

University of Louisville
Institutional Animal Care and Use Committee
Policies and Procedures

Use of Neuromuscular Blocking Agents

Policy: This policy establishes standards and expectations for researchers when performing procedures that require the use of a neuromuscular blocking drug (NMBD) in addition to general anesthesia. NMBDs are administered in cases where self-generated movement must be controlled ex: skeletal muscles and ocular movement. However, the use of these drugs eliminates many of the indicators routinely used to determine appropriate anesthetic depth. Autonomic nervous system changes such as heart rate and blood pressure values must be carefully monitored as indicators of the perception of pain related to an inadequate depth of anesthesia. This policy provides guidance to ensure the use of NMBDs in laboratory animals is carefully and appropriately managed. All studies utilizing NMBDs must provide scientific justification for the necessity and duration as well as monitoring parameters within the IACUC Proposal. NMBDs must always be used in conjunction with general anesthesia. NMBAAs must never be used as a sole agent for euthanasia.

Rationale: The Public Health Service Policy on Humane Care and Use of Laboratory Animals, and the USDA Animal Welfare Act states that procedures performed on 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 (NMBDs). 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 well-being of the animal. 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. The AVMA Guidelines on Euthanasia prohibits and condemns the sole use of neuromuscular blocking drugs as euthanasia agents.

Procedures, Guidelines, and Exceptions:

A. Proposal guidelines:

1. The use of NMBDs must be detailed in the IACUC Proposal and reviewed and approved by the IACUC prior to implementation.
2. The proposal must include the name of the NMBD to be used, dose, route of administration, frequency, and duration of the drug. It must also justify the need for the use of an NMBD in addition to general anesthesia.
3. The proposal must include the following declaration, *“Before the administration of the NMBD and including the duration of the use of the NMBD the animal will be maintained*

in a surgical plane of anesthesia. Heart rate and blood pressure measurements will be made before and during the use of the NMBD. To ensure a surgical plane of anesthesia, the animal will be maintained in a stable plane for at least 15 minutes prior to the administration of the NMBD and the absence of reflexes will be verified prior to the administration of the NMBD. If a 20% elevation in these parameters is noticed during the use of the NMBD, the procedure will be suspended and the anesthesia will be increased to deepen the surgical plane of anesthesia which will be evaluated by a return to baseline. Animals will be on a ventilator prior to, during, and after the administration of the NMBD. The animal will not be removed from the ventilator until they are able to breath on their own.”

B. Special considerations for the use of an NMBD

1. Controlled ventilation (endotracheal tube and ventilator) must be established prior to the administration of the neuromuscular blocking drug.
2. Administration of NMBDs at the start of each procedure should be delayed by at least 15 minutes 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 (e.g. heart rate and blood pressure).
3. Details of all drugs administered and actions taken (e.g., “toe pinch” testing) during the procedure must be documented on the animal’s monitoring record.
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% in any one or a combination of these monitored parameters without other explanations, indicates a pain/stress response and anesthetic levels should be deepened.
5. Use of neuromuscular blocking agents should be confined solely to that phase of the procedure for which they are indicated.
6. 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.
7. Care should be taken to ensure that the animal has recovered control of respiration prior to discontinuing the use of the ventilator.
8. Animals must be monitored until they are fully ambulatory after receiving NMBDs.

References:

1. American Veterinary Medical Association, Guidelines for the Euthanasia of Animals, 2020 edition

2. National Research Council, Guide for the Care and Use of Laboratory Animals, 8th Ed., National Academies Press, Revised 2011
3. USDA Animal and Plant Health Inspection Service, Animal Welfare Regulations. 9 CFR Part 2.38(f)(2)(ii), 2016
4. US Department of Health and Human Services/NIH Public Health Service Policy on Humane Care and Use of Laboratory Animals, 2015