UNIVERSITY OF CALIFORNIA
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Institutional Animal Care and Use Committee

Policy on Labeling Dilutions of Pharmaceutical Compounds Used in Animals

Date Reviewed: 3/11/19

Background
Federal regulations require Investigators to use pharmaceutical-grade compounds for injection in animals.

It is recognized that many experimental compounds used in research may need to be diluted or combined for use in laboratory animal research.

The use of combinations of multiple drugs, or dilution of drugs can introduce unexpected or even toxic effects, and should be avoided whenever possible.

When compounding or dilution is necessary, it must be done using aseptic technique and the final product must be properly labeled and stored. **THIS IS ESPECIALLY TRUE FOR CONTROLLED SUBSTANCES**

Definitions

1. *Pharmaceutical-grade compounds* are drugs, biologics, reagents, etc. which are approved by the FDA or for which a chemical purity standard has been written/established by the United States Pharmacopeia (USP)/National Formulary or British Pharmacopeia **and are intended for injection.**

2. *The United States Pharmacopeia National Formulary (USP-NF)* provides FDA-enforceable quality standards for drugs, dietary supplements, and excipients as well as procedures for tests, assays and analytical methods. *Parenteral articles* meet Pharmacopeia requirements for sterility, pyrogens, particulate matter, and other contaminants, and, where appropriate, contain inhibitors of the growth of microorganisms.

3. *Compounding* is a practice in which a person combines, mixes, or alters ingredients of a drug to create a medication tailored to the needs of an individual patient(s). **Simple dilution is also considered compounding.**

Requirements
All agents used in animals **must** be listed in the IACUC protocol.

If compounding of drugs to be injected in animals is necessary, investigators must ensure:

1. **Aseptic preparation** (compounding) of the drug to include sterile containers, filtration or autoclaving of compounded drug if original components are not sterile. Injectable drugs should never be used if they contain particulate matter, precipitates, turbidity, or discoloration.

2. **Appropriate storage** of the compounded drug to include the use of a secondary container and methods which maintain sterility yet allow repeat draws e.g. use of a sterile injection vial with a rubber stopper is highly encouraged. Alternatively, for single use purposes, a sterile microfuge tube can be used.

3. **Appropriate labeling** of containers for storage of compounded drugs to include**:**

- Name of the compound(s) and diluent (when applicable)
- Final concentration (usually mg/ml)
- Date of Compounding and assigned Expiration date
- The expiration date should be based on the earliest expiration date listed on the stock bottles of agents used
- **For controlled substances, read further tracking and label instructions below.**

Note: The length of time a compounded drug can be used should be based on use frequency and performance. Compounded drugs may result in decreased "shelf-life" compared to the stock drug(s). Furthermore, the potential for bacterial contamination is increased when compounding drugs or when drawing from multi-use vials

Note for controlled substances: The tracking sheet for the controlled substance original tank vial must be updated to indicate the creation of a secondary container and the secondary container/s must be tracked on a "secondary container sheet". The tracking sheet for the original tank vial and the "secondary container sheet" must clearly reference each other to adequately track the use of the controlled substance. The label on the secondary container itself must identify the exact multi-use vial from which the controlled substance was drawn to create the dilution and must contain the following information on each vial created:

- The date of vial creation (dilution)
- The date of expiration of the dilution vial
- The name of the drug/s and diluted concentration/s
- The identity of the parent tank vial to correspond with the identity on the tracking sheet for the controlled substance original tank vial.
- The tracking identity of the daughter vial tp correspond with the identity on the "secondary container sheet".

Note: **It is highly recommended when using compounded drugs that a lab-specific SOP be created to establish proper preparation procedure and creation of an expiration date for the compounded drug vial.**

References

1. USDA APHIS Animal Care, Policy 3, March 14, 2014.