WASHINGTON STATE UNIVERSITY

Washington State University
Institutional Animal Care and Use Committee

"Guideline #12: Compounding Drugs and Chemicals"

Approval Date: 9/3/2021 (Replacing version 1/2020)

A. Purpose

These guidelines define compounding and provide guidance for the preparation, labeling, and storage of compounds, mixtures, and dilutions.

B. Background

Definitions

1. **Pharmaceutical grade compound:** Drug, biologic, reagent, etc. that is approved by the Food and Drug Administration (FDA) or for which a chemical purity standard has been written/established by the United States Pharmacopeia/National Formulary (USP/NF) or British Pharmacopeia (BP). There should be a National Drug Code (NDC) number on the packaging
2. **Non-pharmaceutical grade compound:** Drug, biologic, reagent, etc. that is not approved by the FDA nor an established purity standard from USP/NF or BP and no NDC number. Experimental compounds and materials manufactured for tissue/cell culture are typically non-pharmaceutical grade and require additional care during preparation.
3. **Compounding:** Combining, mixing, or altering the ingredients of a drug to create a medication tailored to the needs of an individual patient.
4. **Vehicle:** a carrier or inert medium used as a solvent or diluent in which the active agent is formulated

The IACUC considers dilutions/mixtures/compounding to be equivalent to pharmaceutical grade as long as all components of the solution/mixture are pharmaceutical grade. If available and possible, pharmaceutical grade compounds should always be used. Please see WSU IACUC Policy #29 on the use of non-pharmaceutical grade substances for additional information.

C. Guideline

Compounding Preparation and Storage Methodologies: Parenteral administration (substances delivered by injection outside of the gastrointestinal tract)

- Substances administered parenterally should be
  - Isotonic (280 mOsmol/L; such as 0.9% saline) and without precipitate or crystallization
  - Close to physiologic pH (6.8-7.2). If the pH is outside of physiologic range, administer through a central blood vessel (such as the jugular or femoral vein), intraperitoneally or buffer or dilute the solution
  - Sterile and delivered aseptically
    - Use all sterile constituents (including vehicle)
    - Mix solutions using sterile technique to minimize any contamination (biosafety cabinet, gloves, open flame, etc.)
    - Use a clean, sterile container for each preparation. For each entry into the container, use a new, sterile needle. Injection vials with injectable rubber stoppers are recommended to maintain sterility

    - If any part of the preparation is not a sterile pharmaceutical grade parenteral product, sterilize by filtering with a 0.22 micron sterile syringe filter into a sterile container after mixing
    - Use sterile needles and syringes for administration. For each entry into the container, use a new, sterile needle.
    - Note: commercially available 0.9% saline for cell culture in one-liter screw top flasks is not pharmaceutical grade and is easily contaminated
  - Stored properly
    - Maintain proper storage environment for the constituents of the solution (proper temperature and light conditions).
    - If permitted, only small amounts of a compound/dilution should be mixed at a time to minimize storage time & opportunity for contamination.
  - Examine injection vials/tubes prior to use for evidence of biological, physical or chemical contamination. Solutions should be discarded if they meet any of the following criteria:
    - Particulate matter
    - Precipitation of solids
    - Turbid or discolored appearance

- Mislabeled or unlabeled container
- Damage to the rubber stopper or cap compromising integrity

Compounding Preparation and Storage Methodologies: Enteral administration (substances delivered *per os* (orally or by mouth) to the gastrointestinal tract)

- Drugs and chemicals delivered orally do not have to be sterile, but consideration should be made to the purity, solubility, mucosal irritability, and potential toxicity of the experimental drug and any vehicles. Odor and taste will affect the voluntary intake in feed or water. Administration can occur orally via capsule, tablet, bolus, paste or liquid; or by addition to the drinking water or feed; or by stomach or gavage tube.

Labeling

- All dilutions and mixtures should be labeled with:
  - Active compound/s
  - Concentration
  - Diluent/vehicle
  - Sterile or nonsterile
  - Route of administration
  - Preparation date
  - Expiration date

Expiration

- Due to risk of contamination and dilution of preservatives, sterile dilutions or mixtures of drugs may result in shorter effectiveness period than the expiration date of the original compounds.
- Mixtures should be labeled and considered expired three months from the date of preparation, or at the earliest expiration date of any single component (if less than three months) unless data can be provided to verify the quality assurance.
- Some non-pharmaceutical experimental drugs or chemicals do not have listed expiration dates and are prohibitively rare or difficult to manufacture. In these circumstances, expiration dates should be based on the compounds' manufacturer's assurance if available or OCV should be consulted on best practices for storage. An example of a possible solution is to aliquot mixtures and store in ultrafreezers at a maximum temperature of -70°C. A description of any special storage parameters should be added to the ASAF.

D. References

1. Taylor, B., et al. *Beyond-use dating of extemporaneously compounded ketamine, acepromazine, and xylazine: safety, stability, and efficacy over time.* J AM Assoc Lab Anim Sci. 2009. 48 (6):718-26.
2. Dodelet-Devillers, A., et al. *Assessment of stability of ketamine-xylazine preparations with or without acepromazine using high performance liquid chromatography-mass spectrometry.* Can. J. Vet Res 2016 Jan; 80(1); 86-89.OLAW FAQ F.4. Last revised November 28, 2017.
3. AAALAC International FAQ. Last updated June 2019.
4. AVMA Drug Compounding Brochure – American Veterinary Medical Association