QUILLEN COLLEGE of MEDICINE
EAST TENNESSEE STATE UNIVERSITY

University Committee on Animal Care

Policy on the Use of Non-Pharmaceutical Grade Drugs and Preparation and Storage of Compounds for Parenteral Administration

Purpose

The purpose of this policy is to provide guidance to the University Committee on Animal Care (UCAC), faculty, staff, and students on the use and storage of chemicals or compounds in laboratory animals.

Policy

The use of pharmaceutical-grade chemicals/compounds in laboratory animals ensures that the chemicals/compounds administered meet the established documentable standards of purity (~97%) and composition established by the United States Pharmacopeia National Formulary (USP/NF) or the British Pharmacopoeia (BP). The indiscriminant use of lower grade chemicals/compounds with higher levels of impurities or poorly formulated non-commercial preparations can introduce unwanted experimental variables or even toxic effects. Although pharmaceutical grade chemicals/compounds should be used in experimental animals whenever possible, the use of non-pharmaceutical-grade chemicals/compounds in experimental animals is an acceptable practice under certain circumstances. The NIH Office of Laboratory Animal Welfare (OLAW) and the United States Department of Agriculture (USDA) both have determined that the use of non-pharmaceutical-grade products 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 UCAC. Cost savings alone is not considered an adequate justification for the use of non-pharmaceutical-grade reagents in laboratory animals. Consideration should be given to the grade/purity of the chemical/compound being proposed, as well as the formulation of the final product. Issues such as sterility, pyrogenicity, stability, pH, osmolality, site/route of administration, pharmacokinetics, physiological compatibility, and quality control should be considered when proposing the use of a non-pharmaceutical-grade agent. When developing and reviewing a proposal to use non-pharmaceutical-grade agents the investigator and UCAC should also consider animal welfare and scientific issues related to the use of the agent, including potential for contamination, safety, efficacy, and the inadvertent introduction of confounding research variables. Whereas, many of the above issues have been addressed in the commercial manufacturing and formulation of pharmaceutical-grade products, the same cannot be said for non-commercial formulations using non-pharmaceutical-grade reagents or those manufactured in the laboratory. Although the possible implications of the use of non-

pharmaceutical-grade chemicals/compounds in non-survival studies appears less evident, OLAW has stated that the scientific issues remain the same and professional judgment, as outlined above, must still apply.
The use of non-pharmaceutical-grade agents in laboratory animals should be clearly delineated and justified in the Animal Study Protocol Form. Where possible the description should include the chemical grade of the agent(s) being used, source of the reagents, as well as a description of the appropriateness of the agent, its formulation and vehicle. Formulations and vehicles may need to be adjusted depending on the route and site of administration, as well as the species under consideration.

Preparation and Handling of Drugs/Chemical Agents

- All necessary and required training must be provided to potentially exposed individuals.
    - Adhere to the guidelines outlined in the SDS (safety data sheet) ensuring all appropriate PPE and Engineering controls are in place.
- The responsibility for controlled substance research compliance rests with the Licensed Individual. The Licensed Individual is responsible for obtaining and renewing both the DEA registration and the TN State Board of Pharmacy license and for assuring that all acquisition, storage, security, inventory, disposal and record-keeping requirements are met.
- Agents to be administered to animals must be handled and stored so as to maintain sterility and efficacy
    - Appropriate closed sterile containers (e.g. injection vials, red-topped blood tubes) must be used, rather than snap-cap or screw-top containers
    - The smallest amount of agent suspension/dilution/mixture should be used to minimize storage time prior to administration
    - The rubber injection port/cap should be swabbed with alcohol prior to insertion of the needle
    - Use a clean, sterile container for each preparation (do not reuse)
    - Use new sterile needles for each entry into a sterile container
    - Maintain needles in a sterile manner prior to injection
        - Do not rest needles on non-sterile surfaces
    - The re-use of needles for multiple animals is strongly discouraged due to loss of sharpness and biosecurity/cross-contamination concerns
- Examine multiple-dose injection vials/tubes prior to use for evidence of physical or chemical contamination
    - Discard any substance meeting any of the following criteria:
        - Particulate matter
        - Precipitation of solids
        - Turbid or discolored appearance
        - Mislabeled or unlabeled container
        - Damage to the rubber stopper compromising integrity
- All containers must be labeled with:
    - Name of the drug(s)/chemical(s) contained
        - The use of a readily available key is acceptable for controlled drugs

- Concentration of the drug/chemical
- Date of expiration (see below)

Expiration of Drug Dilutions/Mixtures

- Sterile dilutions or mixtures of drugs may result in a shorter effective expiration date than the expiration date of the individual components, due to risk of contamination and dilution of preservatives
- An expiration date of six (6) months from the date of preparation, or the earliest expiration date for any single component (if less than six months), is recommended unless scientifically justified otherwise.

Definitions

1. USP/NF: United States Pharmacopeia/National Formulary
2. BP: British Pharmacopeia
3. Pharmaceutical grade chemical: ~97% purity; a chemical that states it meets the USP/NF or BP standard on the label. A certificate of analysis is usually available on request.
4. Analytical Standards: "Certificate of Analysis" a document that goes with each product run. This certificate lists the formula for the ingredients as well as the amount of each raw material/ingredient. The product name and lot number are listed to avoid confusion with other batches. The C of A also may contain results of tests for contaminants.
5. Analytical Grade: ~99% purity; Certificate of Analysis usually available; appropriate preparation is imperative.
6. Reagent ACS: This designates the highest quality commercial chemical. The "ACS" means the American Chemical Society. A Certificate of Analysis is available upon request.
7. Reagent Grade: The highest quality commercial chemical; HOWEVER, ACS has not set specifications for materials. A Certificate of Analysis is usually not available.

Approved by the ETSU University Committee on Animal Care: June 14, 2022