

# STANDARD OPERATING PROCEDURE

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**TITLE:** Post-operative analgesia in mice and rats - Western  
**SOP NO.:** 355-01  
**REVISION:**  
**EFF. DATE:** February 2010  
**SUPERSEDES:** NA

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## APPROVALS

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## 1.0 PURPOSE

- 1.1 To outline standards of care to ensure optimal *post-operative analgesia in weaned mice and rats* used in biomedical research, testing or teaching at UWO.
- 1.2 Animal welfare regulations require that procedures involving research animals avoid or minimize discomfort, distress, and pain.
- 1.3 Pain causes many physiologic alterations, therefore the most sound scientific data is retrieved from research subjects that do not suffer from post-operative pain.
- 1.4 Procedures causing *more than momentary or slight pain and discomfort* to research animals require the appropriate use of sedatives, anesthetics, or analgesics.
- 1.5 Because the anatomic structures and neurophysiologic mechanisms leading to the perception of pain are similar in humans and non-human animals, it is reasonable to assume that if a stimulus is painful to humans, is damaging or potentially damaging to tissues, or induces escape and emotional responses in an animal, it must be considered to be painful to that animal.
- 1.6 Failure to provide post-operative analgesics is a serious offence according the requirements of **University Council on Animal Care**, the guidelines of the **Canadian Council on Animal Care**, the **Ontario Animals for Research Act** and the **Criminal Code of Canada**.

## 2.0 SCOPE

- 2.1 This SOP details commonly used *post-operative analgesic regimes in weaned mice and rats*. Investigators may refer to this SOP in their Animal Use Protocol (AUP) or discuss an alternate SOP with an ACVS veterinarian prior to submission of their AUP, related renewals or modifications and obtain approval from the Animal Use Sub-committee (AUS) on that alternate SOP.
  - 2.2 For rodents other than mice and rats, un-weaned mice and rats, and non-rodent animals, analgesic regimes should be discussed with an ACVS veterinarian prior to submission of their AUP, related renewals or modifications and obtain approval from the AUS.
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2.3 Analgesic regimes used to treat pain and/or distress associated with *non-surgical* procedures is not considered in this SOP.

### 3.0 RESPONSIBILITIES

- 3.1 Investigator
  - 3.1.1 Ensure that an appropriate post-operative analgesic regime is approved on their AUP.
  - 3.1.2 Ensure that the person performing the procedure is properly trained and is listed on the approved AUP.
  - 3.1.3 Ensure appropriate approvals from Health Canada for the use of opioids (ie. buprenorphine) in his/her research laboratory
- 3.2 Person administering the post-operative analgesic.
  - 3.2.1 Ensure timely administration of post-operative analgesics as outlined in the approved AUP.
  - 3.2.2 Contact an ACVS veterinarian if the animal exhibits signs of pain (see point 7.3) in spite of analgesic administration. The animal may require additional medications or treatments.

### 4.0 PROCEDURES

- 4.1 **Level 1 Procedures**
  - 4.1.1 **Representative Procedures:** Thoracotomy, Laparotomy; Orthopedic (including cranial procedures involving defects >2 mm diameter), Limb Amputation
  - 4.1.2 **Minimum Analgesic Requirement:** Pre-emptive injection of an NSAID or Buprenorphine, then additional injections of an NSAID or an opioid, such that effective analgesic levels maintained for **48 hrs post-operatively**
- 4.2 **Level 2 Procedures**
  - 4.2.1 **Representative Procedures:** Tail Biopsy (>21 days age, if > 0.3 cm, since vertebrae could be cut), Digit Amputation (mice >12 days age, rats > 7 days age), Skin incision +/- Major tissue manipulation or Vessel cannulation involving skin incision, Burr holes <2 mm diameter
  - 4.2.2 **Minimum Analgesic Requirement:** Pre-emptive injection of an NSAID or Buprenorphine, then additional injections of NSAID or an opioid, such that effective analgesic levels maintained for **24 hrs post-operatively**
- 4.3 **Level 3 Procedures**
  - 4.3.1 **Representative Procedures:** Ear punch or punch biopsy, Tail Biopsy (<21 days age or >21 days age if <0.3 cm, thus avoiding bone), Digit Amputation (mice < 12 days age, rats < 7 days of age)
  - 4.3.2 **No Analgesia Required**

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#### 4.4 Recommended Drugs, Doses and Schedule for Mice and Rats

4.4.1 **NSAIDs:** *Meloxicam (Metacam<sup>TM</sup>)*: 0.3-1.0 mg/kg IM, IP, SQ (every 24 hours, if repeated injections required)

*Carprofen (Rimadyl<sup>TM</sup>) or Ketoprofen (Anafen<sup>TM</sup>)*: 5 mg/kg IM, IP, SQ (every 24 hours, if repeated injections required)

4.4.2 **Opioids:** *Buprenorphine (Temgesic<sup>TM</sup>)*: 0.05-0.1 mg/kg IM, IP, SQ (every 6-8 hours)

#### 4.5 Considerations for choosing either opioids or NSAIDs

4.5.1 Note that buprenorphine administration in mice and rats routinely causes reductions in food and water consumption in animals not undergoing any additional procedures. Therefore, NSAIDs may be the better choice of analgesic drug following many post-operative procedures.

4.5.2 Additional advantages of NSAIDs over opioids include an anticipated duration of effective analgesia of 24 hours in rodents. Furthermore, NSAIDs are not controlled substances.

4.5.3 Surgeries anticipated to cause severe degrees of pain (ie. craniotomy) may require a combination of opioid and NSAIDs. In this case, administration at the lower range of effective doses is anticipated to provide adequate pain relief. For example, a pre-emptive dose of *Buprenorphine (Temgesic<sup>TM</sup>)*: 0.05 mg/kg SQ, combined with 2 doses of *Ketoprofen (Ketofen<sup>TM</sup>)*, 3 mg/kg SQ, administered pre-emptively and 24 hours following.

4.5.4 Use of opioids requires that the Principle Investigator obtain a controlled substances “Exemption License” from Health Canada, prior to ordering these substances. Storage and record keeping standards are set by Health Canada. Links and information can be found on the [Animal Care and Use Website – Services page](#).

#### 5.0 SUMMARY

5.1 This SOP outlines a regime for post-operative analgesic administration for weaned mice and rats.

#### 6.0 REVISION HISTORY

Revision	Reason(s) for Revision	Initiated by

#### 7.0 REFERENCES / ASSOCIATED MATERIALS

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### 7.1 Definitions

- 7.1.1 Pre-emptive: defined as SQ, IM or IP analgesic administration shortly (ie. up to 30 minutes) before making an incision or other painful procedure.
- 7.1.2 NSAID: Non-steroidal anti-inflammatory drug
- 7.1.3 SQ: subcutaneous
- 7.1.4 IM: intramuscular
- 7.1.5 IP: intraperitoneal

### 7.2 References

- 7.2.1 Brennan MP, Sinusas AJ, Horvath TL, Collins JG, Harding MJ. 2009. Correlation between body weight changes and postoperative pain in rats treated with meloxicam or buprenorphine. *Lab Anim (NY)*. 2009 Mar;38(3):87-93.
- 7.2.2 Raucci FA, Gades NM, Toth LA. 2000. An evaluation of analgesic regimens for abdominal surgery in mice. *Contemp Top Lab Anim Sci* 39:18-23.
- 7.2.3 Roughan JV, Flecknell PA. 2000. Effects of surgery and analgesic administration on spontaneous behavior in singly housed rats. *ResVet Sci* 69:283-8.
- 7.2.4 Roughan JV, Flecknell PA. 2001. Behavioral effects of laparotomy and analgesic effects of ketoprofen and carprofen in rats. *Pain* 90:65-74.
- 7.2.5 Roughan JV, Flecknell PA. 2003. Evaluation of a short duration behaviour-based post-operative pain scoring system in rats. *Eur J Pain* 7:397-406.
- 7.2.6 Roughan JV; Flecknell PA. 2004. Behavior-based assessment of the duration of laparotomy-induced abdominal pain and the analgesic effects of carprofen and buprenorphine in rats. *Beh Pharm* 15: 461-472
- 7.2.7 Stewart LSA, Martin WJ. 2003. Evaluation of postoperative analgesia in a rat model of incisional pain. *Contemp Top Lab Anim Sci* 42:28-34

### 7.3 Pain Recognition in Rodents

- 7.3.1 The most definitive signs of pain in rodents are reduced night-time activity (either locomotor or upward exploratory behavior) and decreases in food and water consumption (and hence, body weight).
- 7.3.2 Most acute or chronic clinical signs are not an absolute indication of pain as they may be associated with other problems, e.g. diseases. Clinical signs which may indicate pain (or disease) in rodents are: anorexia with subsequent loss of weight, abnormal posture, self mutilation of painful area, decreased exploratory behavior, piloerection, hunched posture, rough and ungroomed hair coat and ungroomed appearance, excessive scratching and licking, more aggressive when handled, vocalization when handled, weight loss, porphyrin tearing (rats), twitching of the back and flank (following laparotomy).
- 7.3.3 Research and/or animal care staff must contact ACVS veterinarians if signs of pain are evident at any point during the post-operative procedure.