TITLE: Guidelines for Compounding and Secondary Container Use for Injectable Drugs

PURPOSE: To provide guidance on appropriate secondary containers used for compounding, diluting or transferring drugs and compounds to be administered by parenteral injection to animals.

REVIEW/REVISIONS: The IACUC will review and revise this guidance as needed.

DATE OF LAST REVIEW: 04/05/2017

Secondary containers are vials, bottle or tubes used when drugs or compounds are moved from their original containers. This can occur when drugs or compounds are:

- Transferred
  - Taken out of the primary container and placed into a secondary container (e.g., drugs in glass ampules)
- Diluted
  - Mixed with a diluent to achieve a working concentration (e.g., antibiotics or analgesics for use in rodents)
- Compounded
  - Mixed with one or more drugs or diluents (e.g., a mixture of ketamine, xylazine and diluent)

Containers

The type of secondary container must be compatible with the drug or compound and its intended use (see below for examples).

- Container material
  - Does not react with the drug or compound (e.g., glass, polypropylene or polycarbonate plastic)
  - Opaque, if light sensitive material is to be stored (e.g., covered with foil, brown glass)
  - Supplied sterile or able to be autoclaved
- For solutions that are administered aseptically
  - Contents must be removed aseptically – single or multiple draws

The most common use of secondary containers is for drugs or compounds that are:

- Removed multiple times from the same container
- Removed and administered aseptically

The best type of container for this 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.

Labelling

Any drug or compound transferred to a secondary container must be labelled as follows (see below for examples):

- The name and concentration of each ingredient, including the diluent
- Total amount/volume in the container
- For transferred solutions:
  - The expiration date of the drug or compound
- For diluted or compounded solutions:
  o The preparation date
  o The use-by-date
    ▪ Should not extend past the earliest expiration date of any of the components
    ▪ Should be no longer than 30 days from preparation for compounds or dilutions, unless published or vendor-provided scientific data can be provided to demonstrate a duration of efficacy longer than 30 days, for 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 the 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:
  o The inventory must reflect all disbursements
  o The label must have:
    ▪ The total amount/volume and lot number of each controlled substance
    ▪ The total amount/volume of the combined drugs
    ▪ The concentration of each drug (mg/ml)
    ▪ Date of preparation
    ▪ Date of expiration or use by date, whichever is earliest. See above.
  o For more information on UA oversight of DEA regulated controlled substances, contact RLSS at http://rgw.arizona.edu/compliance/RLSS

Examples of containers

<table>
<thead>
<tr>
<th>Examples of appropriate vials for liquids</th>
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</tr>
</thead>
<tbody>
<tr>
<td>These vials can remain sterile when obtaining multiple doses using separate sterile needles.</td>
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</tr>
</tbody>
</table>

Examples of vials NOT appropriate for liquids. They cannot remain sterile when obtaining multiple doses.
Examples of labelling

**Examples/templates of appropriate container or bottle labeling:**

<table>
<thead>
<tr>
<th>Total: ____ mL</th>
<th>Ketamine (8.25mg/mL) Lot# ___</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acepromazine (0.25mg/mL)</td>
<td>Xylazine (0.83mg/mL)</td>
</tr>
<tr>
<td>Made: <strong>/</strong>/__ Initials _______</td>
<td>Expires/Use by Date: <strong>/</strong>/__*</td>
</tr>
</tbody>
</table>

**Examples/templates of appropriate labeling for bags or transfer containers:**

**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

**Dosage:** 0.30mL/25g BW, IP

*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 the preparation date or the earliest expiration date of any drug in the cocktail if less than 1 month.

**Comments:**

Individual dosages for a mouse:
- 100mg/kg Ketamine (100mg/ml)
- 20mg/kg Xylazine (20mg/ml)
- 3mg/kg Acepromazine (10mg/ml)

**References:**

**Contact Information:**
Name: ______________________
Phone: ______________________

**PROVISOS:**

The following compounds are exempt from this Guidance:

- Test compounds that are prepared for single use and will not be stored past this use.
- Test compounds that are available in small quantities (< 0.5ml), such that use of a septate vial poses a risk of losing the contents in the rubber septum.
- 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.