



University Animal Care Committee Standard Operating Procedure		
Document No: 7.1	Subject: Pain Management in Mice	
Date Issued: February 16, 2012	Revision: 2	Page No: 1

Location: Queen's University

Responsibility: Principal Investigators (PI), 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).

Abbreviations: subcutaneous **SC**, intravenous **IV**, intraperitoneal **IP**, intramuscular **IM**, per os **PO**, each, every **q**

2. Procedures:

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.
- All animals should be observed initially from a distance so their natural behaviour is not inhibited. This should be followed by a closer examination.
- 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:

Mice
<ul style="list-style-type: none">- 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



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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.
- 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	<ul style="list-style-type: none"> - 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: <ul style="list-style-type: none"> - Slower onset of action versus lidocaine but longer duration
Lidocaine/bupivacaine	-	Up to 7 hrs.	<ul style="list-style-type: none"> - Combination allows for rapid onset with longer duration

General Analgesics

Analgesic	Dose	Route	Frequency
Acetaminophen	100 – 300 mg/kg	PO	q 4 hr.
Meloxicam	1 – 2 mg/kg	SC	q 24 hr.
Ketoprofen	5 mg/kg	SC	q 24 hr.
Carprofen	2.5 – 5 mg/kg	SC	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.



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Canadian Council on Animal Care Categories of Invasiveness in Animal Experiments

A. Experiments on most invertebrates or on live isolates.

B. Experiments which cause little or no discomfort or stress.

Possible examples: domestic flocks or herds being maintained in simulated or actual commercial production management systems; the short-term and skillful restraint of animals for purposes of observation or physical examination; blood sampling; injection of material in amounts that will not cause adverse reactions by the following routes: intravenous, subcutaneous, intra-muscular, intra-peritoneal or oral, but not intra-thoracic or intra-cardiac (Category C); acute non-survival studies in which the animals are completely anesthetized and do not regain consciousness; approved methods of euthanasia following rapid unconsciousness, such as anesthetic overdose, or decapitation preceded by sedation or light anesthesia, short period of food and/or water deprivation equivalent to period of abstinence in nature.

C. Experiments which cause minor stress or pain of short duration.

Possible examples: cannulation or catheterization of blood vessels or body cavities under anesthesia; minor surgical procedures under anesthesia, such as biopsies, laparoscopy; short period of restraint beyond that for simple observation or examination, but consistent with minimal distress; short periods of food and/or water deprivation which exceed periods of abstinence in nature; behavioural experiments on conscious animals that involve short-term, stressful restraint; exposure to non-lethal levels of drugs or chemicals. Such procedures should not cause significant changes in the animal's appearance, in physiological parameters such as respiratory or cardiac rate, or fecal or urinary output, or in social responses.

Note: During or after Category C studies, animals must not show self-mutilation, anorexia, dehydration, hyperactivity, increased recumbency or dormancy, increased vocalization, aggressive-defensive behaviour or demonstrate social withdrawal and self-isolation.

D. Experiments which cause moderate to severe distress or discomfort.

Possible examples: major surgical procedures conducted under general anesthesia, with subsequent recovery; prolonged (several hours or more) periods of physical restraints; induction of behavioural stresses such as maternal deprivation, aggression, predator-prey interactions; procedures which cause severe, persistent or irreversible disruption of sensorimotor organization; the use of Freund's Complete Adjuvant (see CCAC Guidelines on Acceptable Immunological Procedures). Other examples include induction of anatomical and physiological abnormalities that will result in pain or distress; the exposure of an animal to noxious stimuli from which escape is impossible; the production of radiation sickness; exposure to drugs or chemicals at levels that impair physiological systems.

Note: Procedures used in Category D studies should not cause prolonged or severe clinical distress as may be exhibited by a wide range of clinical signs, such as marked abnormalities in behavioural patterns or attitudes, the absence of grooming, dehydration, abnormal vocalization, prolonged anorexia, circulatory collapse, extreme lethargy or disinclination to move, and clinical signs of severe or advanced local or systemic infection, etc.

E. Procedures which cause severe pain near, at, or above the pain tolerance threshold of unanesthetized conscious animals.

References:

Fish RE, Brown MJ, Danneman PJ, Karas AZ. Ed. (2008) Anesthesia and Analgesia in Laboratory Animals 2nd Ed. Academic Press, New York

https://www.ccac.ca/Documents/Standards/Policies/Categories_of_invasiveness.pdf

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