March 24, 2006

Re: The use of Tribromoethanol (Avertin®)

Tribromoethanol (TBE), previously available under the trade name Avertin, is a non-pharmaceutical grade anesthetic whose use as a human anesthetic was discontinued in the late 1940’s as it was associated with hepatic damage. TBE continues to be used in laboratory mice because it is a non-controlled substance which rapidly induces surgical anesthesia though its reliability to do so can be variable (1, 2).

The concern for use of TBE is the adverse effects that have been associated with its administration. A number of studies have reported various degrees of pathologic lesions and clinical outcomes following TBE administration – these include intestinal ileus, muscle necrosis, chemical peritonitis of abdominal organs and peritoneal wall, bacterial translocation, sepsis, and death (2-5). Use of TBE has also been associated with post-anesthetic illness and death in the rat (6) and gerbil (7).

These adverse side effects have been attributed to different formulations, various doses, pH changes, mouse strain differences, the lack of a standard method for preparation and storage of TBE, and/or toxic decomposition products, but the exact cause(s) remains unclear. Different commercial sources of TBE powder can also vary in purity, and toxicity can arise during storage of TBE powder in the absence of any solvent (8).

Morbidity rates have been reported to range from 30-60% in mice (24 hours post-administration to weeks after) (2-5) and mortality as high as 35% (5). High mortality is also observed after administration of a second anesthetic dose, regardless of the interval between doses. It is important to note that although animals may appear and act normally, microscopic lesions of fibrous adhesions and peritonitis are still observed in TBE treated animals (6), thus these animals experience discomfort despite looking clinically normal.

Consequently, TBE should not be used for survival surgery in rodents. An alternative injectable anesthesia combination is ketamine/xylazine i.p., which produces adequate surgical anesthesia and results in fewer pathologic changes, and less morbidity and mortality. Xylazine is known to provide analgesia, whereas the analgesic effects and anesthetic mechanism of action for TBE are not known.

If investigators have a specific need to use TBE, written scientific justification must be provided to the Animal Care Committee for review and approval.

References