

# NU – IACUC

## POLICY

Northeastern University Institutional Animal Care and Use Committee

### The Prevention, Recognition, and Treatment of Pain & Distress in Laboratory Animals

The Animal Welfare Act defines a painful procedure as “any procedure that would reasonably be expected to cause more than slight or momentary pain and/or distress in a human being...”. The perception of pain varies between species on a whole, however, the NU-IACUC feels any procedure that would cause pain or distress in humans, would cause pain or distress in animals.

Management of pain or distress is as important as any part of the research experiment. The three main issues we must consider are recognizing an animal is in pain or distress, understanding the degree of pain the animal is involved in, and determining the analgesic regimen that will be administered.

Some procedures that cause pain or distress in animals cannot be alleviated using analgesics. These experiment(s) would be negatively affected by the administration of analgesics. The withholding of analgesics in instances where pain is involved must be scientifically justified in the research protocol and approved by the NU-IACUC. The protocol must clearly define endpoints for all experiments and explain the reasons for withholding analgesics.

#### **Recognition and Management**

Recognition of the level of pain involved in a painful procedure allows for a prediction of animal pain or distress. The physiological responses to pain can include increased blood pressure, respiration, or heart rate, and pupillary dilation. These functions can only be measured if baseline measurements are known.

Identifying changes in behavior is also a useful tool in recognition of pain or distress. These responses vary among individual animals, groups, and species. Response may even vary with the same animal. Important behaviors to look at include: grooming, feeding, drinking, movement, exploration, performance in learning and discriminating tasks, mating behavior, social interactions, and dominance/submissiveness responses within the social system.

#### **Common Behavioral Signs of Pain:**

- Protecting the painful area.
- Vocalizing(especially when handled).

- Licking, biting, scratching, or shaking the painful area.
- Restlessness.
- Lack of mobility.
- Poor hair coat resulting from failure to groom.
- Abnormal posture.
- Lack of normal behavior.

To address the issue of pain/discomfort management, the Principal Investigator must indicate in the protocol:

- The duration and degree of pain/discomfort.
- A literature search that reveals no less painful alternative available (required as part of the animal use protocol).
- The anesthetic/analgesic to be administered with dosage, route and duration.
- The person who will be responsible for the monitoring of the animal(s) along with their level of training.
- If applicable, a justification for the withholding of analgesic medication.
- Endpoints: defined clinical parameters that will indicate the animal must be euthanized prior to the expected experimental endpoint.

Consult with the DLAM veterinarian for species specific clinical indicators.

#### Alleviation of Post-Surgical Pain and Distress:

Pain must be relieved not only during surgical procedures, but during the post-operative period as well. Deviations from this requirement must be justified, in detail, on the protocol form submitted to the NU-IACUC. The DLAM veterinarian may require analgesics be administered if deemed necessary regardless of protocol. It is recommended that post-surgical analgesic be administered to the animal prior to it regaining consciousness. The stress induced by post-operative pain can lead to weight loss, deficiencies in the immunological response, and impairment of wound healing.

Prevention of a painful or stressful condition prior to an animal demonstrating this condition, that is, pre-emptive analgesia, can significantly reduce analgesic requirements and, overall, is a more humane approach to post-operative care.

In recovery from painful procedures, i.e. surgery, animals must be treated with an approved analgesic immediately post-surgery and then as needed depending upon the clinical symptoms. The analgesics are to be provided by an approved member of the protocol team at investigator discretion.

Investigators are encouraged to consult with the DLAM veterinarian prior to beginning a protocol that involves pain. Refer to the NU-IACUC Policy on *Recommended Doses of Anesthetics and Analgesics of Laboratory Animals* for the proper doses and routes of administration of analgesics. This information is also available in the DLAM PI Handbook.

#### Contraindications of Analgesic Administration:

The alleviation of pain and distress may not be a viable option due to the negative effects the medication may have on the experimental outcome; e.g.: the propagation of tumor cells in animals models. In this case, the use of pain medications would interfere with cell growth or angiogenesis.

The protocol submission for such procedures requires the same documentation as stated earlier in this policy. The investigator must explain and scientifically justify, in writing, the reasons that the animals

cannot receive analgesic medication. The literature search must verify that no less painful alternatives are available.

Protocols in which pain and distress cannot be alleviated require the principal investigator to clearly outline the parameters that will be used to measure the level of pain/discomfort in the animal. Specifically, what clinical indications need be present to determine if euthanasia be undertaken to prevent extreme or unnecessary pain and discomfort.

It is at the discretion of the veterinarian as to when treatment or euthanasia is required if not appropriately addressed by the principal investigator.

Euthanasia must be considered when:

- The animal has a weight reduction of more than 20% of overall body weight. (Additionally, an assessment must be done immediately to determine the cause of cachexia. Animals must be weighed daily until there is no further evidence of pain and distress);
- Ambulation is compromised so as to interfere with the ability to take food or water, or to urinate or defecate.
- If a tumor ulcerates, causes any interference with ambulation, or becomes greater than 10-15% of the animal's body weight or is 2 cm across its longest axis.

All methods for pain and distress assessment must be recorded on a post-operative care form.

#### Neuromuscular Blocking Agents:

Neuromuscular blocking agents (pancuronium, succinyl choline) are not anesthetic or analgesic and do not alleviate pain. Thus, when used, constant monitoring is required. These agents are generally used to paralyze skeletal muscle during surgery. When these agents are utilized, many signs used for pain assessment, such as involuntary movement or the palpebral reflex, are eliminated. Sudden changes in heart rate and blood pressure, and/or expired CO<sub>2</sub> > 3.5%; however, can still be used as indicators of pain.

To ensure that anesthetic and analgesic delivery is adequate while paralyzed, the experimenter must either monitor parameters listed above and maintain them at a level appropriate to the species, or remove the paralytic periodically to check for reflex movements.

#### Definitions:

**Pain** – *An unpleasant sensory and emotional experience associated with or described in terms of tissue damage.*

**Distress** – *Mental or physical suffering or anguish.*

**Anesthesia** – *A state characterized by loss of sensation, the result of pharmacological depression of nerve function.*

**Analgesia** – *A condition in which noxious stimuli are perceived but are not interpreted as pain; usually accompanied by sedation without loss of consciousness.*

Approved: