

## Background

This guideline is designed to provide a single source of information for investigators that use rodents models of biomedical disease and discovery. The following tables reference contemporary literature and are a modification of a similar presentation of information in a recently updated chapter from [\*Anesthesia and Analgesia in Laboratory Animals\*](#) (Academic Press; Gaertner et al. 2008). Investigators are always strongly encouraged to consult with [ULAR](#) veterinarians in the design of their animal research projects, including the selection of the most efficacious anesthetic and analgesic regimens for the animals and the model.

(CS) = “[Controlled Substance](#)”. These agents are scheduled as controlled substances by the Drug Enforcement Agency. Special licensing is required in order to procure and prescribe a controlled substance. Applications for licensure may be completed [online](#).

## INDUCTION AGENTS

Some induction agents and premedications calm the animal, smooth anesthetic induction and recovery, and reduce the dose of anesthetic agent needed, but are seldom used prior to rodent anesthesia due to the additional stress of administering a second injection. Pre-emptive analgesia should be administered with the induction agents.

- Anesthetic induction of a rodent with inhalants often requires closer attention than during maintenance of anesthesia due to the relatively high doses used for and the rapid onset of induction.
- When drugs are given by injection, the dosage cannot be reduced after induction. Therefore, drugs at either a low dose or with a wide safety margin should be used for injection.
- Subcutaneous (SC) administration of anesthetics is not recommended because the induction of anesthesia is prolonged and variable in onset.
- Intravenous injections in rodents can be performed by more highly trained personnel.
- For most purposes, general anesthesia in rodents is preferred to localized anesthesia because it is believed to reduce stress to the animal and increase safety for personnel.
- Small mammals require an almost continuous supply of food and water; accordingly fasting and water deprivation should be minimized prior to anesthetic induction.

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INDUCTION AGENT	Species	Dose range (mg/kg, unless otherwise specified)	Route of Administration
Isoflurane	Mice	4%	Inhaled
	Neonatal mice	2-4%	Inhaled
	Rats	5%	Inhaled
Propofol	Mice	26	IV
	Rats	10	IV

## ANESTHETICS

One must administer appropriate anesthesia to animals undergoing procedures that cause more than momentary or slight pain or distress. Anesthetics render the animal unconscious without loss of vital functions. It is important to provide appropriate and gentle restraint, a sufficient amount of analgesia to diminish pain sensation during the procedure, and relaxation of muscle tone to the degree that procedures can be performed quickly and efficiently.

- Inhalant anesthetics provide a safe, reliable, reversible, and reproducible means of rendering rodents unconscious in order to perform surgeries and other intricate or potentially painful procedures.
- Inhalant anesthesia of small rodents is generally maintained utilizing face masks or nosecones. Endotracheal intubation has also become a more common practice in mice and rats and should be considered where appropriate.
- Injectable agents may allow multiple animals to be maintained under anesthesia at the same time. Longer periods of anesthesia can be accomplished by repeated injections or by constant rate infusions (CRI).
- When using parenteral anesthetics it is important to consider accurate dosing with correct multidrug use ratios, storage conditions, and feasibility of immediate use following reconstitution. It is critical to weigh each animal accurately prior to administration of a calculated dose of anesthesia to avoid either over- or underdosing.

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<b>ANESTHETIC</b>	<b>Species</b>	<b>Dose range (mg/kg, unless otherwise specified)</b>	<b>Route of Administration</b>
Alpha chloralose	Mice	114 of a 5% solution	IP
	Rats	31-65	IP
Alphaxolone- alphadolone	Mice	60-150	IM
	Mice	60-120	IP
	Rats	10 - 25	IV
	Rats	25-30	IP
Carbon dioxide	Guinea pigs	80% for 60s	Inhaled
	Mice	80% for 120s	Inhaled
	Rats	80% for 60s	Inhaled
Chloral hydrate	Mice	370-400	IP
	Rats	300-450	IP
	Rats	400-600	SC
Isoflurane	Mice	0.08-1.5%	Inhaled
	Neonatal mice	0.25-2.5 %	Inhaled
	Rats	0.25- 2.5%	Inhaled
Isoflurane / Morphine (CS)	Rats	2% I / 5 M	Inhaled, IP
Ketamine (CS) / Diazepam (CS)	Mice	100 K/5 D	IP
	Rats	40 K/5 D	IP
Ketamine (CS) / Midazolam (CS)	Mice	50-75 K / 1-10 M	IP
	Rats	60 K / 0.4 M	IP
Ketamine (CS) / Xylazine	Mice	90-150 K / 7.5-16 X	IP
	Rats	40-80 K / 5-10 X	IM, IP
Ketamine (CS) / Xylazine / Acepromazine	Mice	100 K / 2.5 X / 2.5 A	IM
	Rats	40 K / 8.0 X / 4.0 A	IM
Medetomidine / Fentanyl (CS)	Rats	200-300 ug/kg / 300 ug/kg	IP
Medetomidine / Sufentanil (CS)	Rats	150 ug/kg / 40- 50ug/kg	SC
Sevoflurane	Rats	2-2.4%	Inhaled

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Sodium pentobarbital (CS)	Mice	30-90	IP
	Rats	30-60	IP
Tiletamine (CS) / Zolazepam (CS)	Rats	20-40	IP
Thiobarbital (Inactin) (CS)	Mice	80	IP
Tribromoethanol (TBE orAvertin)	Mice	125-300	IP
Tribromoethanol / Medetomidine	Rats	150 / 0.5 (reversal 2.5 mg/kg atipamezole)	IP

**ANALGESICS**

Improved pain management for rodents is an important goal in the use of experimental animals. One must administer analgesia to animals undergoing procedures that cause more than momentary or slight pain or distress. Analgesics reduce or relieve pain without loss of consciousness. The avoidance or minimization of discomfort, distress and pain in laboratory animals is a moral imperative for all individuals who work with these species in biomedical research.

- Systemic and/or local analgesics may also reduce the anesthetic requirements, and have a pre-emptive effect on pain perception which persists into the recovery period.
- Not only pre-operative, but also immediate post-operative analgesic administration is important for adequate pain relief in post-surgical rodents.
- The most commonly used analgesics in rodents and other laboratory animal species are opioids and nonsteroidal anti-inflammatory drugs (NSAIDs). The ultimate decision for selection of drug must be based upon the experimental model under study and the specific types of data to be collected.
- Stress, pain, and distress have an effect on the immune system. Several viable options exist for relief of pain in chronic models of inflammation and infection.

<b>ANALGESICS</b>	<b>Species</b>	<b>Dose range (mg/kg, unless otherwise specified)</b>	<b>Route</b>
Acetaminophen (Tylenol®)	Rats	50	SC, IP
	Rats	100	PO

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	Rodents	110-305	PO
	Rodents	110-305	IP
Aspirin	Rats	100	PO
	Rodents	20	SC
	Rodents	100-120	IP
Buprenorphine (Buprenex®) (CS)	Mice	2	SC
	Mice	1.1 mM in DMSO	Topical
	Rodents	0.002-0.055	IV
	Rodents	0.04-0.13	IP
	Rats	0.05-0.5	SC, IP
	Rats	0.4	PO
Butorphanol (CS)	Mice	5	SC
	Rats	2	SC
Carprofen (Rimadyl®)	Rats	5-15	SC
Celecoxib	Rats	10-20	PO
Clonidine	Mice	0.25-0.5	PO
	Mice	0.001-0.1	IP
Clonidine / Morphine (CS)	Rats	0.025 C / 0.5 M	IP
Diclofenac	Mice	9.0-28	IP
Dipyrone	Rats	50-600	SC, IP, IV
Dipyrone / Morphine (CS)	Rats	177-600 D / 3.1-3.2 M	SC, IV
Ethyl carbamate	Rats	1000-1500	IP
Ethyl carbamate / alpha chloralose	Rats	250-400 EC (30 minutes prior to alpha chloralose)	IP
Fentanyl (CS)	Mice	0.025 - 0.6	SC
	Mice	0.032	SC
	Rats	0.01 - 1.0	SC
	Rats	2.0-4.0 g/day	PO
Flunixin meglumine (Banamine®)	Mice	4.0-11	IV

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Ibuprofen (Advil®), Motrin®, Nuprin®)	Mice	40	PO
Ibuprofen / Hydrocodone (CS)	Rats	200 I / 2.3 H	SC
Ibuprofen / Methadone (CS)	Rats	200 I / 1.7 M	SC
Ibuprofen / Oxycodone (CS)	Rats	200 I / 0.5 O	SC
Ketoprofen (Ketofen®)	Rats	5-15	SC
	Rats	10-20	IP
Lidocaine (Xylocaine®)	Rats	0.67-1.3 mg/kg/h CRI	SC-pump
Lidocaine / Buprenorphine (CS)	Mice	0.44 mM L/ 0.18 mM B in DMSO	Topical
Meloxicam (Metacam®)	Mice	1.0-10	IP
	Rats	1.0-4.0	SC, IP
Meloxicam / Tizanidine or Clonidine	Mice	0.5 M/ 0.25 T	PO
Meperidine (CS)	Mice	20	IP
Methadone (CS)	Rats	0.5-3	SC
Morphine (CS)	Mice	10	SC
	Mice	6.1 mM in DMSO	Topical
	Rats	2.0-10	SC
	Rats	2.8	SC-L
Naproxen / Hydrocodone (CS)	Rats	200 N / 1.3 H	SC
Oxymorphone (CS)	Mice	4	SC-L
	Rats	0.03 mg/kg/h CRI	IV
	Rats	0.1	IV
	Rats	1.2-1.6	SC-L
Physostigmine	Rats	50-200 µg/kg	SC
Tizanidine	Mice	0.25-1.0	PO
Tizanidine or Clonidine / Nimesulide	Mice	0.25 T / 1.0 N	PO

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Tramadol	Mice	20-40	IP
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**LOCAL AND TOPICAL ANESTHETICS**

Local anesthetics such as lidocaine, bupivacaine and others may be used to reduce the perception of pain at the surgical site as local or regional anesthetics. In conjunction with other agents, their use may allow reduced levels of general anesthetics, which may speed recovery and minimize mortality. When carefully used, direct injection of a local anesthetic can be a useful adjunct to anesthesia.

LOCAL OR TOPICAL ANESTHETICS	Species	Dose range (mg/kg, unless otherwise specified)	Route
Bupivacaine	Rodents	Local infiltration	SC
Lidocaine / Morphine (CS)	Mice	0.85 mM / 1.7 mM in DMSO	Local
Lidocaine / prilocaine cream (EMLA Cream®)	Rodents	Local application	Topical

**REVERSAL AGENTS**

Reversal leads to early termination of anesthesia which may reduce mortality and allow rapid return of the rodents to the home cage environment. Reversal agents also reverse bradycardia and bradypnea, but do not eliminate the hypothermic effects, thus thermal support remains essential. If reversal agents are used, both the anesthetic and analgesic properties of the drug may be terminated, thus alternative sources of analgesia must be provided.

REVERSAL AGENTS	Species	Dose range (mg/kg, unless otherwise specified)	Route
Atipamezole (Antisedan®)	Rats	0.5	SC
Flumazenil	Rodents	10 nmol	IP
Levallorphan tartrate	Rodents	0.89	SC

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Naloxone hydrochloride	Rodents	20	IP
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**REFERENCES**

Gaertner, DJ, TM Hallman, FC Hankenson, MA Batchelder. 2008. Anesthesia and Analgesia in Rodents. [Anesthesia and Analgesia in Laboratory Animals](#). Second Edition, Academic Press, CA.

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