

## Guidelines for the Use of Neuromuscular Blocking Drugs in Anesthetized Animals

Revised and Re-Approved May 2006

Neuromuscular blocking drugs (NMBDs) may be used in approved Animal Use Protocols (AUPs) to paralyze skeletal muscles during procedures in which general anesthetics have been administered. NMBDs provide no anesthesia or analgesia but are useful in some anesthetic protocols when skeletal muscle movements will interfere with experimental objectives. Typically used indicators of anesthetic depth (e.g., response to noxious stimuli or changes in respiratory rate) are eliminated because of the paralysis. In order to make certain NMBDs are used properly, animal welfare regulations, policy and guidelines hold the IACUC responsible for establishing performance standards designed to ensure that adequate anesthesia is maintained throughout a period of paralysis.

ACUC approval of an AUP that proposes the use of NMBDs requires the following:

1. The proposal to use NMBDs must be justified in terms of the scientific needs of the research.
2. All surgical or otherwise potentially painful procedures must be performed under adequate anesthesia prior to NMBD administration.
3. Establishment of an adequate long-term anesthesia regimen must be verified prior to the administration of NMBDs. After the surgical or painful portion of the protocol is complete, the animal must be maintained without NMBDs at a fixed anesthetic level until physiologically stable. The ACUC requires a period of at least one hour of stable effective anesthesia without change in anesthetic level prior to NMBD administration. Once NMBDs have been administered, the anesthetic level must not be decreased. If animals are anesthetized for several days, anesthetic levels may need to be decreased to allow successful neurophysiological recordings to continue. In such cases, NMBDs must be withdrawn from the animal for a period of time adequate to allow normal muscle responses to return prior to any reduction in anesthetic dosage.
4. The adequacy of anesthesia must be assessed and documented by means of a “toe pinch” immediately prior to administration of NMBDs and periodically after NMBDs have been administered. This toe pinch is performed by applying direct pressure to one digit with a force adequate to elicit an avoidance response in a conscious animal. The heart rate must be carefully monitored for a period of at least 1 minute immediately following the toe pinch. An increase in heart rate of 20% or greater within 1 minute of the toe pinch will be taken as a significant positive response, indicating that the depth of anesthesia must be increased.
  - a. Prior to NMBD administration: After the surgery and/or other potentially painful procedures are complete, there must be a period of at least one hour with 4 consecutive negative “toe pinch” tests every 15 minutes. Then NMBDs can be administered.
  - b. After NMBD administration: The frequency of toe pinch testing after NMBDs have been administered depends on the nature of the recording procedure being performed. In general, the toe pinch test must be performed and recorded at least once every 8 hours after NMBDs have been administered. If a positive “toe pinch” response is elicited, the dosage of anesthetic must then be increased and toe pinch repeated at least once every 15 minutes for one hour until no significant response is elicited.
5. A thorough physiological monitoring record must be kept for all animals. Parameters such as heart rate, EEG, end-tidal CO<sub>2</sub> and rectal temperature must be monitored continuously and documented periodically. Details of the specific parameters to be monitored and frequency of documentation

must be approved as part of the AUP. Monitoring and documentation must be performed at least every 15 minutes during the surgical portion of the procedure but may be extended to every 30 minutes during more stable periods after NMBDs have been administered (e.g., during periods of neurophysiological recordings).

6. 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. Notations must include the time, date (if appropriate) and the name (or initials) of the individual making the comment.
7. A copy of the animal's records, including the monitoring record, must be returned to the Office of the Animal Care and Use Committee within 7 days of completion of the procedure.

#### References:

1. Committee on Guidelines for the Use of Animals in Neuroscience and Behavioral Research, *Guidelines for the Care and Use of mammals in Neuroscience and Behavioral Research*, National Research Council, National Academy Press, Washington, D.C., 2003.
2. Drummond JC, 1996. Use of neuromuscular blocking drugs in scientific investigations involving animal subjects. *Anesthesiology*, 85(4):697-699.