experimental setting only. A new investigational substance would not have chemical purity standards established and by default is considered a **non-pharmaceutical grade** compound.

Availability: Refers to whether a product is commercially available from an active U.S. vendor.

JUSTIFICATION AND USE OF NON-PHARMACEUTICAL GRADE SUBSTANCES

The use of non-pharmaceutical grade substances (including active substance and other active or inactive constituents such as vehicles) must be described and justified in the IACUC protocol. Appropriate scientific justification for the use of non-pharmaceutical grade substances includes:

- No equivalent veterinary or human drug is available for experimental use; this includes new investigational compounds.
- Pharmaceutical grade is not available in the appropriate concentration or formulation, or the appropriate vehicle control is not available.
- Non-pharmaceutical grade is required to generate data as part of an on-going study or to generate data that are comparable to previous work without inadvertent introduction of new variables.

Cost savings alone is not considered an adequate justification for the use of non-pharmaceutical-grade substances

Agents for sedation, analgesia, anesthesia, or euthanasia should be commercially available veterinary or human preparations, unless the use of an investigational chemical or formulation is scientifically necessary, appropriately justified, and approved by the IACUC.

Non-pharmaceutical grade substances must be prepared as described in the Guidelines for Preparing Drugs and Agents for Animal Research. When formulating from bulk drug or chemical, USP grade material should be used when available. If USP grade drug or chemical cannot be obtained, material of the highest purity available, e.g., American Chemical Society (ACS) grade or reagent grade, should be used.

REFERENCES

AAALACi. Frequently Asked Questions, C. Institutional Responsibilities, 9. Non-Pharmaceutical-Grade Compounds. June 2017.

National Research Council of the National Academies. *Guide for the Care and Use of Laboratory Animals,* 8th edition. National Academies Press: Washington, D.C., 2011.

U.S. Department of Health and Human Services. Guidelines for the Use of Non-Pharmaceutical Grade Compounds in Laboratory Animals . National Institutes of Health, Animal Research Advisory Committee: Bethesda, MD, March 4, 2016.

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