Policies and Procedures

SECTION: IACUC	NUMBER: 7.07			
CHAPTER: Miscellaneous Experimental Animal Use Policies	ISSUED: 11/2007	REV. A: 4/7/2009	REV. B: 11/2012	REV. C: 9/2013
POLICY: Non-pharmaceutical grade compounds	REV. D: 11/2013	REV. E:	PAGE 1 OF 5	

PURPOSE:

The purpose of this policy is to establish clear guidelines for the use of non-pharmaceutical grade compounds with animals that is consistent with United States Department of Agriculture (USDA) and Office of Laboratory Animal Welfare (OLAW).

Consistent with USDA policy, non-pharmaceutical grade drugs are not acceptable when pharmaceutical grade compounds are available. "Pharmaceutical-grade" means that the preparation has received FDA approval for human and/or veterinary use. It is important to understand that this guideline pertains to all components, both active and inactive, contained in the preparation to be administered. Therefore, the vehicle used to facilitate administration of a compound is as important of a consideration as the active compound in the preparation. This procedure is approved by the Creighton University Institutional Animal Care and Use Committee (IACUC). All investigators will follow this policy unless scientific justification is provided and approved by the IACUC.

DEFINITIONS:

- **Pharmaceutical grade compound:** Drug, biologic, reagent, etc. which is approved by the FDA or for which a chemical purity standard has been written/established by USP/NF, BP
- **Analytical grade bulk chemical:** ~99% purity; Certificate of Analysis is usually available
- **Non-availability:** Not commercially available from an active US vendor; includes formulations supplied as tablet, capsule, injectable, etc.
- **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
- **USP/NF:** United States Pharmacopeia/National Formulary
- **BP:** British Pharmacopeia
- **FDA:** Food and Drug Administration; FDA approved compounds are manufactured using USP/NF compounds

POLICY OUTLINE: This policy provides a definitive position on the use of non-pharmaceutical grade substances. 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.

1. When selecting compounds the following order of choice should be applied:
   a. FDA-approved veterinary or human pharmaceutical substances;
   b. FDA-approved veterinary or human pharmaceutical substances used to compound a needed dosage form;
   c. USP/NF or BP pharmaceutical grade substance used in a needed dosage form (also includes compounded products from sources such as compounding pharmacies);
   d. Analytical grade bulk chemical used to compound a needed dosage form (requires justification);
2. Other grades and sources of substances (requires justification)

   NOTE: For new investigational drugs the grade and formulation is not optional, but the investigator and IACUC can verify health and safety issues described above

3. For a majority of common substances used in laboratory animal research, pharmaceutical grade (USP or NF grade) substances are available and should be used. Examples of common substances that are available in USP or NF grades include:

   • Saline
   • DMSO
   • Corn oil
   • Tamoxifen
   • Tetracycline
   • Analgesics (e.g., buprenorphine)
   • Anesthetics (e.g. ketamine)
   • Euthanasia reagents (e.g. Euthasol)
   • MS222

4. When a non-pharmaceutical grade substance is proposed and when developing and reviewing a proposal to use non-pharmaceutical grade substances, the investigator and IACUC should consider animal welfare and scientific issues related to the use of the substances, including potential for contamination, safety, efficacy, and the inadvertent introduction of confounding research variables. **For all non-pharmaceutical grade substances used in animals, the IACUC shall consider the 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, and quality**

control. The IACUC may use a variety of administrative methods to review and approve the use of such agents. For example, the IACUC may establish acceptable scientific criteria within the institution, rather than on a case-by-case basis. The use of non-pharmaceutical-grade compounds in laboratory animals shall be clearly delineated and justified in the protocol document and/or covered by an IACUC policy developed for their use.

5. **Examples for use of Non-Pharmaceutical-Grade Substances:** It would be reasonable for the IACUC to review and the Committee may approve the use of non-pharmaceutical-grade substances in the following situations:

    a. 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.
    b. 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.
    c. Although an equivalent veterinary or human drug is available, dilution or change in formulation is required.

        - If adulteration by dilution, addition, or other change in formulation is required, there may be no additional advantage to be gained by using the USP formulation.
        - Use of the highest-grade reagent may have the advantage of single-stage formulation and also result in purity that is equal to or higher than the human or veterinary drug.
        - Professional judgment should be used to determine the appropriate test material and to ensure use of an agent with the least likelihood for causing adverse effects.

    d. The available human or veterinary drug is not concentrated enough to meet experimental requirements.
    e. The available human or veterinary drug does not meet the non-toxic vehicle requirements for the specified route of injection.

For more information, see the web page ‘Guidelines for Alternates to Non-Pharmaceutical Agents”.

Application

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

- scientific necessity; or
- no equivalent veterinary or human drug is available for experimental use; and
- specific review and approval by the IACUC.

Investigators should consider relevant animal welfare and scientific issues including safety, efficacy, and the inadvertent introduction of new variables. 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.

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 animals after specific review and approval by the IACUC for reasons such as scientific necessity or non-availability of an equivalent veterinary or human pharmaceutical-grade product.

Refer to Creighton University IACUC policy on the Use of Secondary Containers for labeling purposes.

Refer to the Creighton University IACUC policy for the Use of Avertin

References:

U.S. Department of Agriculture, Animal and Plant Health Inspection Service, Animal Care, Policy 3-Veterinary Care, April 14, 1997.

Frequently asked questions about the public health service policy on humane care and use of laboratory animals. Wolff A, Garnett N, Potkay S, Wigglesworth C, Doyle D, Thornton V. Lab Animal (NY). 2003 Oct; 32(9):33-6.

Office of Laboratory Animal Welfare: Educational Resources: Non-Pharm Use
http://grants.nih.gov/grants/olaw/educational_resources.htm