

# COMPARATIVE MEDICINE AND LABORATORY ANIMAL FACILITIES

## STANDARD OPERATING PROCEDURES FOR

Protocols requiring the use of neuromuscular blocking agents (paralytics)

- 1.0 Purpose: The SOP outlines the CMLAF's policy on using neuromuscular blocking agents (paralytics) as a method of anesthesia for surgical procedures
- 2.0 Scope: All Principal Investigators approved for the use of paralytic agents.
- 3.0 Background:
  - 3.1 Neuromuscular blocking agents (eg. Pancuronium) are sometimes used to paralyze skeletal muscles during surgery, in which general anesthetics have been administered. Since this paralysis eliminates many signs and reflexes used to assess anesthetic depth, autonomic nervous system changes (eg., sudden changes in heart rate and blood pressure values) can be indicators of pain related to an inadequate depth of anesthesia.
  - 3.2 According to the Public Health Service Policy on Humane Care and Use of Laboratory Animals, and the Animal Welfare Act, 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.
  - 3.3 The Guide for the Care and Use of Laboratory Animals states that neuromuscular blocking drugs do not provide relief from pain, and recommends 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.
  - 3.4 According to The Guide for the Care and Use of Laboratory Animals and the PHS Policy, any proposed use of neuromuscular blocking drugs (paralytics) must carefully be evaluated by the Veterinarian and the IACUC to ensure the wellbeing of the animal.
  - 3.5 The AVMA Guidelines on Euthanasia prohibits and condemns the sole use of neuromuscular blocking drugs as euthanasia agents.

#### 4.0 Procedure:

- 4.1 Surgical procedures on animals using paralytic drugs should not be performed before first conducting a pilot study to determine the appropriate amount of anesthetic needed to achieve the proper anesthetic depth for that protocol.
  - 4.1.1 An animal of the same species, strain, sex, and age, without the paralytic should be anesthetized and the same surgery performed to determine degree, dosage and settings of anesthetic and analgesic necessary to carry out the procedures at a sufficient anesthetic depth.
- 4.2 Administration of paralytic at the start of each surgery should be delayed to establish initial anesthetic depth. A fixed anesthetic level, with the animal not exhibiting any changes in physiological state, must be well-established 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 (heart rate and blood pressure).
- 4.3 Controlled ventilation (endotracheal tube and ventilator) must be established prior to the administration of the neuromuscular blocking drug.
- 4.4 During the period of paralysis, multiple physiologic indicators of pain and stress must be monitored at a minimum of every 10 minutes or 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% (as established in 4.1 above) in any one or a combination of these monitored parameters without other explanations, indicates a pain/stress response and anesthetic levels should be deepened.
- 4.5 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 must be present at all times during any procedures using neuromuscular blocking agents, as the clinical status of the animal can change quickly and require immediate intervention.
- 4.6 The use of analgesics is recommended in addition to the general anesthetic(s).
- 4.7 During surgery, the paralytic should be allowed to wear off periodically to reassess anesthetic depth and adjust administration of anesthetic drugs.
- 4.8 Use of neuromuscular blocking agents should be confined solely to that phase of the procedure for which they are indicated.

- 4.9 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.
- 4.10 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.
- 4.11 Care should be taken to ensure that the animal has recovered control of respiration and locomotion prior to discontinuing the use of the ventilator and before it is returned to the home cage.
- 4.12 Prior to using neuromuscular blocking drugs in a procedure, the IACUC may require a Veterinarian to observe the procedure using the proposed method of anesthesia and analgesia, but without administration of the neuromuscular blocking drug, to assure that the anesthetic technique is sufficient to relieve any pain or distress associated with the procedure.
- 4.13 Animals displaying any signs of pain or distress post operatively must be evaluated by the Veterinarian and should be relieved from pain or be humanely euthanized if necessary.