Rodent Anesthesia and Analgesia Guidelines

Introduction
The purpose of this guideline is to provide Principal Investigators with basic information to facilitate completion of Animal Care and Use Protocols. It is important that individuals be familiar with the normal biology and physiology of the species they propose to study. Additionally, it is critical that anesthetic and analgesic selection be made based upon individual familiarity with the agents, species specific sensitivity and response to agents and consideration of effects these agents may have on specific research models. The information contained in this guideline is intended to present:

- Basic methods used to monitor rodents during and after anesthesia and/or surgery.
- General dosing considerations and recommended routes of administration.
- Recommended anesthetic and analgesic agents for each species.
- Anesthetic agents, analgesic agents and basic biological parameters for each species.

The investigator is reminded that strain, stock, age and gender differences, as well as underlying medical/experimental conditions of the animals may alter individual response to anesthetic and analgesic agents. Therefore, the doses provided in the species charts are to be considered guidelines. When first investigating a new model, it may be necessary and advantageous to administer anesthetic doses starting at the low end of the acceptable range and increasing as needed. Additionally, because this guideline is not intended to be exhaustive, but rather provide a reference source for agents and doses in common use, there are anesthetic agents, doses and combinations which have not been included in this guideline. **Investigators are encouraged to contact an ARC veterinarian to discuss individual study needs.**

Injectable agents used for sedation, anesthesia, and analgesia with few exceptions are controlled substances, which are regulated by governmental drug enforcement agencies based on their medicinal applications versus their habit-forming potential. Use of these agents requires each PI to obtain a state and federal controlled substances license and arrange DEA-approved locked storage within their laboratories. The IACUC requires disclosure of the controlled substance(s) license holder for agents described for use in the animal care and use protocol. Examples of commonly used agents in rodents include, but are not limited to, Ketamine and Buprenorphine. For more information on controlled substances, please refer to the [Controlled Substance Policy](#).

Proper procedures for dilutions
Anesthetic and/or analgesic drugs transferred to another container for immediate use need to be labeled with drug contents and concentration. For storage of mixed or diluted drugs, date of expiration (i.e., the date of the drug which is expiring the earliest) must also be included. Sterile procedures and containers should be used for all cocktails and dilutions. Medications must only be stored in sterile multi-dose vials with an injection port on top, not in screw top containers.
Administration of Anesthesia

**General Anesthetic Considerations**

1) Accurately weighing every animal to be anesthetized and proper calculation of doses cannot be over-emphasized.

2) Rodents generally do not need to be fasted, or have water restriction preoperatively, unless there is scientific justification.

*Example*: The difference in accurate dosing between a 20 gram and a 30 gram mouse can equate to complications ranging from inadequate anesthesia or analgesia to anesthetic or analgesic overdose.

When dosing multiple animals with slightly different weights, having a chart prepared in advance listing weights in small increments and associated calculated doses and injection volumes for each agent to be administered can help facilitate dosing accuracy and safety for the animal.

Many drugs have to be diluted in order to administer accurate doses in rodent species. When calculating dilutions, it is important to consider the total volume that will be administered to the animal. Volumes less than 0.1 ml (100µl) are often too small for dosing accuracy and volumes greater than 0.5 ml (500µl) may be excessive for the size of the animal and/or route of administration.

**General Support**

While anesthetized, animals should be given supportive care. This includes, but is not limited to, the application of a sterile eye lubricant to negate dryness and the possibility of corneal damage while the animal is anesthetized. Animals should also be kept warm while under anesthesia as they will have a decrease in body temperature. Supplemental heat sources to counter hypothermia include slide warmers, chemical heat packs, warm water blankets, heat lamps and forced air heaters such as Bair Huggers. Another means of supportive care is the administration of sterile fluids subcutaneously. Warmed (not hot) saline or lactated ringers solution can be given at 2ml/100g during or immediately after surgery. When using injectable anesthetic combinations such as ketamine + xylazine, it is recommended to provide supplemental oxygen whenever possible to prevent hypoxia and reduce the likelihood of anesthetic-related death.

**Route of Drug Administration**

**General Anesthesia:**

*Injectable agents* are most often given by intraperitoneal (IP) or subcutaneous (SC) injection in rodent species.

*Intra-peritoneal (IP)* injection is a convenient route of administration for most properly restrained rodents.

*Subcutaneous (SC)* injections require minimal restraint and are associated with few injection site complications.

*Intramuscular (IM)* injections are discouraged in most rodent species due to their relatively small muscle mass. Intramuscular injections often result in localized inflammation, tissue necrosis, and/or neuropathies followed by self-trauma.
Intravenous (IV) injection of anesthetic agents is possible but technically challenging. Administration of anesthetics by the IV route is usually or commonly reserved to those studies which require vascular cannulation for reasons other than anesthesia alone.

<table>
<thead>
<tr>
<th></th>
<th>Subcutaneous</th>
<th>Intramuscular</th>
<th>IV (bolus)</th>
<th>IV (infusion)</th>
<th>Intraperitoneal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mouse</strong></td>
<td>5</td>
<td>Not recommended</td>
<td>5</td>
<td>25</td>
<td>5–10</td>
</tr>
<tr>
<td><strong>Rat/Hamster</strong></td>
<td>5</td>
<td>Not recommended</td>
<td>5</td>
<td>20</td>
<td>5–10</td>
</tr>
<tr>
<td><strong>Guinea Pig</strong></td>
<td>5</td>
<td>0.1 ml/site</td>
<td>1</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td><strong>Rabbit</strong></td>
<td>2.5</td>
<td>0.25</td>
<td>1–5</td>
<td>10</td>
<td>3–5</td>
</tr>
</tbody>
</table>

Gas anesthetics are administered by inhalation (IH) to desired effect. Induction of gas anesthesia for mice and rats is done in an induction chamber attached to a precision vaporizer anesthetic machine with proper scavenging system. Animals should be monitored closely and once unconscious moved out of the chamber for maintenance on a tightly-fit nose cone attached to the machine. The gas range should be from 0.5–5.0%, using medical grade 100% oxygen and must be maintained at a rate that will keep the animal at a surgical plane of anesthesia for the duration of the procedure. The range may also vary depending on the health status of the animal, and the use of other drugs, such as injectable anesthetics, and analgesics.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Type &amp; Common Uses</th>
<th>Mouse</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoflurane - Inhalant</td>
<td>General inhalant anesthetic useful for major and minor procedures</td>
<td>Induction: 0.5–4% Foundation; Maintenance: 2–3% Maintenance of effect</td>
<td>Induction: 0.5–4% Foundation; Maintenance: 2–3% Maintenance of effect</td>
</tr>
<tr>
<td>Ketamine + Xylazine</td>
<td>Anesthetic dosage for major procedures such as entry into a body cavity</td>
<td>90–120 mg/kg IP 5–10 mg/kg IP Redose at 30–60 minutes at 1/3 the original dose of Ketamine only</td>
<td>40–80 mg/kg IP 5–10 mg/kg IP Redose at 20–30 minutes at 1/3 the original dose of Ketamine only</td>
</tr>
<tr>
<td>Ketamine + Xylazine Surgical Procedures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketamine + Xylazine Non-surgical Sedation</td>
<td>Sedation dosage useful for brief, minor procedures such as blood draws</td>
<td>50–80 mg/kg IP 5–10 mg/kg IP</td>
<td>50–65 mg/kg IP 5 mg/kg IP</td>
</tr>
<tr>
<td>Yohimbine*</td>
<td>Reversal agent for xylazine</td>
<td>0.5–1 mg/kg IV</td>
<td>0.5–1 mg/kg IV</td>
</tr>
<tr>
<td>Atipamezole*</td>
<td>Reversal agent for xylazine, medetomidine or dexmedetomidine</td>
<td>1 mg/kg SC, IP, IV</td>
<td>1 mg/kg SC, IP, IV</td>
</tr>
</tbody>
</table>
*Please note that both Yohimbine and Atipamezole are both effective reversal agents; however, Atipamezole has a faster onset of action. Reversal agent dosing volume should be calculated ahead of time in case of emergency use. When reversing animals due to an anesthetic emergency (ie respiratory depression, apnea), ensure that the animal is surgically stable (ie body cavities are closed and no hemorrhage is present) before administering reversal.

**Recommended Anesthetic Agents and Sedatives for Other Rodents**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Type &amp; Common Uses</th>
<th>Guinea Pig</th>
<th>Hamster</th>
<th>Gerbil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoflurane - Inhalant</td>
<td>General inhalant anesthetic useful for major and minor procedures</td>
<td>2–5% Inhalation to effect</td>
<td>1–4% Inhalation to effect</td>
<td>1–4% Inhalation to effect</td>
</tr>
<tr>
<td>Ketamine + Xylazine</td>
<td>Anesthetic dosage for major procedures such as entry into a body cavity</td>
<td>20–40mg/kg IM 3–5 mg/kg IM Redose at 1/3 the original dose of Ketamine only</td>
<td>50–150 mg/kg IP 5–10 mg/kg IP Redose at 1/3 the original dose of Ketamine only</td>
<td>50–70mg/kg IP 2–3 mg/kg IP Redose at 1/3 the original dose of Ketamine only</td>
</tr>
<tr>
<td>Surgical Procedures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yohimbine*</td>
<td>Reversal agent for xylazine</td>
<td>0.5–1 mg/kg IV</td>
<td>0.5–1 mg/kg IV</td>
<td>0.5–1 mg/kg IV</td>
</tr>
<tr>
<td>Atipamezole*</td>
<td>Reversal agent for xylazine, medetomidine or dexmedetomidine</td>
<td>0.5–1 mg/kg IV</td>
<td>0.5–1 mg/kg IV</td>
<td>0.5–1 mg/kg IV</td>
</tr>
</tbody>
</table>

*Please note that both Yohimbine and Atipamezole are both effective reversal agents; however, Atipamezole has a faster onset of action. Reversal agent dosing volume should be calculated ahead of time in case of emergency use. When reversing animals due to an anesthetic emergency (ie respiratory depression, apnea), ensure that the animal is surgically stable (ie body cavities are closed and no hemorrhage is present) before administering reversal.

**Other Anesthetic and Sedation Choices for Mice and Rats (please contact a vet)**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Type &amp; Common Uses</th>
<th>Mouse</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketamine + Xylazine +</td>
<td>Anesthetic combination for major procedures such as entry into a body cavity. Acepromazine can provide a smoother induction and reduce the amount of anesthetic required.</td>
<td>65–85 mg/kg IP 10–13 mg/kg IP 2–5 mg/kg IP</td>
<td>60–80 mg/kg IP 5–10 mg/kg IP 2.3–2.5 mg/kg IP</td>
</tr>
<tr>
<td>Acepromazine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketamine + Medetomidine</td>
<td>Anesthetic dosage for major procedures such as entry into a body cavity, medetomidine is a more specific alpha-2 agonist than xylazine</td>
<td>65–80 mg/kg IP 1 mg/kg IP</td>
<td>60–80 mg/kg IP 0.5 mg/kg IP</td>
</tr>
<tr>
<td>Agent</td>
<td>Type &amp; Common Uses</td>
<td>Guinea Pig</td>
<td>Hamster</td>
</tr>
<tr>
<td>----------------------------</td>
<td>-------------------------------------------------------------------------------------</td>
<td>------------</td>
<td>---------</td>
</tr>
<tr>
<td>Ketamine + Xylazine + Acepromazine</td>
<td>Anesthetic combination for major procedures such as entry into a body cavity. Acepromazine can provide a smoother induction and reduce the amount of anesthetic required</td>
<td>22–64 mg/kg IM 2–5 mg/kg IM 0.75 mg/kg IM</td>
<td>NA</td>
</tr>
<tr>
<td>Ketamine + Diazepam Sedation</td>
<td>Sedation dosage useful for brief, minor procedures such as blood draws</td>
<td>20–50 mg/kg IP, IV 3–5 mg/kg IP, IV</td>
<td>40–100 mg/kg IP 2–5 mg/kg IP</td>
</tr>
<tr>
<td>Pentobarbital</td>
<td>Oxybarbiturate with a very narrow margin of safety that can be used for surgical anesthesia – use with caution</td>
<td>37 mg/kg IV</td>
<td>70–90 mg/kg IP</td>
</tr>
</tbody>
</table>

### Animal Monitoring

**General Monitoring Considerations**

Sophistication of anesthesia monitoring will vary with procedures, species and available equipment. It is recommended to have at least one person present who is non-sterile to assist the sterile surgeon. Animals having minor procedures performed such as blood collection or injections may only require monitoring of respiratory rate, pattern and response to painful stimuli such as toe pinch. Animals having prolonged anesthesia may require the use of electronic monitoring devices such as heart rate monitors, electrocardiograms (ECG), pulse oximetry and body temperature monitoring. It is important to continually monitor the animal being manipulated.

**Anesthesia Monitoring Parameters**

Toe pinch is used to assess perception of pain in an anesthetized rodent. If the toe or distal paw has pressure applied using a digital pinching action, withdrawal of the limb or overt movement of the animal signals response to stimulus and pain. This test is often used during anesthesia induction to determine when an animal has achieved an adequate level of anesthesia to begin a painful procedure. This test is used intermittently during anesthesia to assess continued depth of anesthesia and lack of response to painful stimuli. **If after having lost the toe pinch response, the animal begins to regain it, or**
shows other signs of movement this is an indication that additional anesthetic doses may need to be administered.

Heart rate (HR) is difficult to assess accurately in most rodent species due to their rapid heart rates. If electrocardiography or pulse oximetry is being used, measurement of heart rate may be possible and trends can be observed over the anesthetic interval. Increases in heart rate may indicate pain perception and the need for additional anesthesia. Conversely, if heart rate decreases, this may be an indication that the animal is reaching a deeper plane of anesthesia and additional anesthetic is not needed or that too much has been administered.

Respiratory rate (RR) is one of the simplest and most effective methods of monitoring anesthetic depth in rodents. Respiratory rate can be measured by counting the number of breaths over 15 seconds and multiplying by 4 to provide a rate of breaths per minute. The normal respiratory rate for mice anesthetized with isoflurane is 60-100 breaths/ min, and the normal respiratory rate for mice anesthetized with injectable anesthetics such as ketamine + xylazine is 150-200 breaths/ min. Trends in respiratory rate and character can be judged over time to help assess anesthetic depth. Increases in respiratory rate and shallow breaths may indicate that an animal is responding to manipulations being performed and may need additional anesthetic. Alternately, if respiratory rate decreases or the animal demonstrates exaggerated respiratory effort, this may be an indication that the animal is reaching a deeper plane of anesthesia and additional anesthetic is not needed. Translucent draping material is recommended so that respiratory rate and effort may be easily observed throughout the anesthetic event.

Temperature monitoring during anesthesia is important as decreases in body temperature (hypothermia) are commonly encountered when animals are anesthetized. Hypothermia enhances anesthetic effect such as respiratory and cardiovascular depression which can adversely affect recovery and survival from anesthesia. Whenever possible, temperatures should be monitored and supplemental/external heat sources provided. Rectal thermometers and probes allow for accurate measurement of body temperature. Supplemental heat sources to counter hypothermia include slide warmers, chemical heat packs, warm water blankets, infrared light heating pads, heat lamps and forced air heaters such as Bair Huggers. All of these have the potential to cause thermal burns, and there should be a barrier such as a disposable absorbent pad between the heat source and the animal. Commercial heating pads are discouraged because of their increased risk for thermal burns compared to the other sources. Close temperature monitoring is required to prevent overheating of the unconscious animal.

Post Procedural Monitoring
All animals must be monitored continuously until they have regained their righting reflex (sternal recumbency) and ability to safely move around in their cage.
- Failure to stimulate anesthetized animals until they regain consciousness may lead to gradual decreases in respiration resulting in gradual oxygen deficiency which could ultimately lead to cardiac failure and death.
- Animals should be provided heat support during the recovery period. This can be accomplished by placing the recovery cage partway on the slide warmer to provide a gradient of heat. Animals which are pair or group housed should receive particular attention during the post-anesthesia recovery phase as individuals may recover at varying rates. Animals recovering sooner than others may harm those still in the recovery stage.
- Following surgery animals should be monitored for pain and surgical complications on a regular basis.

Physiologic Parameters of Awake Mice and Rats
Parameter | Mouse | Rat
--- | --- | ---
**Adult Body Weight** | 20–40g | 250–520g
**Body Temperature** | 36.5–38°C/97.7–100.4°F | 35.69–37.5°C/96.6–99.5°F
**Heart Rate** | 400–600 beats per minute | 250–450 beats per minute
**Respiratory Rate** | 100–220 breaths per min | 70–115 breaths per minute

*Please note that all parameters are approximate and may vary based on the animal’s health status and genetic background*

### Physiologic Parameters of Other Rodents

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Guinea Pig</th>
<th>Hamster</th>
<th>Gerbil</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adult Body Weight</strong></td>
<td>700–1200g</td>
<td>85–150g</td>
<td>55–100g</td>
</tr>
<tr>
<td><strong>Body Temperature</strong></td>
<td>37.2–39.5°C/99–103.1°F</td>
<td>37–38°C/98.6–100.4°F</td>
<td>37–38.5°C/98.6–101.3°F</td>
</tr>
<tr>
<td><strong>Heart Rate</strong></td>
<td>230–380 beats per minute</td>
<td>250–500 beats per minute</td>
<td>360 beats per minute</td>
</tr>
<tr>
<td><strong>Respiratory Rate</strong></td>
<td>40–130 breaths per minute</td>
<td>35–135 breaths per minute</td>
<td>90 breaths per minute</td>
</tr>
</tbody>
</table>

*Please note that all parameters are approximate and may vary based on the animal’s health status and genetic background*

### Analgesia

#### General Considerations

- Procedures which are expected to cause only momentary pain or distress (e.g. blood collection, injections) may not require administration of analgesic agents.
- Any procedure expected to cause pain or distress in a human must also be considered to cause pain or distress in laboratory animals.
- Analgesics should be administered prior to a painful procedure.
- Local anesthetics may be used to prevent or alleviate pain in conjunction with general anesthesia and/or analgesics.

**Scientific justification must be provided and approved in the protocol if analgesia must be withheld from animals undergoing painful procedures.**

#### Analgesic Classes

**Non-Steroidal Anti-Inflammatory Drugs**

Generally, the NSAID classification applies to drugs that inhibit one or more steps in the metabolism of arachidonic acid (AA). NSAIDs act primarily to reduce the biosynthesis of prostaglandins by inhibiting cyclooxygenase (COX). NSAIDs are effective for pain associated with inflammation. On their own, NSAIDs are effective against pain of mild to moderate intensity. Potential side effects include gastric or intestinal ulceration, disturbance of platelet function, and changes in renal function.

**Opioids**

Opioids exert their effects on the opiate receptors in the central nervous system. Opioids are effective for acute, deep, or visceral pain. The most commonly used opioid in laboratory animal medicine is...
buprenorphine, which manages mild to moderate pain. Potential side effects include respiratory depression, nausea, vomiting, pica (rats), and constipation. All opiates are controlled substances, and their use requires special record keeping.

*Local Anesthesia*
Local anesthetics block passage of sensory nerve impulses responsible for the generation and conduction of pain perception. When used superficially, they block sensory nerve endings and pain associated with local, superficial, painful procedures. When used to infiltrate nerve trunks, the effect is regional blockage of pain perception and propagation. Bupivacaine (Marcaine) is a local anesthetic with a relatively long duration of effect, approximately 6–8 hours. Because of this long duration of effect, bupivacaine is often used in rodent species both for its local anesthetic effect and also as a local analgesic based on its duration of effect. It supplements, but does not replace a systemic analgesic.

Ideally, local anesthetics are injected using a small gauge needle (25–30 gauge). The needle is injected up to the hub, following the line of the surgical site. The drug is slowly administered as the needle is pulled out. They may also be applied by “splash” block, where the solution is put in the open surgical site. The proper calculated dose of the drug must be used in both methods.

*Analgesic Administration*
Animals subjected to procedures that are expected to produce mild to moderate pain will typically benefit from preemptive analgesic agents (e.g. local anesthetic + NSAID + opioid) plus 48 hours post-operative analgesia (NSAID or opioid). Multi-modal analgesic regimens such as these combinations are the most efficacious for pain management. Frequency of administration should be based upon anticipated pain response to a procedure, duration of effect of the analgesic being administered and ongoing monitoring of the animal for signs of pain. Standardized analgesic regimens for typical surgical procedures are listed below:

- **For skin incision**: one dose meloxicam or buprenorphine preemptive
- **For craniotomy**: one dose meloxicam AND buprenorphine preemptive
- **For soft tissue removal**:
  - One dose meloxicam preemptive OR
  - One dose buprenorphine preemptive and one additional dose 8–12 hours later
- **For laparotomy**:
  - One dose meloxicam AND buprenorphine preemptive and one additional dose of meloxicam 24 hours later OR
  - One dose meloxicam AND buprenorphine preemptive and three additional doses of buprenorphine at 8–12 hour intervals OR
  - One dose meloxicam AND Ethiqa XR® preemptive
- **For orthopedic procedure and thoracotomy**:
  - One dose meloxicam AND buprenorphine preemptive and five additional doses of buprenorphine at 8–12 hour intervals AND two additional doses of meloxicam at 24 hour intervals OR
  - One dose meloxicam AND Ethiqa XR® preemptive and two additional doses of meloxicam at 24 hour intervals

Note: Please make sure the frequency of dosing is based on when the pre-emptive dose is administered and not when the surgical procedure ends. This is especially important for lengthy surgical procedures.
**Monitoring Animals for Signs of Pain**

Efficacious analgesia may decrease morbidity and reduce mortality following surgical manipulations and poor pain management can potentially invalidate research results, as uncontrolled pain may initiate a stress response, resulting in hormonal, metabolic and physiologic imbalances. **Animals must be monitored at a frequency which will allow for observation of signs of pain as the analgesic is wearing off and at intervals appropriate for re-dosing of analgesic drugs as indicated.** Drugs may be redosed anytime within the drug’s time range of effectiveness.

**Example:** An analgesic with expected duration of effect of 12 hours is administered at 10:00 a.m., at the start of anesthesia. Evaluation of the animal for pain should not be longer than 12 hours later, which is the maximum time of expected analgesic effect. The animal could be evaluated prior to 10:00 p.m. and given additional doses of analgesic if determined to be needed, or for reasons of practicality, the animal could receive a second dose of analgesic at 7:00 p.m. (9 hours following the initial dose) and then be re-assessed at 7:00 a.m. to evaluate the need for additional analgesic doses. The animal may then be monitored at 12 hour intervals until need for further analgesia has passed.

**Rodent manifestations of pain** are most commonly observed as hunched posture, lack of grooming/nest building, excessive grooming of incision sites, lethargy (lack of rearing up on hind limbs, lack of climbing on wire bars), and animals not being observed to eat or drink. It should be kept in mind that rodents are prey species and tend to hide signs of pain or distress. A minimum number of redoses should be outlined in your protocol beforehand, based on the level of pain the surgery is expected to cause to prevent this problem. Familiarity with overt signs of pain unique to each species is important to ensure that pain assessment is adequately evaluated and interpreted.

### Recommended Analgesic Agents for Mice and Rats

<table>
<thead>
<tr>
<th>Agent</th>
<th>Type &amp; Common Uses</th>
<th>Mouse</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>mu-agonist-antagonist narcotic good for moderate to severe pain</td>
<td>0.1–0.2 mg/kg SC every 8–12 hrs</td>
<td>0.03–0.05 mg/kg SC every 8–12 hrs</td>
</tr>
<tr>
<td>Ethiq XR®</td>
<td>Extended release Buprenorphine that provides 72 hrs of pain relief</td>
<td>3.25 mg/kg SC every 72 hrs</td>
<td>0.65 mg/kg SC every 72 hrs</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>NSAID useful for mild pain or use with an opioid for major pain management</td>
<td>5-10 mg/kg SC every 24 hrs</td>
<td>1 mg/kg SC every 24 hrs</td>
</tr>
</tbody>
</table>

### Other Analgesic Choices for Mice and Rats (please contact a vet)

<table>
<thead>
<tr>
<th>Agent</th>
<th>Type &amp; Common Uses</th>
<th>Mouse</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketoprofen</td>
<td>NSAID useful for mild pain or for use with an opioid for major pain management</td>
<td>20 mg/kg SC every 24 hrs</td>
<td>5 mg/kg SC every 24 hrs</td>
</tr>
<tr>
<td>Carprofen</td>
<td>NSAID useful for mild pain or for use with an opioid for major pain management</td>
<td>20 mg/kg SC every 24 hrs</td>
<td>5 mg/kg SC every 24 hrs</td>
</tr>
</tbody>
</table>
### Bupivacaine

Long-acting local anesthetic that can be combined with opioids to reduce pain in minor and major procedures.

| Max dose: 1.0–2.0 mg/kg (less than 100ul of 0.25% solution) |
| Max dose: 1.0–2.0 mg/kg (less than 240ul of 0.25% solution) |

### Recommended Analgesic Choices for Other Rodents

<table>
<thead>
<tr>
<th>Agent</th>
<th>Type &amp; Common Uses</th>
<th>Guinea Pig</th>
<th>Hamster</th>
<th>Gerbil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>mu-agonist- antagonist narcotic good for moderate to severe pain</td>
<td>0.05–0.5 mg/kg SC every 6–12 hrs</td>
<td>0.1 mg/kg SC every 6–12 hrs</td>
<td>0.1 mg/kg SC every 6–12 hrs</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>Injectable NSAID useful for mild pain or for use with an opioid for major pain</td>
<td>1 mg/kg SC, IM every 24 hrs</td>
<td>5 mg/kg SC every 12 hrs</td>
<td>5 mg/kg SC every 12 hrs</td>
</tr>
</tbody>
</table>

### Other Analgesic Choices for Other Rodents (please contact a vet)

<table>
<thead>
<tr>
<th>Agent</th>
<th>Type &amp; Common Uses</th>
<th>Guinea Pig</th>
<th>Hamster</th>
<th>Gerbil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carprofen</td>
<td>NSAID useful for mild pain or for use with an opioid for major pain management</td>
<td>4 mg/kg PO, SC every 12–24 hrs</td>
<td>5 mg/kg SC every 12 hrs</td>
<td>5 mg/kg SC every 12 hrs</td>
</tr>
</tbody>
</table>

### Neonatal Rodent Anesthesia and Analgesia

**General Considerations:**

- The neonatal rodent is especially predisposed to developing side effects associated with traditional injectable anesthetics. The most commonly reported complications are hypotension, bradycardia, apnea, hypothermia, and hypoglycemia.
- Rodents are born with underdeveloped kidneys, liver, lungs, and hearts; all of these organs don’t finish development until weeks after the post-natal period.
- Intraoperative monitoring should be performed before, during, and after the anesthetic event. This may include toe pinching, observing for response to stimuli, checking for a righting reflex, and ensuring the pup is pink.
  - A source of warmth (40°C) must be provided for pups undergoing inhalant and injectable anesthesia.
  - 100% flow-by oxygen should be delivered to the pup before surgery and for the delivery of inhalant anesthetics.
  - The pup should be returned to the dam as soon as it has fully recovered as they are unable to adequately combat hypoglycemia and hypothermia by themselves.

Because of these complications and the rapid post-natal development and growth that occurs, the appropriate anesthetic protocol must be selected for the right procedure and neonate age. Below are recommendations for anesthetic protocols and their indications. For all other inquiries that are not addressed in this document, please contact a veterinarian.
1. **Inhalant Anesthesia (Isoflurane):** The use of inhalant anesthesia should be performed in a ducted biosafety cabinet that can remove waste gas. A down-draft table can also be used.
   a. **Age/ Indication:** Neonates from 0-21 days of age, and for more invasive surgical procedures.
   b. **Method:** Neonates have lower requirements for oxygen and therefore require larger doses of inhalant anesthetics to achieve a surgical plane of anesthesia. The higher doses of inhalant anesthetics must be delivered at a lower flow rate of oxygen to account for the smaller lung volume and longer expiratory time that neonates have.
      i. **Induction:** 3-5% per 1-2 L/min oxygen
      ii. **Maintenance:** 1.5-4.5% per 1-2 L/min oxygen

2. **Cryoanesthesia**
   a. **Age/ Indication:** Neonates 0-7 days of age, and for minimally invasive surgical procedures lasting 10 minutes or less.
   b. **Method:** Direct contact of neonate skin/ tissues with crushed ice can lead to significant damage. Always ensure that there is no direct contact with the ice.
      i. Prepare a container of crushed ice.
      ii. Place the neonate on a section of cut latex glove or an opened plastic tube. Ensure that the crushed ice comes up to the level of the neck and that the neonate is able to breathe ambient air.
      iii. Anesthetic induction takes 5-10 minutes, and the surgical plane lasts for only about 10 minutes. The surgical plane can be extended by placing the animal on an ice pack, with a drape or towel to prevent direct contact to the neonate’s skin.
      iv. Recover the animal in an incubator set at 33°C or a warm heating pad (40°C) until movement and toe-pinch response has returned. Temperatures higher than 40°C may result in rapid re-heating and consequent tissue damage.

3. **Injectable anesthetics:** Injectable anesthesia is unpredictable and it may result in a high mortality among patients. Please see a veterinarian prior to selecting this method of anesthesia.
   a. **Age/ Indication:** Neonates older than 7 days of age. For minimally invasive procedures lasting 20-30 minutes. Because of the unreliable response to medications, frequent intraoperative monitoring of the anesthetic plane is warranted (ex: toe pinching, response to stimuli, examining skin color).
   b. **Method:**
      i. Maximum volume: The maximum volume of medication to be prescribed to a pup will depend on the pup’s weight. The following recommendations are based off our “Injections and Gavage” Guidelines.
         1. Max. Volume for subcutaneous injections: 5ml/kg or 5ul/g
         2. Max. Volume for intraperitoneal injections: 5-10ml/kg or 5-10ul/g

<table>
<thead>
<tr>
<th>Agents</th>
<th>Mouse</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medetomidine, Midazolam, Butorphanol</td>
<td>(0.3mg/kg) + (4mg/kg) + (5mg/kg), IP or SC</td>
<td>(0.3mg/kg) + (4mg/kg) + (5mg/kg), IP or SC</td>
</tr>
<tr>
<td>Medetomidine, Midazolam, Fentanyl</td>
<td>(0.5 mg/kg) + (5mg/kg) + (0.05mg/kg), SC</td>
<td>This protocol has safely been studied only with an atipamezole-flumazenil-naloxone reversal administered SC. Please note: Efficacy has not been demonstrated.</td>
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</tbody>
</table>
Post-Anesthesia Monitoring & Care: Whenever possible, neonates should recover after surgery with their littermates, to provide companionship and warmth in groups, and they should be reintroduced to the dam as soon as they have recovered. Aside from providing warmth, measures should be taken to prevent dam rejection and/ or cannibalism. Cannibalism of pups can be triggered by stress, unusual or foreign scents on pups, and any pups displaying signs of morbidity. To reduce the likelihood of the dam cannibalizing her pups, the following steps can be taken:

- Recover pups in an area with "used" bedding from the home cage to mask smells from procedure. A fecal bath can be created for pups less than two days old.
  - Fecal Bath Method: Collect feces from the home cage and place in a disposable container. Add tap-water to create a "slurry" like consistency. Warm the fecal bath to 33-40°C. Clean the pups off after surgery (to remove the smell of medications or disinfectants). Gently coat the pups with a fecal bath using a cotton swab and avoid the surgical site.

- Do not place recovering or overly sick pups back in the cage with the dam.
  - Pups that do not recover after anesthesia in the anticipated period of time should be euthanized.

- Attempt to minimize stress in the dam
  - The dam should remain in the home cage, with her litter, while pups are being anesthetized. If multiple pups from the same litter will be anesthetized at the same time, please refrain from removing all the pups at once. Remove the pups, anesthetize them, and recover them in smaller groups. Remember to return pups to the dam once they have fully recovered.
  - Whenever possible, the dam should be placed somewhere with minimal vibrations and investigator activity.
  - Handling and olfactory conditioning of the dam 7-10 days prior to birthing may help reduce stress during the pups’ procedure. This can be accomplished with gentle handling at 5-minute intervals 2-3 times a day.
  - Please seek a veterinarian should you pursue procedures involving more than one separation from the dam within 24 hours.

- Post-operatively, the pups should be monitored at least twice a day to identify rejection of the pups early on. Seeing a pup outside of the nest is a strong indicator of rejection. In the event the dam rejects the litter, a foster mother can be provided.

References for Neonatal Anesthesia and Analgesia

