

Title: **Use of Non-Pharmaceutical Grade Compounds**

Effective Date: **May 19, 2020** Revision # **00**

Standard Operation Procedure Number: **IACUC-RVW-036** Last Committee Review: **May 19, 2020**

Purpose and Scope

This policy establishes standards of review for the IACUC to ensure animal welfare is preserved. The use of non-pharmaceutical grade compounds can present a risk to animal welfare due to concerns over consistency, contamination, or preparation. This policy has been developed to ensure that MSU complies with the Guide for the Care and Use of Animals, 8th Edition, and the Animal Welfare Act and Regulations. This policy applies to all animals cared for at MSU.

References

- a. NIH Office of Animal Care and Use, Guidelines for the Use of Non-Pharmaceutical Grade Compounds in Laboratory Animals (Last Revised, 2013)
(http://oacu.od.nih.gov/ARAC/documents/Pharmaceutical_Compounds.pdf)
- b. OLAW Position Statement 3) Non-Pharmaceutical-Grade Substances
(http://grants.nih.gov/grants/olaw/positionstatement_guide.htm#nonpharma)

Background

The use of pharmaceutical-grade substances in laboratory animals ensures that the substances administered meet established documentable standards of purity and composition. This in turn helps ensure research animal health and welfare, as well as the validity of experimental results. The use of lower grade substances/compounds with undefined or higher levels of impurities or poorly formulated non-commercial preparations can introduce unwanted experimental variables or even toxic effects, and so should be avoided if at all possible. Although pharmaceutical grade substances should be used in experimental animals whenever possible, the use of nonpharmaceutical-grade substances in experimental animals is an acceptable practice under certain circumstances. For example, in the case of new investigational compounds, they would be the only grade and formulation available.

The NIH Office of Laboratory Animal Welfare (OLAW) and the United States Department of Agriculture (USDA) both have determined that the use of nonpharmaceutical-grade substances should be based on:

- (1) scientific necessity,
- (2) non-availability of an acceptable veterinary or human pharmaceutical-grade compound, and
- (3) specific review and approval by the institutional IACUC. The use of chemical grade substances must be clearly delineated and justified in the IACUC proposal. Cost savings alone is not considered an adequate justification for the use of non-pharmaceutical-grade substances in laboratory animals.

Definitions

1. Pharmaceutical Grade Substances: drugs, biologics, or reagents that are 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).
2. New investigational compound: Supplied by its manufacturer for testing in an experimental setting only and for this reason would not have chemical purity standards established; by default is considered a non-pharmaceutical grade compound.

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Policy

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 nonavailability of an acceptable veterinary or human pharmaceutical-grade product. Cost savings nor administrative burden of acquiring a DEA License are not an adequate justification for using non-pharmaceutical grade compounds on regulated animals.

The investigator must also provide sufficient information to the IACUC to permit the IACUC to assess the potential of the non-pharmaceutical grade drug to harm animal health or well-being. This should include specifics regarding the toxicity of the drug components if known, and details regarding the drug preparation where the drug is not a pharmaceutical grade drug and is not compounded by a licensed pharmacist.

The IACUC is responsible for evaluating the potential adverse consequences of such agents when used for research. The IACUC should consider the as applicable and relevant to the specific circumstance: grade/purity being proposed, the formulation of the final product, and issues such as sterility, pyrogenicity, stability, pH, osmolality, site/route of administration, pharmacokinetics, physiological compatibility, storage, and quality control.

Procedures

When developing and reviewing a proposal to use non-pharmaceutical grade compounds the investigator and IACUC will consider animal welfare and scientific issues related to the use of the compounds, including potential for contamination, safety, efficacy, and the inadvertent introduction of confounding research variables.

The IACUC may approve the use of non-pharmaceutical-grade substances in the following situations:

1. If no equivalent veterinary or human drug is available for experimental use, then the highest-grade equivalent chemical reagent should be used and formulated aseptically and with a non-toxic vehicle as appropriate for the route of administration. It is expected that this will be maintained in a sterile container, unless specifically justified by the PI, and labeled to provide the name and concentration of the compound as well as its expiration date.
2. Although an equivalent veterinary or human drug is available for experimental use, the chemical-grade reagent is required to replicate methods from previous studies because results are directly compared to those of replicated studies.
3. Although an equivalent veterinary or human drug is available, dilution or change in formulation is required.
4. The available human or veterinary drug is not concentrated enough to meet experimental requirements.

Reviewed:

IACUC Chairperson

Date

Research Compliance Director

Date