Analgesia Guidance for Rodent Procedures

Important tips:
1. Expected post-procedural pain level is based on procedure being performed optimally by skilled personnel. Sub-optimal performance of any procedure is likely to produce more pain than is typical.
2. Consider the effects of using the specific analgesic (NSAID or opioid) on the scientific objectives of the study.
3. Include multiple (or all) options in your protocol to maintain flexibility. See additional information on drugs below chart.
4. Animals should be monitored as follows: moderate pain → at least once daily; severe pain → at least twice daily until analgesia is done and animal is stable (see green post-op card instructions).
5. Analgesia lasting longer than required is permitted (e.g. sustained release formulas).
6. Other analgesic regimens may be proposed. Contact a veterinarian to discuss available alternatives. All analgesic regimens must be reviewed and approved by the IACUC prior to use.
7. Multi-modal pain relief (e.g. a combination of local anesthetic, opioid, and NSAID) is generally superior to single-modality analgesia.

<table>
<thead>
<tr>
<th>Rodent Procedure Examples</th>
<th>Expected Post-procedural Pain Level</th>
<th>Analgesic Options (see additional info that follows)</th>
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</thead>
<tbody>
<tr>
<td>IP, SC, or IV injection</td>
<td>No Pain or Minimal Pain</td>
<td>• Analgesia is not required.</td>
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<td>Percutaneous catheter insertion</td>
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<td>• Any of the “mild pain” options may be used if desired.</td>
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<tr>
<td>Tail snip</td>
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<td>In general, if anesthesia is not required, then analgesia is not required.</td>
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<td>Toe clip</td>
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<td>Ear notch</td>
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<tr>
<td>SC tumor implant by needle</td>
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</tbody>
</table>
| Retro-orbital blood collection or injection (typically requires general anesthesia) | Mild Pain (analgesia to last at least 8 hours) | Option 1: Local anesthetic (incisional)  
Option 2: 1 dose of buprenorphine  
Option 3: NSAID (to last at least 8 hours)  
General anesthesia is required. |
| Skin incision only (any site) |                                    |                                                   |
| Subcutaneous implant (e.g., osmotic pump, pellet, transponder) | |                                                   |
| Catheter placement via cut down |                                    |                                                   |
| Punch biopsy of skin       |                                    |                                                   |
| Vascular access port implantation |                                |                                                   |
| Ocular (eye) procedure—minor |                                    |                                                   |
### Rodent Analgesia

- **Embryo transfer via lumbar incision**
- **Castration / Vasectomy**
- **Intracranial surgery** — minor
- **Thyroidectomy**
- **Thymectomy**
- **Mammary fat pad manipulation**
- **Orthopedic procedures** — minor
- **Ocular (eye) procedure** — moderate
- **Tissue dissection/transection** (e.g. incisional biopsy or tumor removal)

#### Moderate Pain (analgesia needs to last 12-24 hours)

| Option 1: | Lidocaine or Bupivacaine local at the time of surgery followed by NSAID (12-24 coverage) |
| Option 2: | Buprenorphine + injectable NSAID (12-24 hour coverage) |
| Option 3: | Buprenorphine + oral NSAID (12-24 hour coverage) |
| Option 4: | 1 dose of Buprenorphine-SR (lasts 72 hours) |

- **Thoracotomy** (use of local anesthetic on incision site is highly desirable — see following pages)
- **Laparotomy** (for C-section, GI, kidney, spleen, liver, reproductive, or other abdominal procedures)
- **Craniotomy** — with bone removal — major
- **Laminectomy/Vertebral surgery**
- **Nerve surgery**
- **Ocular (eye) procedure** — major
- **Orthopedic procedure** — major

#### Severe Pain (analgesia needs to last 24-48 hours)

| Option 1: | Lidocaine or Bupivacaine local at the time of surgery followed buprenorphine +/- NSAID (thoracotomy) |
| Option 2: | Buprenorphine + injectable NSAID (24-48 hour coverage) |
| Option 3: | Buprenorphine-SR given 1 hour prior to surgery; +/- local anesthetic; +/- oral NSAID to reduce swelling and increase comfort |

*Minor procedures typically do not result in permanent or chronic impairment. Healing is rapid with little obvious change in the area or organ.

*Major procedures require more extensive tissue resection and organ involvement resulting in delayed healing or chronic inflammation.

### Additional Information on Rodent Analgesics

I. **Systemic analgesics**
   A. **Buprenorphine (Buprenex®)**
      - Narcotic/Opioid (Schedule III)
      - Drug concentration in ampule: 0.3 mg/ml
      - Analgesic duration: 8-12 hours
      - Dosages:
        - Rats: 0.01 - 0.05 mg/kg given SC or IP every 8-12 hours *
        - Mice: 0.05 - 0.1 mg/kg given SC or IP every 8-12 hours
      - *may cause pica (eating of non-food substances) in rats; use lower dose range for Sprague-Dawley rats
B. Buprenorphine-Sustained Release ("Bup-SR")  
Narcotic/Opioid (Schedule III) from ZooPharm  
Drug Concentration: 1 mg/ml (5 ml vial)  
Analgesic duration: 72 hours  
Dosages:  
   Rats: 1.0 - 1.2 mg/kg* [for a single 72-hour SC injection]  
   Mice: 0.5 – 1.0 mg/kg* [for a single 72-hour SC injection]  
Additional information at SR Veterinary Technologies

C. Carprofen (Rimady®) Non-steroidal anti-inflammatory (NSAID)

1. Carprofen Oral (chewable tabs): from Bio-serv  
Flavored chewable tablet containing 2 mg carprofen/5 gram tablet.  
How to use: Placebo tab (no carprofen) can be used 3 days prior to surgery to acclimate the animal. Place on the cage floor for easy access. The tablet is nutritionally complete, stimulates appetite, and allows animals time to recover undisturbed.  
Dosages:  
   Rats: One 5 gm tablet per rat per day  
   Mice: ¼ tablet per mouse per day (one 5 gm tablet for up to 4 mice)

2. Carprofen Oral (Drinking water):  
Drinking water is treated with injectable carprofen (50mg/ml) to provide therapeutic levels.  
How to use: Determine size of water bottle used in cages (most commonly 400 ml bottles).  
Dosages:  
   Rats: 0.05mg to 0.1mg carprofen per ml water (Add 0.1 to 0.2 ml carprofen per 100 ml water)  
   Mice 0.05mg carprofen per ml water (0.1 ml carprofen (50 mg/ml) per 100 ml water)

3. Carprofen Injectable:  
Drug concentration in bottle: 50 mg/ml  
*Store at 4˚ C  
How to use: Drug is viscous and needs to be diluted in sterile water 1:10 or more.  
Administer injectable solution as below using a 25 or 27g needle.  
Dosages:  
   Rats: 5 mg/kg IP or SC every 6-8 hours **  
   Mice: 5 mg/kg IP or SC every 6-8 hours **  
   **or 8-12 hours if supplemented with chewable NSAID
D. **Meloxicam (Metacam<sup>®</sup>)** Non-steroidal anti-inflammatory (NSAID)

1. **Meloxicam Oral (chewable tab):** available from Bio-Serv
   Flavored, nutritionally complete chewable 5 gram tablet
   **How to use:** Placebo tab (no meloxicam) can be used 3 days prior to surgery to acclimate the animal. Place on the cage floor for easy access.
   **Dosages:**
   - Rats: One 5 gm tablet/rat/day (0.5 mg meloxicam/tablet)
   - Mice: One 5 gm tablet/mouse/day (0.125 mg meloxicam/tablet)

2. **Meloxicam Injectable:** (5 mg/ml)
   **How to use:** Administer injectable solution as below using a 25 or 27g needle.
   **Dosages:**
   - Rats: 1 mg/kg once daily up to 3 days
   - Mice: 5-10 mg/kg once daily up to 3 days

3. **Meloxicam SR (sustained release) injectable:** (2mg/ml)
   (SR formulation recommended for RATS only)
   **How to use:** Store at 4 degrees. Warm to room temperature before use. Use a 16- or 18-gauge needle to draw Meloxicam SR from the vial and then replace with a 23-gauge needle for injection into the animal. Administer SC up to 1 hour before surgery. Contraindicated in animals with impaired hepatic, cardiac, or renal function. Avoid use in dehydrated or hypovolemic animals.
   **Dosages:**
   - Rats only: Administer 4 mg/kg SC [lasts up to 72 hours]
   - Additional Information at [SR Veterinary Technologies](#)

4. **Meloxicam Oral Solution (for oral dosing):** (1.5 mg/ml)
   **How to use:** Drug must be diluted with sterile diluent 1:10 prior to use. Specific training in oral dosing by gavage is required. Contact DCM to arrange training.
   **Dosages:**
   - Rats: 0.5 mg/kg PO every 12 hours up to 3 days
   - Mice: 2.5 - 5 mg/kg PO every 12 hours up to 3 days

II. **Local anesthetics that provide analgesia**
   General considerations for local analgesics:
   - Provides local pain relief, and is most effective when injected BEFORE making the incision.
   - Use in the skin around the **planned** incision site for surgeries. Intradermal injection is preferred.
   - For thoracotomies, inject into the intercostal space (rib muscles) at the planned site of incision. Can be used to supplement systemic analgesia (opioids, NSAIDS)
A. **Bupivacaine (Marcaine®) 0.5%**
   Concentration: 5 mg/ml (0.5%); sold in a 50ml vial
   Analgesic duration: 4 – 8 hours, slow onset
   **How to use:** Dilute in sterile water to 2.5mg/ml (0.25%).

   Dose: Do not exceed 8mg/kg SC

B. **Lidocaine (Xylocaine®) 2%**
   Concentration: 20 mg/ml (2%); sold in a 50 ml vial
   Analgesic duration: 1 hour, fast onset
   **How to use:** Some formulations of lidocaine include epinephrine to promote vasoconstriction (to keep anesthetic agent in area longer). Do not use if epinephrine will complicate research study. Dilute with sterile water to final concentration of 5 mg/ml (0.5%) before use.

   Dose: Do not exceed 7 mg/kg

III. **Documentation of Analgesic Administration**

   Administration of post-operative analgesics must be documented. Federal regulators and inspectors consider a lack of documentation to mean analgesics were not provided and would classify that event as non-compliance. Please use the links below for more information about how to document analgesic administration.

   Post-Surgical Monitoring Records (Green Cards) are required for all survival surgery procedures. They may also be required for prolonged anesthesia exposure or other painful procedures as described in your approved IACUC protocol.

   1. [https://research.wustl.edu/green-card-instructions/](https://research.wustl.edu/green-card-instructions/).
   2. [https://research.wustl.edu/avery-green-sticker-templates/](https://research.wustl.edu/avery-green-sticker-templates/)