ADA Forsyth®

Animal Program Policy

Title:	**Administration of Analgesia in Rats and Mice**
Date Created:	12/5/2011
Date Reviewed:	11/20/2024

Some research protocols involving the use of animals, especially those involving surgery, are likely to result in pain and/or distress for the animals. It is the policy of the IACUC that such pain and/or distress be identified, minimized or eliminated wherever possible. Administration of analgesics is encouraged as a means to reduce or eliminate pain and distress.

Specific analgesia should be specified in the protocol, but modification of dose, duration, route of administration, or may be enacted **following consultation with the Consulting Veterinarian** without submission of a protocol amendment. Upon confirmation by the Veterinarian that the requested change is consistent with this policy, the change can be implemented. PI and or the Veterinarian must convey in writing to the IACUC that this change has taken place. This record of the change will be maintained with the protocol. Additional information on pain assessment and management can be found in the American College of Laboratory Animal Veterinarians (ACLAM) publication on rodent analgesia.

General Considerations

A procedure which would be expected to be painful if it was done on a human must be considered painful to the animal. When there is a question of whether or not a procedure is painful, the animal should receive the benefit of analgesia. Analgesia should be provided at an appropriate dose, duration and frequency to control pain. Any deviation from this procedure must be justified by the investigator and approved by the IACUC. Every effort should be made to determine the least painful procedure (such as literature searches or consultation with experts).

Assessment of Pain

Some research protocols, particularly those involving the study of inflammation, may be anticipated to produce pain. In these cases, the IACUC may request the investigator to document the extent of pain experienced by experimental animals. Animals should be observed at appropriate frequencies for signs of pain and distress. The IACUC suggests implementation of the following pain scoring system. In each case, a normal healthy animal would receive a score of 0.

1. Activity (Score 1, relatively distressed; score 2, significantly distressed): hypo activity (huddled, lethargic), hyperactivity, restlessness, lack of inquisitiveness, and reduced food intake
    a. Spontaneous Behavior: These observations are made without disturbing the animal, e.g., vocalization, self-trauma, (isolation from cage mates).
    b. Provoked Behavior: These observations are made when the animal is disturbed or even prodded, e.g., vocalization, hiding, aggressiveness, and minimal response.
2. Fur and skin (score 1, relatively distressed; score 2, significantly distressed) - e.g., unkempt, greasy or dull fur; porphyrin staining around eyes and nostrils; pale or congested mucous

membranes or skin (ears, feet, tail); soiled anogenital area.

3. Posture and locomotion (score 1, relatively distressed; score 2, significantly distressed)
    a. Posture: hunched back (a sign of abdominal pain, score 2, tucked abdomen, head tucked down.
    b. Locomotion: gait, ataxia, lameness, action of each limb, position of tail when ambulating.

When any animals under experimentation show a total of pain score more than 2, analgesia should be administered. In addition, endpoints should be specified in the case of unrelieved pain.

An alternative method of assessing pain and distress is the Body Condition Score. Scoring the body condition of rodents is a non-invasive method for assessing health and establishing endpoints for adults where body weight is not a viable monitoring tool, such as with tumor models, ascites production and pregnancy, or for young growing animals.

Body condition scores (BCS) range from 1 (emaciation) to 5 (obesity). An anticipated BCS of 2 – under conditioned – or lower, requires justification in the protocol.

Scores are determined by frequent visual and hands-on examination of each animal. The hands-on evaluation is done by gently holding the mouse by the base of the tail and passing a finger over the sacroiliac bones. The findings are matched to the descriptions and diagrams below to determine a score.

BC 1

Mouse is emaciated.
- *Skeletal structure extremely prominent; little or no flesh cover.*
- *Vertebrae distinctly segmented.*

BC 2

Mouse is underconditioned.
- *Segmentation of vertebral column evident.*
- *Dorsal pelvic bones are readily palpable.*

BC 3

Mouse is well-conditioned.
- *Vertebrae and dorsal pelvis not prominent; palpable with slight pressure.*

BC 4

Mouse is overconditioned.
- *Spine is a continuous column.*
- *Vertebrae palpable only with firm pressure.*

BC 5

Mouse is obese.
- *Mouse is smooth and bulky.*
- *Bone structure disappears under flesh and subcutaneous fat.*

A "+" or a "-" can be added to the body condition score if additional increments are necessary (i.e. ...2+, 2, 2-...)

Anesthesia Options

1. Extended-release buprenorphine (Ethiqa) is the only analgesia in use at Forsyth as of 11/24. This is a controlled substance and is provided on request by animal facility staff. Contact Desal or Yoga. **Details of Ethiqa handling and dispensing are described in Standard Operating Procedure P9 "Use of Ethiqa XR as pain relieving medication."**

   Ethiqua is supplied as a sterile solution at 1.3 mg/ml. It is a viscous solution and must be administered subcutaneously in the loose skin at the back of the neck, using a 23 gauge needle. It may not be diluted.

   The dose for mice is 3.25mg/kg and for rats the dose is 0.65 mg/kg.

   Ethiqa should be administered one time prior to the start of the painful procedure, and should provide pain relief for 72 hours. If signs of pain are observed during the 72 hour period, contact the consulting veterinarian for advice.

2. Additional anesthesia for surgery
   Even with general anesthesia, the topical, subcutaneous (at surgical incision site) administration of a local anesthetic is recommended to provide additional post-surgical analgesia. Local anesthetics should not be used alone to provide post-surgical/post-procedural analgesia, and should be administered prior to surgery

Agent	Species	Onset	Duration*	Topical Use	Infiltration Use	Maximum Dose
Lidocaine	2:1mouse	Fast	2 hours	24%	0.5--1%	10 mg/kg
Bupivicaine (Marcaine)	8:1mouse	Int	4-8 hours	-	0.25%	5 mg/kg
Lidocaine	rat		2 hours	2%	2%	10 mg/kg
Bupivicaine (Marcaine)	rat		4-8 hours		.5%	5 mg/kg

3. Non-Opioid Analgesia
   There are non-opioid options for analgesia in rodents.

   These include Carprofen (2.5 – 5.0 mg/kg, s.c. every 24 hr) for mice or rats or
   Meloxicam (1 – 2 mg/kg s.c. every 24 hr)for rats

   Use of non-opioid analgesia must be discussed with the Director of Animal Care and the Consulting Veterinarian prior to including in a protocol. Only pharmaceutical grade analgesia formulations are allowed; contact the Director of Animal Care for information.

References

Body condition scoring: a rapid and accurate method for assessing health status in mice. Ullman-Culleré MH, Foltz CJ. Lab Anim Sci. 1999 Jun;49(3):319-23. PMID: 10403450

Sustained-Release Buprenorphine Improves Postsurgical Clinical Condition but Does Not Alter Survival or Cytokine Levels in a Murine Model of Polymicrobial Sepsis. Herndon NL, Bandyopadhyay S, Hod EA, Prestia KA. Comp Med. 2016 Dec 1;66(6):455-462. PMID: 28304248 Free PMC Article

Efficacy of Sustained-Release Buprenorphine in an Experimental Laparotomy Model in Female Mice. Kendall LV, Wegenast DJ, Smith BJ, Dorsey KM, Kang S, Lee NY, Hess AM. J Am Assoc Lab Anim Sci. 2016 Jan;55(1):66-73. PMID: 26817982 Free PMC Article

Guidelines for the Assessment and Management of Pain in Rodents and Rabbits Ch 14 in Anesthesia and Analgesia in Laboratory Animals, Melissa Dyson, Paulin Jirkof, Jennie Lofgren, Elizabeth Nunamaker, Daniel Pang, eds 3rd edition, Academic Press 2023