IACUC Guidelines on the use of Non-pharmaceutical Grade Sodium Pentobarbital in Animal Use Protocols

Pentobarbital is a class II controlled substance. The investigator must have appropriate DEA licensing and all personnel using it must be listed with the DEA.

The University of Maryland School of Medicine (UM SOM) Institutional Animal Care and Use Committee (IACUC) has developed the following guidelines to describe the necessary information investigators need to provide to obtain IACUC approval to use non-pharmaceutical grade sodium pentobarbital. This document also provides guidance on acceptable methods of preparation and use.

Sodium pentobarbital has a long history of effective use in laboratory animals. In recent years, the medication has fallen out of favor with human healthcare use and, consequently, most pharmaceutical companies have ceased producing or selling pentobarbital as an injectable pharmaceutical grade product. While most researchers are able to convert to alternative medications, for certain applications and certain studies, scientific necessity requires continued use of this barbiturate.

The NIH has stated "*The exorbitant cost of this product has placed it logistically into the unavailable category. Regulatory guidance on this matter specifically allows for use of non-pharmaceutical-grade compounds due to non-availability and with IACUC approval.*" Therefore, the IACUC will consider and may approve requests to use a non-pharmaceutical grade of pentobarbital under the following circumstances:

The preparation and use of this anesthetic must be:

- Scientifically necessary,
- Appropriately justified,
- Prepared from a reagent or analytical-grade powder; properly prepared by a pharmacist or other knowledgeable individual (e.g., chemist, veterinarian, researcher), with assurance of appropriate storage and handling, and
- Approved by the IACUC. In making its decision, the IACUC must consider the side effects, stability, storage requirements, and other considerations associated with the preparation of this agent (the PI must provide this information for IACUC consideration).

Please note that even non-pharmaceutical grade pentobarbital is a DEA schedule II controlled substance, and therefore must be obtained, stored, dispensed, administered, and properly disposed of in accordance with the UMB Environmental Health and Safety (EHS) Policy. **Use must be recorded as a Schedule II controlled substance.**

STERILE PREPARATION OF NON-PHARMACEUTICAL GRADE SODIUM PENTOBARBITAL

1) Combine the measured amount of powder and sterile diluents to achieve a concentration not to exceed 60 mg/ml (*as in the recipe below*).
2) The drug must be prepared using a Biological Safety Cabinet (BSC) with final solution filtered through a 0.22 µm filter into a sterile vial for injection for storage.
3) If the resultant sodium pentobarbital contains visible particulates and a clear solution is not present in the final solution, do NOT inject it into an animal.

RECIPE FOR SODIUM PENTOBARBITAL STOCK SOLUTION

1) Ingredients:
    a. 6 grams sodium pentobarbital
    b. 10 mL ethanol (95%) USP
    c. 40 mL propylene glycol USP
    d. Water for injection USP qs 100 mL
    e. Sodium hydroxide USP or hydrochloric acid USP as required bringing pH to ~ 9.5
2) Steps:
    a. Dissolve the pentobarbital powder completely in 10 mL of 95% ethanol.
    b. Add 40 mL of propylene glycol, again mixing thoroughly.
    c. Bring up to the final volume (100 mL) with sterile water for injection.
3) The final product must have a label with the following information, at minimum:
    a. Compound name, final concentration (mg/ml) and total volume (ml) in vial for injection.
    b. Preparation date and initials of preparer.
    c. Expiration date of not more than 7 days from reconstitution date.

SPECIAL NOTES FOR THE USE OF PREPARED SODIUM PENTOBARBITAL

Drug solutions prepared and stored properly in a suitable injection vial must be used within 7 days of preparation. Prepare only as much as can be used in a reasonable period of time. Solutions must not be used if they are cloudy, discolored, precipitated, or have become otherwise altered in appearance since initial preparation. Though filtered for sterility PIs should be aware pyrogens may be present in final solution.

1) Recipe may be adjusted to make smaller quantities of solution if all components are adjusted proportionately.
2) Final concentration 60 mg/ml or diluted solutions must be protected from light.
3) Do not administer above concentration of 60 mg/ml or if solution has reached expiration date.
4) Powered and compounded solutions (expired solutions) must be stored as a class II controlled substance.
5) If able to secure Pentobarbital for injection from a compounding pharmacy, the prepared drug expiration date is to be 30 days post first accessing the vial for use or by the labeled expiration date (whichever occurs first).
6) Expired stock or working solutions of pentobarbital must be labeled "EXPIRED – DO NOT USE" and discarded through UMB EHS.
7) Pentobarbital cannot be transported to the VA. For use in the VA, it must be obtained via the VA pharmacy as mandated by VA policy.

For examples of appropriate drug bottles / vials, please review the Drug Dilution & Storage Guidelines.