Washington State University Institutional Animal Care and Use Committee



Title: Preparation of Dimethyl Sulfoxide (DMSO)

Standard Operating Procedure #1

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Standard Operating Procedures for Preparation of Dimethyl Sulfoxide (DMSO)

1.0 Purpose:

1.1 To provide guidance on the preparation of dimethyl sulfoxide for use as a vehicle for administration of compounds to laboratory mice and rats and prevent adverse events associated with high concentrations of DMSO, which have been previously reported. Note: DMSO is available in pharmaceutical grade. Use of DMSO for compounding must be consistent with Guideline #12 - Compounding Drugs and Chemicals.

2.0 Background

- **2.1** DMSO is commonly used as a solvent for therapeutic and toxic agents that are not water soluble.
- **2.2** Because DMSO easily penetrates biologic membranes it is frequently used as a drug delivery system. Use of non-medical grade DMSO can introduce harmful impurities.
- **2.3** DMSO is not an inert vehicle. It has anti-inflammatory, analgesic and diuretic properties, impacts platelet aggregation and provokes histamine release. It has anticholinesterase activity and inhibits alcohol dehydrogenase so can potentiate different drugs such as alcohol, insulin and atropine.
- 2.4 Possible toxic effects of DMSO include:
 - **2.4.1** Teratogenic effects in certain species;
 - **2.4.2** Renal tubulonephritis and hepatic, pancreatic and splenic necrosis when given intraperitoneally (IP) for repeated doses;
 - 2.4.3 Intravascular hemolysis or coagulation and pulmonary edema when given intravascularly or at high concentrations IP;
 - **2.4.4** Acute morbidity and mortality can occur with no characteristic gross and microscopic lesions.
- 2.5 Additionally, 100% solution of DMSO when mixed with blood or body fluids (peritoneal fluid) can generate heat by chemical reaction. Therefore, it is recommended to test the solubility of compounds in different combinations of solvents before selecting DMSO as the only vehicle (see 4.4 for suggested combinations) and keep the percentage of DMSO to a minimum.

3.0 Preparation:

- **3.1** DMSO should be stored in airtight containers away from light. It may react with some plastics so should be stored in glass or in the container provided by the manufacturer.
- 3.2 Handle DMSO in a in well ventilated, cool, and dry location away from heat or

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ignition.

- **3.3** Wear PPE: lab coat, tight fitting protective eye wear, and butyl rubber gloves or double nitrile gloves (change after 25 minutes).
- 3.4 For injection, use sterile technique to dilute DMSO to a maximum concentration of 10% solution (v/v) using sterile 0.9% (physiological saline) sodium chloride solution.
- **3.5** It is recommended to indicate not only the concentration of DMSO used but also the mg/kg body weight dosage on the ASAF.

4.0 Additional Recommendations:

- **4.1** Due to the potential toxicity of DMSO, it is advisable to have an untreated control group in addition to DMSO (vehicle) control.
- **4.2** Potential interactions of DMSO with other agents should be considered, even if such interactions have never been reported.
- **4.3** Suggested combinations of solvents are 10% DMSO/10% Tween 80/80% water; or 10% ethanol/40% PEG/50% water.
- **4.4** If a compound needs to be dissolved in DMSO as the only solvent, it is recommended to keep the percentage of DMSO to a minimum (ideally, <1% v/v solutions for *in vivo* injections). If higher concentrations of DMSO are needed, these should not be higher than 10% v/v solutions.

5.0 References:

- **5.1** IACUC <u>Policy #29</u> "Use of Non-Pharmaceutical Grade Substances" https://iacuc.wsu.edu/policies/
- **5.2** Indiana University IACUC Policy "<u>Use of Non-Pharmaceutical Grade Chemicals and Compounds in Laboratory Animals</u>", 2014.
- **5.3** UCDAVIS Veterinary Medical Teaching Hospital SOP "<u>Dimethyl sulfoxide (DMSO)</u> <u>Use</u>", 2011.
- **5.4** Brayton CF. <u>Dimethyl Sulfoxide (DMSO): A Review</u>. *The Cornell veterinarian*, 1986;76:61-90.
- **5.5** Caujolle FM, Caujolle DH, Cros SB, Calvet MM. Limits of toxic and teratogenic tolerance of dimethyl sulfoxide. *Ann N Y Acad Sci.* 1967;141(1):110-126. doi:10.1111/j.1749-6632.1967.tb34871.x
- **5.6** Galvao, J., Davis, B., Tilley, M., Normando, E., Duchen, M.R. and Cordeiro, M.F. (2014), Unexpected low-dose toxicity of the universal solvent DMSO. The FASEB Journal, 28: 1317-1330. https://doi.org/10.1096/fj.13-235440
- **5.7** Plumb, D.C. (2008) *Plumb's Veterinary Drug Handbook*. Blackwell Publishing Professional.