

NEUROMUSCULAR BLOCKING AGENTS

I. Background

- A. The Guide for the Care and Use of Laboratory Animals states that neuromuscular blocking drugs do not provide relief from pain. It is recommended that prior to the use of paralytic agents, the appropriate amount of anesthetic be established for the procedure using the anesthetic of choice without a blocking agent.
- B. According to the Public Health Service Policy on Humane Care and Use of Laboratory Animals, procedures with animals that may cause more than momentary or slight pain or distress should be performed with appropriate sedation, analgesia or anesthesia. Surgical or other painful procedures should not be performed on un-anesthetized animals paralyzed by chemical agents.
- C. Animal Welfare regulations states that procedures that may cause more than momentary or slight pain or distress to the animals will not include the use of neuromuscular blocking agents without anesthesia.

II. Sources

- Mason D.E. and Brown M.I. (1997) Monitoring of Anesthesia.
- D.F. Kohn, S.K. Wixson, W.J. White, G.J. Benson (eds.), *Anesthesia and Analgesia in Laboratory Animals*. San Diego: Academic Press.
- NRC. (1996) Guide for the Care and Use of Laboratory Animals, Washington, DC: National Academy Press.
- NIH (2002) Public Health Service Policy on Humane Care and Use of Laboratory Animals, Bethesda, MD: Office of Laboratory Animal Welfare.

III. Policy

- A. Neuromuscular blocking drugs paralyze skeletal muscles but they do not produce analgesia or loss of consciousness. Neuromuscular blocking agents such as succinyl choline, tubocuraine chloride, atracurium beslyate, gallamine triethiodide, vecuronium bromide, and pancuronium bromide, pipecuronium, and doxacurium are not to be used alone for surgical restraint or in painful procedures. They may be approved for research procedures when the animal needs to be immobilized completely, but only in conjunction with drugs that produce surgical anesthesia. Procedures that may cause more than momentary or slight pain or distress to the animals may not include the use of paralytics without anesthesia. Due to the inherent difficulties in assessing the level of surgical anesthesia in paralyzed animals, the use of these drugs will be approved only if it is clearly established that they are essential for the proposed research, and the investigator is able to monitor the animal appropriately for signs of pain and distress and prepare to take the necessary steps to ensure the animal remains unconscious during the period of paralysis.

- B. The use of neuromuscular blocking agents may be approved for research procedures where scientific justification is provided in detail for paralysis of the animal. Proposed use will be reviewed by the IACUC on a case-by-case basis.
- C. Veterinary consultation is required in preparation of protocols requiring the use of neuromuscular blocking agents.
- D. Because neuromuscular blocking drugs readily cross the placental barrier, the use of these drugs in pregnant animals is not recommended.

IV. Guidelines

- A. The following requirements are necessary during procedures using neuromuscular blocking agents:
 1. A surgical plane of anesthesia must be established and verified and the animal intubated prior to administration of the neuromuscular blocking drug. A fixed anesthetic level, with the animal not exhibiting any changes in physiological state, must be well-established prior to beginning the administration of paralytic drugs, to ensure that the animal is at a stable plane of anesthesia. This period should also be used to establish and validate the physiological signs that will be monitored under paralysis to document that the animal is being maintained in a suitable condition.
 2. A surgical plane of anesthesia must be maintained during the entire time that the neuromuscular blocking drug is present and effective.
 3. The use of analgesics is recommended in addition to the general anesthetic.
 4. Use of neuromuscular blocking agents should be confined solely to that phase of the procedure for which they are indicated.
 5. Controlled ventilation should be established prior to the administration of the neuromuscular blocking drug.
 6. During the period of paralysis, multiple physiologic indicators of pain and stress must be monitored at a minimum every 10 minutes as appropriate to the species and recorded on the intra-operative record (e.g., heart rate, respiratory rate, blood pressure, oxygen saturation, body temperature, mucous membrane color, capillary refill time). An increase of >20% in any one or combination of monitored parameters without other explanations, indicates a pain/stress response. If noted, anesthetic levels should be deepened.
 7. Monitoring of electroencephalography (EEG) and bispectral analysis may also be helpful. However, the normal EEG appearance differs with different types of anesthetics, and confirmation of an anesthetized state may not always be possible based on the EEG. Therefore, the investigator should be thoroughly familiar with the expected EEG pattern for the particular anesthetic used.
 8. Core temperature and fluid balance must be maintained within normal levels during the period of paralysis. If animals will be

paralyzed for long periods of time (e.g., greater than 4 hours) provision must be made for periodic voiding of the urinary bladder.

9. The details on the specific physiologic measures to be monitored and the frequency and means of documentation will be determined on a case-by-case basis. The use of automated monitoring devices cannot substitute for direct monitoring of the animal by a human observer, and a human observer should be present at all times any procedures using neuromuscular blocking agents, as the clinical status of the animal can change quickly and require intervention.
10. Care should be taken to ensure that the animal has recovered control of respiration and locomotion before it is returned to the home cage.
11. Monitoring data should be filed by experiment and animal and kept for at least the duration of the overall protocol.
12. Prior to using neuromuscular blocking drugs in a procedure, the IACUC may require a veterinarian to observe the procedure using the proposed methods of anesthesia and analgesia, but without administration of the neuromuscular blocking drug, to assure that the anesthetic technique is sufficient to relieve any pain and distress associated with the procedure.