University Animal Care Committee Standard Operating Procedure		
Document No: 7.1	**Subject:** Pain Management in Mice	
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Location: Queen's University

Responsibility: Principal Investigators, Research Staff, Veterinary Staff

Purpose: The purpose of this Standard Operating Procedure (SOP) is to describe methods for assessing and treating pain in rodents.

1. **Introduction and Definitions:**
   - Based on the definition of pain from the American College of Laboratory Animal Medicine (ACLAM), pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage and should be expected in an animal subjected to any procedure or disease model that would be likely to cause pain in a human.
   - It is generally agreed that pain adversely impacts the welfare of animals and that in research protocols, pain, if not controlled, is a variable which can confound the interpretation of experimental results.
   - Procedures expected to cause more than slight or momentary pain (e.g., pain in excess of a needle poke or injection) require the appropriate use of pain-relieving measures unless scientifically justified in an approved animal use protocol (AUP).
   - Pain management is an important ethical and moral issue but is challenged by inconsistency related to lack of evidence based effective doses for different strains, the challenge of assessing pain and the ability to reduce pain. This results in extrapolation from other species to rodents for dose rates.
   - The following tables provide some options for general analgesics and local analgesics that can be used. Multi-modal pain management is utilized frequently as well as regional analgesia.

Abbreviations: Animal Care Services **ACS**, Principal Investigator **PI,** subcutaneous **SC**, intravenous **IV**, intraperitoneal **IP,** intramuscular **IM**, per os **PO,** per rectum **PR**

2. **Materials:**
   a) **Clinical Assessment of Post-Procedural Pain**
      - The most reliable signs of pain and distress in rodents are changes in

animal behaviour, thus it is important that the animal user has a good knowledge of species specific and individual behaviour. The animal user should also be aware of any strain differences that could affect the animal's response to pain and or the medications used to treat said pain.

- All animals should be observed initially from a distance, so their natural behaviour is not inhibited. This should be followed by a closer examination. The use of additional aides to interpret the presence of pain can also be utilized eg) the Grimace scale
- Frequency of observation should be procedure specific, but not less than once per day.
- Contact veterinary staff if any changes in animal behaviour are observed.
- Common clinical signs of pain and distress include:
    - Reduced grooming
    - Reduced level of spontaneous activity
    - Piloerection
    - Rough hair coat
    - Hunched posture
    - Increased aggression when handled.
    - Isolation/separation from cage mates
    - Reduced food/water intake
    - Pale extremities
    - Sunken eyes/dehydration
    - Squinty eyes
    - Wound licking
    - Orbital tightening
    - Abnormal gait
    - Vocalization when handled.

b) Management of Pain:

- Non-pharmacological considerations:
    - Providing appropriate housing, handling and restraint as well as using appropriate experimental techniques can support pain management.
    - Fluid and heat therapy are generally provided for rodents displaying signs of pain.
    - Easy access to moist chow or lab-diet gel. Lab diet gel must be replaced daily.
- Pharmacological considerations:
    - If not contraindicated by the experimental protocol, preemptive, multi-modal analgesia should be used. For example, administration of a

combination including an opioid, non-steroidal anti- inflammatory (NSAID) and a local analgesic.

- Local Anesthetics:
  - Local anesthetic should be infiltrated at the site where the painful stimulus will be induced:

Local Analgesics	Dose	Duration	Notes
Lidocaine	< 2 mg/kg	30 – 60 minutes	- Due to acidic nature, dilute 3:1 with sodium bicarbonate injectable solution for a conscious rodent - If administered in an anesthetized patient, dilution with sodium bicarbonate is not necessary. - Fast onset of action with moderate duration - Lidocaine with epinephrine is not recommended for rodents
Bupivacaine	< 2 mg/kg	4 – 7 hrs.	As above with the exception: - Slower onset of action versus lidocaine but longer duration
Lidocaine/bupivacaine	-	Up to 7 hrs.	- Combination allows for rapid onset with longer duration

General Analgesics:

Analgesic	Dose	Route	Frequency
Acetaminophen	100 – 300 mg/kg	PO	q 4 hr.
Meloxicam (Long Term)	1 – 6 mg/kg	SC, PO	q 12-24 hr.
Meloxicam (Post-surgical – 3 days)	10mg/kg	SC, PO	q 12-24 hr.
Ketoprofen	5 mg/kg	SC	q 12- 24 hr.
Carprofen	2.5- 5 mg/kg	SC, IP	q 24 hr.
Tramadol	20 – 40 mg/kg	SC, IP	q 24 hr.
Buprenorphine	0.05 – 0.1 mg/kg	SC, IP	q 6 – 12 hr.
Buprenorphine SR	0.1 mg/kg	SC, IP	q 48 hr.

References:

- Fish RE, Brown MJ, Danneman PJ, Karas AZ. Ed. (2008) Anesthesia and Analgesia in Laboratory Animals 2nd Ed. Academic Press, New York
- University of Michigan-Guidelines on Anesthesia and Analgesia in Mice –Approved May 19, 2023
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SOP Revision History:

Date	New Version
January 28th, 2016	Update
February 28th, 2019	Triennial Update
February 28th, 2022	Triennial Update
October 17th, 2023	Drug dose update, format change