UCSD Guidelines for Dilution, Mixture, and Use of Secondary Containers for Injectable Drugs Used in Animals

Parenteral (injectable) drugs for use in animals should be prepared and handled in a manner that preserves the sterility, purity, stability, and efficacy of the drug(s). Dilution, mixing, and even transferring drugs to another container can affect the suitability of the drugs for animal use. For example, diluting a drug also dilutes any preservatives that may be present, which may affect the stability of the preparation.

For the purpose of these guidelines, “drug” means any compound intended to be given to animals, whether for therapeutic or experimental purposes. UCSD has separate guidelines for the preparation of Avertin and Urethane (see References).

Avoid storing drug dilutions or mixtures. Whenever possible, drugs should be prepared the same day they will be used so that dilutions and mixtures of drugs are not stored. If drugs will be stored, prepare only the smallest amount in order to minimize storage time prior to administration. Any drug that will not be used must be disposed of properly (see Resources).

Use a suitable sterile container. Containers used should allow for the aseptic preparation and removal of drugs. Some drugs are affected by plastic and/or rubber and should not be stored in plastic vials or in syringes. Falcon, Eppendorf, or snap-cap tubes should not be used since it is difficult to maintain sterility of the contents.

> **Generally, the best container to use is a sterile, glass, multi-dose vial.** Examples are empty sterile vials or red-topped blood collection tubes with no additives (see Supplies).
>
> A new, sterile vial should be used for each batch. The rubber stopper of sterile vials should be swabbed with 70% alcohol before each use.

Use new, sterile needles and syringes when preparing and removing drug preparations from vials with a rubber stopper. If other containers are used, the preparation should be made and accessed in a properly working tissue culture or other hood capable of maintaining a sterile environment.

Store drug preparations according to the manufacturer’s recommendations. Some drugs need to be protected from light, refrigerated, or used within a specified period of time from when the original container was opened. Store controlled substances (CS) and mixtures containing them in the lab’s EH&S-approved CS storage area (denoted with a CS Storage Area sticker).

Order stock drugs in suitable containers whenever possible. For example, buprenorphine is traditionally supplied in glass ampoules, but is now also available in multi-dose vials which may be ordered through the CS Program. Multi-dose vials are a better choice for dosing most animals and transfer of remaining drug to a secondary container is avoided.

Use the correct diluent. Diluents should be sterile, pharmaceutical preparations such as normal saline for injection, bacteriostatic saline for injection, or lactated Ringer’s solution for injection. Bench-made diluents should not be used, even if sterilized, as these may contain pyrogens that cannot be removed by filtration or heating. Isotonic diluents should be used whenever compatible with the drugs to be diluted.

> **Note**: Vials of saline or water for injection are often over-filled. When using these to dilute drugs, withdraw all of the contents, then add back the measured volume required.

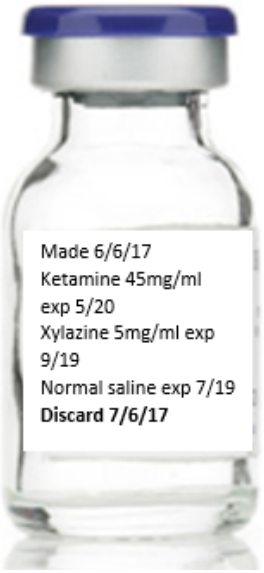
Drug preparations for terminal use (animal is anesthetized and never recovers from anesthesia) do not need to be prepared aseptically; however, stock bottles of drugs should not be contaminated when making the preparation.

Label each container properly. Each container of prepared drug or mixture should be labeled with the following:

- **The date the dilution or mixture was prepared**
- **Full name of each drug and diluent in the container**
- **Final concentration of each drug in mg/ml**
- **Expiration dates of each drug and diluent**
- **The "Discard date" for the preparation**

  Unless otherwise specified by the manufacturer, the discard date is the earliest expiration date of drug or diluent in the container, or thirty (30) days from the preparation date unless published data indicate the mixture is safe and effective for a longer period of time, whichever is earlier. Secondary containers of drugs that are not diluted, mixed, or otherwise adulterated may be used until the expiration date found on the original container.

  Published data have shown that mixtures of Ketamine, Xylazine, and Acepromazine remain safe and effective for 180 days (6 months) after mixing.



Follow all requirements of your Controlled Substance Use Authorization (CSUA) and the Chemical Hygiene Plan's labeling requirements.

Check before you inject. Drug preparations, even those for terminal use, should be examined prior to administration for evidence of contamination or degradation. Check for:

- Particulate matter, turbidity, or discoloration.
- Damage to the rubber stopper that may lead to contamination.
- Proper labeling.

Contaminated or degraded preparations should not be used. Dispose of the preparation properly (see Resources).

Refrigerated solutions for injection should be room temperature before injecting, unless otherwise directed by the manufacturer.

Supplies: You can place a miniRequest in Marketplace to order the following items. After selecting miniRequest, search for 'MWI' under suppliers. Choose the 'Non-Controlled Substances Only' listing. These items are also available from other sources.

Sterile multi-dose vials - Empty Sterile Vials Clear 25 x 10ml Catalog No: 012286

Red top blood tubes – Bld Col Tube 5cc Red No Add B100 Catalog No: 002402

Sterile saline (10ml) - Sodium Chloride 0.9% Inj 25 x 10ml Catalog No: 033500

Sterile bacteriostatic saline (30 ml) – Sod Chlor .9% Inj 30ml Bx25 Bacteriostatic Catalog No: 035830

Resources:

Drug Disposal – non-controlled: https://blink.ucsd.edu/safety/research-lab/hazardous-waste/pharmaceuticals.html

Drug Disposal – Controlled Substances (CS): https://blink.ucsd.edu/safety/research-lab/controlled-substances/dispose.html

CS Program: https://blink.ucsd.edu/safety/research-lab/controlled-substances/index.html

CS Solution Usage Log: http://blink.ucsd.edu/_files/safety-tab/research/CS_Solution_Usage_Log.pdf

Calculation Sheet For Making Drug Preparations & Conversion Factors For Dosages: http://ncifrederick.cancer.gov/Lasp/Acuc/Frederick/Media/Documents/ACUC39.pdf

References:

Non-pharmaceutical grade compounds policy**:** http://blink.ucsd.edu/_files/sponsor-tab/iacuc/Policy%2031%20Non-Pharmaceutical.pdf

Expired Medical Materials policy: http://blink.ucsd.edu/_files/sponsor-tab/iacuc/Policy%2032%20Expired%20Medical%20Materials.pdf

Anesthesia policy: http://blink.ucsd.edu/_files/sponsor-tab/iacuc/Policy%2034%20Anesthesia.pdf

Guidelines for the Use of Avertin: http://blink.ucsd.edu/_files/sponsor-tab/iacuc/GuidelinesForUseOfAvertin.pdf

Guidelines for the Use of Urethane: http://blink.ucsd.edu/_files/sponsor-tab/iacuc/Urethane%20Guidelines%203-2016.pdf

Beyond-Use Dating of Extemporaneously Compounded Ketamine, Acepromazine, and Xylazine: Safety, Stability, and Efficacy over Time Brett J Taylor, et al. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2786925/