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.

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 see:
      ▪ ORCBS Chemical Safety Manual for details regarding DEA Regulated Controlled Substances at the University of Arizona (p. 37-39)
        • http://orcbs.arizona.edu/files/forms/Laboratory%20Chemical%20Safety%20Manual.pdf
      ▪ ORCBS Transfer Form:
        • http://orcbs.arizona.edu/files/forms/DEA%20Controlled%20Substances%20Internal%20Transfer%20Form%202-5-2013.pdf

Examples of containers

<table>
<thead>
<tr>
<th>Examples of appropriate vials for liquids</th>
<th>Examples of appropriate vials for liquids. These vials can remain sterile when obtaining multiple doses using separate sterile needles.</th>
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</thead>
<tbody>
<tr>
<td>Examples of vials <strong>NOT</strong> appropriate for liquids</td>
<td>Examples of vials <strong>NOT</strong> appropriate for liquids. They cannot remain sterility when obtaining multiple doses.</td>
</tr>
</tbody>
</table>
Examples of labelling

Examples/templates of appropriate container or bottle labeling:

| Total: ___ mL |
| Ketamine (8.25mg/mL) Lot# ___ |
| Acepromazine (0.25mg/mL) |
| Xylazine (0.83mg/mL) |
| Made: __/__/__ Initials _______ |
| Expires/Use by Date: __/__/__* |

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.