

Recommended Rodent Anesthetics and Analgesics

Note: Doses provided are approximations and must be titrated to the animal’s strain, age, sex, individual responses, and use of other concurrently administered drugs. Significant departures from these doses should be discussed with a CMRU veterinarian.

All doses are listed as milligrams per kilogram (mg/kg) unless otherwise noted. Dilution of injected drugs allows more precise dosing, but dilution must be performed using pharmaceutical grade diluents in sterile, diaphragmed ([example](#)) bottles. Please see IACUC Policy Use and Labelling of Drug Compounds, Dilutions, and Chronic-Use Fluids. Note: PBS is not considered a pharmaceutical grade diluent. Exceptions to recommendations may be study specific and must be described and justified. All drugs must be approved in a UofL IACUC *Proposal* prior to use.

Multimodal analgesia is recommended by CMRU veterinarians and is standard practice. Multimodal analgesia is defined as the use of a combination of analgesic drugs from different classes, typically one NSAID and one opioid, and/or local anesthesia in lieu of an NSAID or opioid if one of those classes of drugs would interfere with the study. Multimodal analgesia may allow for reduced dosages of these drugs, as well as minimize potential adverse effects of the analgesics. For further information, please see [IACUC Policy Use of Postoperative Analgesia](#).

Anesthetic and Analgesic agents have been associated with nausea in a small subset of all mammalian species including rodents^{2,24,30}. Common signs of nausea in rodents include a facial grimace²³, excessive self-licking/gnawing of forepaws³⁰, and pica behavior^{2,24}. Onset of behavior can occur for up to 3 days post administration. If symptoms of nausea are noticed, please contact a CMRU veterinarian for treatment options.

Please note that recent literature^{3,18,21} has shown that oxygen supplementation is required to prevent hypoxia in anesthetized rodents. CMRU veterinarians *recommend* supplemental oxygen to all anesthetized rodents unless oxygenation status is being monitored (ie. pulse oximeter) with oxygen supplementation being administered as needed.

Abbreviations:

IM = intramuscularly	IP = intraperitoneally	PO = <i>per os</i> (by mouth)
SC = subcutaneously	h = hour(s)	q = every

Anesthetics:

Drug Name	Dose (mg/kg) & Route	Frequency	Notes
<i>Inhalation anesthetics</i>			
Isoflurane	Up to 5% for induction; 1-3% (to effect for maintenance)	Duration of anesthetic period	<i>Highly recommended</i> ; survival surgery should have concurrent pre-emptive analgesia; precision vaporizer usually required.
<i>Ketamine Combinations for Injection</i>			
Ketamine - Dexmedetomidine	<i>Mouse:</i> 50-100mg/kg + 0.5-1.0mg/kg IP <i>Rat:</i> 75-100mg/kg + 0.5-1.0mg/kg IP	As needed; expected duration 30-45 minutes	May be mixed in the same syringe; if re-dosing, use 1/4-1/2 dose of ketamine alone; dexmedetomidine may be partially reversed with <i>atipamezole</i> . Survival surgery should have concurrent pre-emptive analgesia.

Ketamine - Xylazine	<i>Mouse:</i> 80-100mg/kg + 5-10mg/kg IP <i>Rat:</i> 75-100mg/kg + 5-10mg/kg IP	As needed; expected duration 30-45 minutes	May be mixed in the same syringe; if re-dosing, use 1/4-1/2 dose of ketamine alone; xylazine may be partially reversed with <i>atipamezole</i> . Survival surgery should have concurrent pre-emptive analgesia.
Ketamine – Xylazine - Acepromazine	<i>Mouse:</i> 70-100mg/kg + 5-10mg/kg + 2-3mg/kg IP <i>Rat:</i> 75-100mg/kg + 2-6mg/kg + 1-2mg/kg IP	As needed; expected duration 30-45 minutes	May be mixed in the same syringe; if re-dosing, use 1/4-1/2 dose of ketamine alone; xylazine may be partially reversed with <i>atipamezole</i> . Survival surgery should have concurrent pre-emptive analgesia.

<i>Reversal agents</i>			
Atipamezole	<i>Mouse or Rat:</i> 0.5-1.0mg/kg SC or IP	Once	Most specific for <i>dexmedetomidine</i> , but may also be used for <i>xylazine</i> .

<i>Other injectable anesthetics</i>			
Pentobarbital (Nembutal®)	<i>Mouse or Rat:</i> 40-50mg/kg IP	As needed; expected duration 20-40 minutes	Recommended for terminal/acute procedures only, with booster doses as needed, although may occasionally be appropriate for survival procedures; consider supplemental analgesia (opioid or NSAID) for invasive procedures, especially when used for survival surgery.

Analgesics:

<i>Opioids</i>			
EthiqaxR (buprenorphine extended-release)	<i>Mouse:</i> 3.25mg/kg SC <i>Rat:</i> 0.65mg/kg SC	q72h Recommend administration prior to surgery	<i>Strongly recommended;</i> EthiqaxR is an FDA-approved extended release buprenorphine and is similar to buprenorphine except will not need to be redosed unless needed for >72h. More information can be found at www.ethiqaxr.com
Buprenorphine SR**	<i>Mouse:</i> 0.5-1mg/kg SC <i>Rat:</i> 1-1.2mg/kg SC	q48h Recommend administration prior to surgery	<i>Highly recommended;</i> **sustained release buprenorphine (ZooPharm – Bruprenorphine SR-LAB) is similar to buprenorphine except will not need to be redosed unless needed for >48h.† Buprenorphine SR-LAB: Dosing from the same bottle may be extended to 6 months, which is extra-label use. ³⁰ Please contact CMRU veterinarian for specific information about ordering/storing Buprenorphine SR if unfamiliar.
Buprenorphine HCl	<i>Mouse:</i> 0.1-0.5mg/kg SC <i>Rat:</i> 0.05-0.1mg/kg SC or IP	q4-8h Recommend first dose prior to surgery.	Recent literature shows that this drug requires more frequent dosing than 12-hour intervals† consider multi-modal analgesia with an NSAID or administration of sustained-release buprenorphine; high doses of buprenorphine may lead to pica and sedation in rats.

† Buprenorphine has been shown to provide variable/inconsistent analgesia for rodents. Regular buprenorphine in mice may only last 4 to 6 hours^{9,15,16,17,18}. Buprenorphine SR may only provide adequate analgesia in mice for as little as 12 hours⁹ and up to 48 hours in other instances^{17,18}. Buprenorphine SR in rats

has been determined to be effective for 48 hours²⁴ up to 72 hours⁶. Because of the varying clinical efficacies, it is recommended that frequent cageside observation of body posture, activity level, appetite, overall appearance, and scoring of facial grimace be employed as practical methods for assessing adequate analgesia in rodents. Rodents may need to be observed more often than once daily depending on the analgesic regimen used, procedure performed, and the potential for breakthrough pain.

<i>Non-Steroidal Anti-Inflammatory Drugs (NSAID)</i>			
Carprofen	<i>Mouse: 10-20mg/kg SC</i> <i>Rat: 5mg/kg SC</i>	q24h mice q24h rats Recommend first dose prior to surgery.	<i>Highly recommended;</i> depending on the procedure, may be used as sole analgesic, or as part of a multimodal analgesic plan.
Meloxicam	<i>Mouse: 10-20mg/kg SC</i> <i>Rat: 1-5mg/kg SC</i>	q24h mice q24h rats Recommend first dose prior to surgery.	<i>Highly recommended;</i> depending on the procedure, may be used as sole analgesic, or as part of a multimodal analgesic plan.

Note: Carprofen or Meloxicam doses must not exceed a cumulative daily dose of 20 mg/kg. Prolonged use of NSAIDs may be associated with renal, gastrointestinal, or other adverse effects. It is recommended to administer NSAIDs with additional sterile saline or physiologic fluids to aid in proper hydration and to reduce adverse effects.

<i>Local anesthetic/analgesics</i>			
Bupivacaine liposome injectable suspension§	<i>Mouse and Rat: Dilute appropriately, do not exceed 5.3mg/kg total dose, SC or intra-incisional</i>	Once for 72h duration of action	<i>Highly recommended;</i> § NOCITA (bupivacaine liposome injectable suspension) is similar to bupivacaine with the exception of 72h duration of action. Dosing from the same bottle may be extended to 4 days, which is extra-label use ⁴ . Please contact a CMRU veterinarian for specific information about ordering/storing/administering NOCITA if unfamiliar.
Lidocaine hydrochloride	<i>Mouse and Rat: Dilute appropriately do not exceed 10 mg/kg total dose, SC or intra-incisional</i>	Use locally before making surgical incision	Faster onset than bupivacaine but short (<1 hour) duration of action
Bupivacaine or Ropivacaine	<i>Mouse and Rat: Dilute appropriately, do not exceed 3 mg/kg total dose, SC or intra-incisional</i>	Use locally before making surgical incision	Slower onset than lidocaine but longer (~4-8 hour) duration of action

Recommended analgesia/post procedure plans:

<i>Procedure Type:</i>	<i>Non-painful procedure</i>	<i>Minor surgery/procedure</i>	<i>Major surgery/procedure</i>
Examples:	Imaging (ultrasound, CT, MRI, etc)	Surgical catheter placement, SC minipump placement, SC surgical tumor placement, minor skin incisions, intratracheal injections	Laparotomy, thoracotomy, procedures involving bone, craniotomy or cranial implant

Recommended analgesia	No analgesic recommended	Local anesthetic (if applicable), one NSAID and/or Opioid	Local anesthetic (if applicable), one NSAID and Opioid
Duration of analgesia recommended	N/A	48h	48-72h
Monitoring frequency recommended	N/A	Once daily	Twice daily
Other:	Provide supplemental heat. SC or IP fluids if warranted (prolonged anesthetic event; >1h)	Provide supplemental heat. SC or IP fluids, cage alteration (food on floor, gel diet) if warranted	Provide supplemental heat. SC or IP fluids, cage alteration (food on floor, gel diet) and frequent checking when possible.

References:

1. Alamaw ED, Franco BD, Jampachaisri K, Huss MK, Pacharinsak C. 2022. Extended-release buprenorphine, an FDA-indexed analgesic, attenuates mechanical hypersensitivity in rats (*Rattus norvegicus*). *J Am Assoc Lab Anim Sci* PMID: PMC8786384
2. Batra VR, Schrott LM. 2011. Acute oxycodone induces the pro-emetic pica response in rats. *J Pharm and Exp Therp* 339:738-45
3. Blevins CE, Celest NA, Marx JO. 2021. Effects of oxygen supplementation on injectable and inhalant anesthesia in C57BL/6 mice. *J Am Assoc Lab Anim Sci* 60: 289-297.
4. Cantara S, Gergye C, Lee V, Huerkamp M. Sterility of sustained-release buprenorphine. *J Am Assoc Lab Animal Sci.* 61(2): 208-210. Carlson AR, Nixon E, Jacob ME. 2020. Sterility and concentration of liposomal bupivacaine single-use vial when used in a multiple-dose manner. *Vet Surg* 49:772-777.
5. Carpenter, James Wyman, and Christopher J. Marion. *Exotic Animal Formulary*. Elsevier, 2013.
6. Chum HH, Jampachaisri K, McKeon GP, Yeomans DC, Pacharinasak C, Felt SA. 2014. Antinociceptive effects of sustained-release buprenorphine in a model of incisional pain in rats (*Rattus norvegicus*). *J Am Assoc Lab Anim Sci* 53:193-197.
7. Clark TS, Clark DD, Hoyt RF. 2014. Pharmacokinetic Comparison of Sustained-Release and Standard Buprenorphine in Mice. *J Am Assoc Lab Anim Sci.* 53(4): 387-391.
8. Durst MS, Arras M, Palme R, Talbot SR, Jirkof P. 2021. Lidocaine and bupivacaine as part of multimodal pain management in a aC57BL/6J laparotomy mouse model. *Sci Rep* 11, 10918.
9. Flecknell PA. 2009. *Laboratory animal anesthesia*, 3rd ed. London (United Kingdom): Academic Press.
10. Fish RE, Brown MJ, Danneman PJ, Karass AZ. 1997. *Anesthesia and analgesia in laboratory animals*. 2nd ed. London (United Kingdom): Academic Press.
11. Foley PL, Kendall LV, Turner PV. 2019. Clinical management of pain in rodents. *Comp Med* 69: 468-489.
12. Fox JG, Anderson LC, Otto G, Pritchett-Corning KR, Whary MT. 2015. *Laboratory animal medicine*. 3rd ed. London (United Kingdom): Academic Press.
13. Fox JG, Barthold SW, Davisson MT, Newcomer CE, Quimby FW, Smith AL. 2007. *The mouse in biomedical research*. 2nd ed. London (United Kingdom): Academic Press.
14. Gades NM, Danneman PJ, Wixson SK, Tolley EA. 2000. The magnitude and duration of the analgesic effect of morphine, butorphanol, and buprenorphine in rats and mice. *Contemp Top Lab Anim Sci* 39:8-13.
15. Jirkof P, Tourvieille A, Cinelli P, Arras M. 2014. Buprenorphine for pain relief in mice: repeated injections vs sustained-release depot formulation. *Lab Anim* 49: 177-1
16. Kendall LV, Hansen RJ, Dorsey K, Kang S, Lunghofer PJ, Gustafson DL. 2014. Pharmacokinetics of sustained-release analgesics in mice. *J Am Assoc Lab Anim Sci* 53:478-484
17. Kendall LV, Wegenast DJ, Smith BJ, Dorsey KM, Kang S, Lee NY, Hess AM. 2016. Efficacy of Sustained-Release Buprenorphine in an Experimental Laparotomy Model in Female Mice. *J Am Assoc Lab Anim Sci.* 2016 Jan; 55(1): 66-7.
18. Kim J, Cannon BA, Freeman LE, Tan S, Knych HK, Kendall LV. 2023. High-dose Meloxicam Provides Improved

Analgesia in Female CD1 Mice: A Pharmacokinetic and Efficacy Study. *J Am Assoc Lab Anim Sci.* 62:74-80.
McKenna BA, Weaver HL, Kim J, Bowman MW, Knych HK, Kendall LV. 2023. A Pharmacokinetic and Analgesic Efficacy Study of Carprofen in Female CD1 Mice. *J Am Assoc Lab Anim Sci.* Online. DOI: 10.30802/AALAS-JAALAS-23-000041

19. Lee C, Jones TA. 2018. Effects of ketamine compared with urethane anesthesia on vestibular sensory evoked potentials and systemic physiology in mice. *J Am Assoc Lab Anim Sci* 57:268-277.
20. Levinson BL, Leary SL, Bassett BJ, Cook CJ, Gorman GS, Coward LU. 2021. Pharmacokinetic and histopathologic study of an extended release, injectable formulation of buprenorphine in Sprague-Dawley rats. *J Am Assoc Lab Anim Sci* 60: 462-469.
21. Matthews KA, Taylor DK. 2011. Assessment of sterility in fluid bags maintained for chronic use. *J Am Assoc Lab Anim Sci.* 50(5):708-12.
22. Mechelinck, M, Kupp C, Kruger JC, Habigt MA, Helmedag MJ, Olba RH, Rossaint R, Hein M. 2019. Oxygen inhalation improved postoperative survival in ketamine-xylazine anaesthetized rats: an observational study. *PlosOne* <https://doi.org/10.1371/journal.pone.0226430>
23. Nunamaker EA, Goldman JL, Adams CR, Fortman JD. 2018. Evaluation of Analgesic Efficacy of Meloxicam and 2 Formulations of Buprenorphine after Laparotomy in Female Sprague-Dawley Rats. *J Am Assoc Lab Anim Sci.* 57(5): 498-507.
24. Roughan JV, Bertrand HGMJ, Isles HM. 2016. Meloxicam prevents COX-2 mediated post-surgical inflammation but not pain following laparotomy in mice. *Eur J Pain* 20:231-240.
25. Sarbia-Estrada R, Cowman A, Tyler BM, Guarnieri M. 2017. Association of nausea with buprenorphine analgesia for rats. *Laboratory Animals* 46(6): 242-44
26. Seymour TL, Adams SC, Felt SA, Jampachaisri K, Yeomans DC, Pacharinsak C. 2016. Postoperative Analgesia Due to Sustained-Release Buprenorphine, Sustained-Release Meloxicam, and Carprofen Gel in a Model of Incisional Pain in Rats (*Rattus norvegicus*) *J Am Assoc Lab Anim Sci.* 2016 May; 55(3): 300-305
27. Shientag LG, Wheeler SM, Garlick DS, Maranda LS. 2012. A Therapeutic Dose of Ketoprofen Causes Acute Gastrointestinal Bleeding, Erosions, and Ulcers in Rats. *J Am Assoc Lab Anim Sci.* 51(6):832-841.
28. Simonek GD, Alarcio GG, Brignolo LL. 2017. Sterility and Stability of Diluted Carprofen in a Multidose Vial in the Laboratory Animal Setting. *J Am Assoc Lab Anim Sci.* 56(3):296-298.
29. Suckow MA, Weisbroth SH, Franklin CL. 2006. *The laboratory rat.* 2nd ed. London (United Kingdom): Academic Press.
30. Quesenberry, Katherine E., and James W. Carpenter. *Ferrets, Rabbits, and Rodents Clinical Medicine and Surgery.* Elsevier/Saunders, 2012.
31. Wright-Williams SL, Courade J, Richardson CA, Roughan JV, Flecknell PA. 2007. Effects of vasectomy surgery and meloxicam treatment on faecal corticosterone levels and behaviour in two strains of laboratory mouse. *Pain* 130:108-118.
32. Yamamoto K, Tatsutani S, Ishida T. 2017. Detection of nausea-like response in rats by monitoring facial expression. *Front Pharm.* 7. PMID: PMC5222820