IACUC GUIDELINE: ADMINISTRATION OF NON-PHARMACEUTICAL-GRAND OR CONTROLLED SUBSTANCES TO ANIMALS

DATE IMPLEMENTED: December 11, 2009

DATE(s) REVISED: July 7, 2011; January 20, 2012; December 17, 2013; August 25, 2015

This IACUC guideline was created to provide guidance to investigators and to set clear expectations on the conditional use of non-pharmaceutical-grade substances. This document also clarifies the record keeping, storage, and labeling expectations for all laboratories administering controlled substances to animals.

The Office of Laboratory Animal Welfare (OLAW)\(^1\), Office of Extramural Research NIH, and Animal and Plant Health Inspection Service (APHIS)\(^2\), United States Department of Agriculture (USDA) have clarified the following requirements regarding the use of non-pharmaceutical-grade substances and expired drugs or medical materials:

1. “Pharmaceutical-grade substances\(^3\), 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.”\(^1\)
2. “The IACUC is responsible for evaluating the potential adverse consequences of non-pharmaceutical-grade substances when used for research.”\(^1\)
3. “The use of expired pharmaceuticals, biologics, and supplies is not consistent with acceptable veterinary practice or adequate veterinary care. Euthanasia, anesthesia and analgesia agents should not be used beyond their expiration date, even if a procedure is terminal. Other expired materials should not be used unless the manufacturer verifies efficacy beyond the expiration date, or the investigator is able to document to the satisfaction of the IACUC that such use would not negatively impact animal welfare or compromise the validity of the study. The veterinarian and IACUC must maintain control over the use of expired medical materials in order to meet their responsibilities to avoid or minimize discomfort, pain or distress to animals.”\(^4\)

IACUC Expectations:
Approval for the use of non-pharmaceutical-grade substances will be made on a case-by-case basis by weighing the potential adverse consequences to the animal against scientific criteria for the use of these substances. “Cost savings alone are not an adequate justification for the use of non-pharmaceutical-grade substances in animals. However, unavailability or shortages of pharmaceutical-grade substances may lead to cost increases and the IACUC may determine that this justifies the use of the non-pharmaceutical-grade substitution.”

In order to protect animal welfare, due consideration must be given to the preparation (grade, purity, sterility, biocompatibility, and stability) and storage of any non-pharmaceutical-grade substance that is administered to animals. The IACUC recommends the following procedures for preparing non-pharmaceutical-grade compounds:

- Use chemicals of the highest grade and purity.
- Use only sterile and biocompatible (physiological pH and osmolality) solutions to dissolve or dilute the non-pharmaceutical-grade chemical, compound, or formulation.
- Sterilize all drug solutions prior to parenteral administration (i.e. IV, IP, IM, or SC). Use of a syringe-top filter (0.2 µm) is recommended for solutions that cannot be sterilized by other methods.
- Water-containing formulations should be used as soon after preparation as possible, but not later than 14 days after preparation when stored at cold temperatures between 2-8°C.
- All formulations should be labeled with a preparation and use by date.

The acquisition, storage, and research use of controlled substances (e.g. ketamine, pentobarbital, or cocaine) must conform to DEA regulations and the Best Practices Guide from the UC Office of the President (BUS 50), and in the future the UCSB Controlled Substance Program administered by EH&S. At a minimum, all controlled substances should be securely stored; each drug vial or container should be uniquely identified and clearly labeled with the name, concentration, and expiration date of the drug; and the research use of controlled substances should always be properly documented to enable audit tracking by UCSB officials (i.e. IACUC or EH&S) or federal agents (i.e. DEA or USDA). Further, it is recommended that the following information should be documented: the name of the drug, date of use, brief description of use (e.g. anesthesia, or euthanasia), species and number of animals dosed, amount of drug used, calculated balance of drug remaining in the vial, and the initials of the individual dispensing and administering the drug.

**Resources for Locating Pharmaceutical-Grade Substances for In-Vivo Use**

**Online**

- DailyMed
- FDA Orange Book, which list approved human drug products.
- Animal Drugs @ FDA

**Publications**

Pharmaceuticals for use in humans and animals: *Physician’s Desk Reference* (which is also accessible electronically) and the *Veterinary Pharmaceuticals and Biologicals*, and a search on a web search engine may provide a monograph for any compound labeled for human or animal use. It is suggested that both these resources be considered. Drug monographs will also list brand names with formulations and concentrations that are offered.

**Reference:**
1. OLAW FAQ: “May investigators use non-pharmaceutical-grade substances in animals?”


3. A pharmaceutical-grade substance is any active or inactive drug, biologic, reagent, etc., manufactured under Good Manufacturing Practices (GMP) which is approved, conditionally approved, or indexed by the Food and Drug Administration (FDA) or for which a chemical purity standard has been written or established by a recognized compendia (e.g., United States Pharmacopeia-National Formulary (USP-NF), British Pharmacopeia (BP)). OLAW FAQ: “May investigators use expired pharmaceuticals, biologics, and supplies in animal?”