Use and Labeling of Drug Compounds, Dilutions,and Chronic-Use Fluids

Policy:.

This policy outlines the standards and expectations for ensuring the safety and efficacy of drug compounds, dilutions, and chronic-use fluids intended for administration to laboratory animals. It does not apply to topical applications for fish or amphibians; however, any dilutions or reconstitutions of drugs (e.g., MS-222) for these animals must be included in the respective Institutional Animal Care and Use Committee (IACUC) Proposal. The use of adulterated drugs, which result from compounding (combining two or more drugs) or diluting drugs, can affect drug bioavailability and efficiency, decrease stability, compromise sterility, and release toxic excipients. These factors pose potential risks to animal welfare and may introduce unwanted variables into research. Therefore, such practices should be avoided whenever possible. When compounding or diluting agents is necessary, it is essential to employ aseptic techniques and use sterile, pharmaceutical-grade agents. All substances administered to animals, including their dosages and routes of administration, must receive approval on the IACUC Proposal prior to their use.

Rationale:

The IACUC acknowledges that it may be necessary to dilute or compound medications for laboratory animals. This customization allows for tailored treatments, anesthesia, and analgesia for specific animals or groups, particularly when specific mixtures or concentrations are not available. It is important to note that compounded and diluted animal drugs are not FDA-approved. FDA approval signifies that the FDA has verified that the drug is safe, effective, manufactured to high-quality standards, and accurately labeled. Since compounded and diluted animal drugs do not have FDA approval, they lack the same guarantees regarding safety and efficacy.

Due to concerns about the stability and effectiveness of adulterated drugs that can pose potential risks to animal welfare, the IACUC has implemented a conservative policy. While some published studies suggest that certain compounded mixtures may remain stable for longer than 30 days, the available data is inconsistent and not conclusive. Also, factors such as storage temperature, vial type, the number of times the vial is punctured, and the diluent used can influence stability and sterility.

To ensure the safety and effectiveness of drugs used in laboratory animals, the IACUC requires that all compounded and diluted mixtures have a standard expiration period of 30 days post-mixing and/or diluting. If any ingredient in the mixture has an earlier expiration date than 30

Original Approval: 20 January 2022
Revised: 14 July 2025
Latest Approval 17 July 2025

days, that date should be observed instead.

Procedures, Guidelines, and Exceptions:

1. All in-house made compounds and diluted medications must use sterile, pharmaceutical-grade compounds (unless justification has been provided and approved for the use of non-pharmaceutical-grade drugs in a UofL IACUC Proposal), must be combined using sterile technique, and must be stored in a sterile vial in a cool place and away from light. Appropriate storage necessitates the use of a secondary container and methods which maintain sterility yet allow repeat withdrawals (e.g., use of a sterile injection vial with a rubber stopper). Sterile injection vials with rubber stoppers are available for purchase from the Comparative Medicine Research Unit (CMRU). The top of the container should be disinfected with 70% alcohol on clean gauze or cotton prior to accessing with sterile needle and syringe. Alternatively, for single use purposes a ***sterile*** microfuge tube can be used.
2. All adulterated drugs (compounds and dilutions) must be labeled with the drug names, diluent, final concentration of each component, date prepared, expiration date,and the initials of the person preparing the compound. All agents stored within CMRU vivaria must also be labeled with the Principal Investigator's name.

   Example:

   Ketamine 10 mg/ml & 0.1 mg/ml Dexemedetomidine in sterile saline
   Date prepared / / by ____ Expires / /
   Mouse dose: K 100 mg/kg and 1 mg/kg Dexemedetomidine
   Directions: Give 0.2 mls per 20 grams body weight IP Do not redose.

3. All adulterated drugs (compounds and dilutions) must be prepared aseptically and stored in sterile vials and must be discarded within 30 days of preparation or the expiration date of the original stock, ***whichever is earlier***.
4. Fluid bags (ex: NaCl, LRS) for chronic use must be labeled with the date opened/date of first puncture and discarded within ***30 days of opening/first puncture***. All fluids stored within the Comparative Medicine Research Unit (CMRU) vivaria must also be labeled with the Principal Investigator's name.
5. Fluid bags with added agents must be labeled to indicate any agents added. If agents are light sensitive, bags should be protected from direct light exposure using black plastic bags or other means. Fluids with added agents must be discarded according to the expiration of the added agent or within 30 days of opening/puncturing the fluids whichever comes first. All fluids/agents stored within the Comparative Medicine Research Unit (CMRU) vivaria must also be labeled with the Principal Investigator's name
6. If compounds or dilutions display cloudiness, particulate matter, or bacterial/fungal growth, they must be discarded immediately and not used for animal procedures.
7. If drugs, compounds, dilutions or fluids are found within the CMRU vivaria without appropriate labelling, they will be discarded by CMRU staff as they are found or the IACUC during inspections.
8. All substances should be discarded in compliance with the Department of

Environmental Healthand Safety standards. Contact DEHS to arrange for proper disposal of controlled and hazardous substances (https://louisville.edu/dehs/contact-us).

References

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