

## Institutional Animal Care and Use Committee

### THE UNIVERSITY OF MISSISSIPPI MEDICAL CENTER

#### POLICY STATEMENT

##### **Use of Non-Pharmaceutical-Grade Chemical/Compounds in Laboratory Animals**

To assure compliance with the Office of Laboratory Animal Welfare (OLAW), the United States Department of Agriculture – Animal and Plant Health Inspection Service (USDA – APHIS), and the 8<sup>th</sup> Edition of the Guide for the Care and Use of Laboratory Animals, the IACUC requires the use of pharmaceutical-grade compounds in laboratory animals. The use of non-pharmaceutical-grade chemicals/compounds should be based on:

- Scientific necessity;
- No availability of an acceptable veterinary or human pharmaceutical-grade compound;  
and
- Specific review and approval by the IACUC.

##### **Chemical and Compounds with No Acceptable Pharmaceutical-Grade Alternatives**

The IACUC recognizes that many test compounds and experimental agents are used in research and generally classify these agents as non-pharmaceutical grade compounds **without** an acceptable pharmaceutical grade alternative (**and is acceptable practice**). However, PI's should use all available knowledge of the compounds to ensure that the non-pharmaceutical grade agents are prepared under sterile condition and stored properly.

1. When drugs or chemicals are formulated for **injection**, they must be prepared in a **sterile manner**. This requires sterile constituents (e.g. sterile powder, sterile diluents), a sterile container and a means of keeping the preparation sterile.
2. **Diluents or vehicles** must be specified in the animal use protocol. Use of solvents will be evaluated on a case-by-case basis.
3. Containers must be **labeled** with the drug, concentration, and date of preparation.
4. When possible, prepared solution should be passed through a syringe **filter** at the time of preparation. If filtering is not possible, sterile components should be mixed using sterile technique.
5. Prepare only as much as can be used in a reasonable period of time. Drug solutions prepared and stored properly in a suitable container can be stored for a time frame that is in-line with a similar commercial product. Drugs must be stored properly (e.g. freezer, refrigerator, etc.). Solutions must not be used if they are cloudy, discolored, precipitated, etc.

6. **Expired drugs** must be disposed of properly. **Controlled substances** cannot be discarded without appropriate paperwork. All controlled substances must continue to be stored in a secure locked location.
7. **pH** of solutions must be between pH 4.5 and 8.0. Use of a solution with a pH outside of this range must be addressed in the animal use protocol.
8. **Pyrogens** may cause fever when injected into an animal. All pharmaceutical drugs are tested for pyrogens. Sterility does not assure that pyrogens are not present. Filtering does not remove pyrogens. Pyrogen testing is not practical for small lots of prepared drug. Pyrogenicity is a potential experimental variable that researchers should be aware of when using non-pharmaceutical grade drugs.

### **Chemicals and Compounds for which a Pharmaceutical Grade Alternative Exist**

Although pharmaceutical grade chemicals/compounds should be used in experimental animals whenever possible, the use of non-pharmaceutical-grade chemical/compounds in experimental animals is an acceptable practice under certain circumstances. For uses of anesthesia and analgesia, the animal's welfare must come first.

### **Justification for use of a non-pharmaceutical-grade compound**

When considering the use of non-pharmaceutical-grade compounds, the following criteria can be used:

- Justification that is acceptable:
  - Known impact on measured outcomes, which is substantiated by data or published reports.
  - Not available from a veterinary or medical supplier
  - Not available from a veterinary or medical supplier in the needed concentration
  - Required in order to produce data that is comparable to previous years' data
  - More pure in a reagent grade version than a pharmaceutical grade version
  - Pharmaceutical grade contains unwanted fillers
  - Pharmaceutical grade only available in form not suited for chosen route of administration
- Inadequate justification, when no additional justification is present:
  - Cost savings
  - Administration burden of acquiring and maintaining a DEA license
  - Consideration/elimination of only one pharmaceutical-grade alternative

Where possible the description should include the chemical grade of the agent(s) being used, source of the reagents, as well as a description of the appropriateness of the agent, its formulation and vehicle. Formulations and vehicles may need to be adjusted depending on the route and site of administration, as well as the species under consideration.

## **Non-survival Procedures**

OLAW has stated that the scientific issues remain the same in non-survival procedures and professional judgment, as outlined above, must still apply. The IACUC will expect a justification of non-survival use. Remember that cost savings alone is not considered adequate justification.

## **Commonly Used Compounds**

[Recipe for Inactin](#)

[Recipe for Sodium Pentobarbital](#)

[Recipe for MS-222](#)

## **Regulatory Guidance**

OLAW - [FAQ](#)

USDA – [Policy #3](#)

### **Pharmaceutical-Grade Compounds in Research**

Investigators are expected to use pharmaceutical-grade medications whenever they are available, even in acute procedures. Non-pharmaceutical- grade chemical compounds should only be used in regulated animals after specific review and approval by the IACUC for reasons such as scientific necessity or non-availability of an acceptable veterinary or human pharmaceutical-grade product. Cost savings is not a justification for using non-pharmaceutical-grade compounds in regulated animals.

[8<sup>th</sup> Edition of the Guide for the Care and Use of Laboratory Animals](#)

“The use of pharmaceutical grade chemicals and other substances ensures that toxic or unwanted side effects are not introduced into studies conducted with experimental animals. Pharmaceutical grade chemicals should be used, when available, for all animal-related procedures (NIH 2008; USDA 1997b). There may be circumstances when the use of a nonpharmaceutical grade chemical or substance is necessary to meet the scientific goals of a project or when a veterinary or human pharmaceutical grade product is unavailable. The use of non-pharmaceutical grade chemicals or substances should be described and justified in the animal use protocol and be approved by the IACUC (Wolff et al. 2003). Consideration should be given to the grade, purity, sterility, pH, pyrogenicity, osmolality, stability, site and route of administration, formulation, compatibility, and pharmacokinetics of the chemical or substance to be administered, as well as animal welfare and scientific issues relating to its use (NIH 2008).”

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