NDSU NORTH DAKOTA STATE UNIVERSITY Institutional Animal Care and Use Committee Guiding Principles and Procedures	Effective: 2/20/2014 Revised:
Title: Tribromoethanol (Avertin)	Page 1 of 3

Guiding Principle

The use of Tribromoethanol (TBE) as an anesthetic in adult mice will only be approved on an individual basis when scientifically justified. Tribromoethanol will be approved only for a single survival procedure (boosted as necessary during the procedure). If TBE administration is to be repeated for a subsequent procedure, the animal must be euthanized prior to recovery from anesthesia.

Background

Tribromoethanol was first used in human clinical practice in the 1920's at a time when other choices for general anesthesia were limited to diethyl ether and chloroform. As a pharmaceutical-grade anesthetic, TBE was once marketed under several proprietary names including Avertin®. However, commercial production of pharmaceutical-grade TBE was discontinued several years ago as better alternatives became widely available for both human and veterinary use.

As an anesthetic, TBE is easy and inexpensive to make in the laboratory from readily available non-pharmaceutical-gram reagents, requires no special equipment for administration, and is not subject to federal or state drug enforcement regulations. However, adverse reports about the efficacy and safety of TBE, combined with the availability of effective pharmaceutical-grade alternatives, have made the continued use of TBE for rodent anesthesia controversial.

Many of the problems associated with TBE relate to improper storage and handling. This can lead to the formation of toxic degradation products which are potent gastrointestinal irritants. Adverse effects such as intestinal ileitis, serositis and peritonitis have been widely reported as a leading cause for morbidity and mortality in rodents following intra-peritoneal administration of TBE. Even under ideal conditions, many have concluded that TBE should not be used in laboratory animals because it produces an anesthetic state which is often inconsistent and variable.

Requirements

Reference 9CFR Animal Health and Husbandry Standards, 3.110 Veterinary Care, USDA Animal Care Resource Guide Policies, March 25, 2011, Policy #3 Veterinary Care:
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.

Guide for the Care of and Use of Laboratory Animals, ILAR, NAS, Eighth Edition 2011, pg 31: 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. They should therefore be used, when available, for all animal-related procedures (USDA 1997b). 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).

Procedure

1. When a Principal Investigator (PI) is considering the use of TBE in a protocol, the PI should consider using other available anesthetics.
   1.1. Consult with the Attending Veterinarian prior to submitting the protocol to the IACUC for review to discuss options for alternate anesthetics.
   1.2. Scientific justification must be included in the protocol for the use of TBE to be considered.
2. When developing and reviewing a protocol requesting the use of TBE as an anesthetic, the PI and IACUC should consider the following:
   2.1. Animal welfare and scientific issues related to the use of TBE.
   2.2. Potential for contamination, safety and efficacy.
3. Protocols are approved to use TBE as an anesthetic require the PI and research staff to follow these procedures:
   3.1. Sterile filtration with a .22 micron filter must be used when mixing TBE solutions.
   3.2. TBE must be stored in an amber bottle or wrapped with foil at 2-8^{o} C (due to degradation of material in the presence of heat or light).
   3.3. TBE Stock solution must be dated.
   3.4. TBE must be discarded **two (2)** weeks after the mix date.
      3.4.1. It is recommended that TBE be mixed fresh for use.

References

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