

Institutional Animal Care and Use Committee		UNTHSC
Title: Guidelines for Compounding and Secondary Container Use for Injectable Drugs		
Document #: 055	Version #: 01	
Approved by IACUC Date: May 29, 2019		

A. BACKGROUND INFORMATION

- a. These guidelines are developed to ensure sterility and effectiveness of drugs when secondary containers are used for compounding, diluting, or transferring drugs and compounds to be administered by injection to animals.

B. RESPONSIBILITIES

- a. It is the responsibility of the Principal Investigator to adhere to these guidelines when using secondary containers for compounding, diluting, or transferring drugs and compounds.

C. DEFINITIONS

- a. **Secondary Containers:** Vials, bottles or tubes used when drugs or compounds are moved from their original container.
- b. **Transferred:** When drugs or compounds are taken out of the primary container and placed into a secondary container (e.g., drugs in glass ampules).
- c. **Diluted:** When drugs or compounds are mixed with a diluent to achieve a working concentration (e.g., antibiotics or analgesics for use in rodents).
- d. **Compounded:** When drugs are mixed with one or more drug or diluents (e.g., mixture of ketamine with xylazine and diluent).

D. PROCEDURES

- a. **Types of Secondary Containers:**
The type of secondary container must be compatible with the drug or compound and its intended use.
 - 1. Container Material:
 - a. Does not react with the drug or compound (e.g., glass, polypropylene, or polycarbonate plastic).
 - b. Opaque if light sensitive material is to be stored (e.g., covered with foil, brown glass)
 - c. Supplies are sterile or able to be autoclaved.
 - 2. Aseptically Administered:

- a. Contents must be removed aseptically – single or multiple draws.
3. The most common use of secondary containers is for drugs or compounds that are:
 - a. Removed multiple times from the same container
 - b. Removed and administered aseptically

The best type of container for the use is a vial with a septum in the cap (search septum or crimp top vial on a scientific supply website). The sterile drug or compound can be dispensed into the vial and the contents can be removed aseptically with a sterile needle and syringe. The top of the septum should be disinfected with 70% alcohol prior to use. As a second choice, a red capped (untreated) blood collection tube can be used as a secondary container.

The use of screw capped tubes should be avoided as it is difficult to remove the contents aseptically.

b. Labeling:

Any drug or compound transferred to a secondary container must be labelled as follows:

1. The name and concentration of each ingredient including the diluent.
2. Total amount/volume in the container
3. For transferred solutions
4. The expiration date of the drug or compound

For diluted or compounded solutions, secondary containers must also include the following:

1. The Preparation Date
2. The use-by-date
 - a. Should not extend past the earliest expiration date of any of the components.
 - b. Should be no longer than 30 days from preparation for compounds or dilutions, unless published or vendor-provided scientific data can demonstrate a duration of efficacy longer than 30 days.
 - c. EXAMPLE: Compounded Ketamine anesthetic cocktails have a use by date of 6 months (or the earliest expiration date of any drug in the compounded solution, if < 6 months) on a basis of the publication Taylor, BJ et al.2009. Beyond-use dating of extemporaneously compounded

Ketamine, Acepromazine, and Xylazine; safety, stability, and efficacy over time. JAALAS 48:718-726.

For Controlled substances, per DEA Guidelines, the inventory must reflect all disbursements and the label must include the following:

1. The total amount/ volume and lot number of each controlled substance.
2. The total amount/ volume of the combined drugs
3. The concentration of each drug (mg/ml)
4. Date of preparation
5. Date of expiration or use by date, whichever is earliest.

c. Exceptions:

The following compounds are exempt from this Guidance

- i. Test compounds that are prepared for single use and will not be stored past this use.
- ii. Test compounds that are available in small quantities (,0.5 ml), such that use of a septate vial poses a risk of losing the contents in the rubber septum.
- iii. Test compounds that consist of hazardous materials (BSL-2/3, CSL-2/3, Radioisotopes), such that the additional handling needed to place the material into a septate vial increases the risk of accidental exposure.

These compounds must be prepared and handled using sterile technique, as appropriate. All containers must be identified with a description of the contents. Note that this exception does not apply to veterinary drugs, i.e., anesthetics, analgesics, or euthanasia drugs.

E. REFERENCES

1. FDA, "Sterile Drug Products Produced by Aseptic Processing Current Good Manufacturing Practice." September 2004, <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/sterile-drug-products-produced-aseptic-processing-current-good-manufacturing-practice>. Accessed 5/22/2019

Examples of containers

<p>Examples of appropriate vials for liquids. These vials can remain sterile when obtaining multiple doses using separate sterile needles.</p>			
<p>Examples of vials NOT appropriate for liquids. They cannot remain sterility when obtaining multiple doses.</p>			

Examples of labeling

<p>Examples/templates of appropriate container or bottle labeling:</p>
<p>Ketamine (8.25mg/mL) Lot # _____ Acepromazine (0.25mg/mL) _____ Xylazine (0.83mg/mL) _____ Made: ___/___/___ Initials _____ Expires / Use by Date ___/___/_____</p>

<p>Examples/templates of appropriate labeling for bags or transfer containers</p>	
<p>Components In Sterile Vial, mix: Acepromazine Maleate (10mg/mL) 1.2 mg.0.12mL +Ketamine HCl (100mg/mL): 41 mg, 0.41mL + Xylazine HCL (20mg/mL); 4.2 mg, 0.21mL + Sterile Water for injection: 4.26ml</p> <p>Dosage: 0.30mL/25g BW, IP</p> <p>*Ketamine cocktails expire 6 months after made, or the earliest expiration date of any drug in the cocktail if less than 6 months. ** All other cocktails/compounds expire 30 days after preparation date or the earliest expiration date of any drug in the cocktail if less than 1 month.</p>	<p>Comments: Individual dosages for a mouse: 100mg/kg Ketamine (100mg/ml) 20mg/kg Xylazine (20mg/ml) 3mg/kg Acepromazine (10mg/ml)</p> <p>References: Arras M et al, 2001. Optimicization of Intraperitoneal (IP) injection anesthesia in mice; drugs, dosages, adverse effects, and anesthesia depth. Comp Med, 51:443-56.</p> <p>Contact information: Name: _____ Phone: _____</p>