

Drexel University Animal Care and Use Committee Guidelines for Use of Non- Pharmaceutical-Grade Agents or Mixtures of Pharmaceuticals (Cocktails)

OBJECTIVE: To assure appropriate IACUC review and approval for the use of Non-Pharmaceutical Agents and Mixtures of Pharmaceuticals.

RESPONSIBILITY: The Investigator is responsible for ensuring that everyone working on an applicable protocol adheres to this policy.

REGULATORY BACKGROUND:

OLAW (NIH) and USDA Policy

The use of non-pharmaceutical grade chemical compounds in experimental animals under certain circumstances has been, and will continue to be, a necessary and acceptable component of biomedical research. OLAW and USDA have determined that their use should be based upon:

- a) scientific necessity;
- b) non-availability of acceptable veterinary or human pharmaceutical-grade compound(s); and
- c) specific review and approval by the IACUC.

Although one can assume that issues such as sterility, pyrogenicity, stability, pharmacokinetics and quality control have been addressed during the course of pharmaceutical-grade drug production, one cannot ensure the same for substances produced in the research laboratory using non-pharmaceutical-grade chemical compounds. A number of related animal welfare and scientific issues should be considered by investigators and by IACUCs when use of non-pharmaceutical-grade compounds is proposed. These issues include: a) safety; b) efficacy; and c) the inadvertent introduction of research-complicating 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.

PROCEDURES

Use of these compounds must be detailed in the IACUC protocol or amendment and approved by the IACUC.

A. Pharmaceutical Mixtures (Cocktails, e.g., Ketamine/Xylazine)

- 1) Should be prepared and used on "acute" basis only (1-7 days)
- 2) Must be prepared/maintained under sterile conditions
- 3) MUST be clearly labeled with compound names, concentrations, and date of preparation (expiration date shall be 7 days after date of preparation).
- 4) Should be compounded according to methods of successful use/efficacy in published scientific literature.

B. Non-Pharmaceutical Grade Agents

- 1) MUST be justified by scientific necessity and/or lack of availability of pharmaceutical-grade, commercially available preparations in the IACUC protocol. (cost alone is not valid justification for use).
- 2) MUST be prepared and maintained under sterile conditions.
- 3) MUST be evaluated to assure physiological compatibility (pH, pyrogenicity, osmolality, etc.)
- 4) MUST be clearly labeled with compound names, concentrations, and date of preparation. Since shelf-life of such compounds is unknown, these compounds should not be stored longer than 30 days after preparation. Regardless of age, solutions should be discarded if changes in color and/or precipitation occur.

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 (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.

A listing of pharmaceutical-grade drugs and biologics is available through the [FDA database](#). The [Orange Book](#) is the reference for FDA-approved human drugs. The [Green Book](#) is the reference for FDA-approved veterinary drugs.

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: <https://www.avma.org/KB/Resources/Reference/Pages/Compounding.aspx> for more information about federal regulations.

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