Anesthesia and Analgesia in Mice

This is not intended to be an inclusive tutorial on all possible drug combinations that can be used in rats. The following guidelines are also general recommendations and consequently do not include reference to specific research-associated concerns. If you have questions about the use of anesthetics or analgesics for your particular situation, or if you have questions or comments about this document, please contact an IAS veterinarian.

*Anesthesia does not necessarily equate to analgesia.

Inhalational Anesthetics	**Dosage**	**Comments**
Isoflurane **Recommended**	3-5% for induction 1-3% for maintenance	300 μl in a 500 ml container- chamber induction for brief anesthesia. Maintenance requires use of a calibrated vaporizer.
Injectable Anesthetics	**Dosage & Route**	**Comments**
Dissociatives		
Ketamine + xylazine[#] **Recommended**	Ket 80-100 mg/kg IP + Xyl 5-10 mg/kg IP	**Thermal support is crucial.** To prolong anesthesia, supplement with 1/3 dose of ketamine only.
Ketamine + Acepromazine	Ket 100 mg/kg IP + Ace 5 mg/kg IP	Immobilization/anesthesia
Ketamine + xylazine + acepromazine	Ket 80-100 mg/kg IP + Xyl 10-20 mg/kg IP + Ace 2-3 mg/kg IP	Surgical anesthesia
Ketamine + Midazolam	Ket 100 mg/kg IP Mid 5 mg/kg IP	Immobilization/anesthesia
Barbiturates		
Pentobarbital (Nembutal®)	40-60 mg/kg IP	Considerable dose variation. Start at low end of range. NOTE: Euthanasia dose is >=90-100 mg/kg.
Local Anesthetics		
Lidocaine 0.5%	7 mg/kg (0.7 ml/kg)	5 min onset of action, duration 0.5-1 hr
Bupivacaine 0.25%	Up to 8 mg/kg SC, intraincisional	15-30 min onset of action, duration 4-8 hr, can combine with lidocaine
Other		
Propofol (Diprivan®)	12-26 mg/kg IV	Titrate as needed
Tribromoethanol (Avertin)	200-500 mg/kg IP	Non-pharmaceutical grade. Requires special preparation and storage. Adverse effects likely with repeated dosing.
Urethane	1000-1500 mg/kg IP	**Caution! Prolonged anesthesia; terminal procedures only carcinogenic and mutagenic**

Subcutaneous (SC), Intraperitoneal (IP), Intravenous (IV), oral (PO)

*Ketamine alone is not adequate for deep anesthesia or procedures that are painful. It is only to be used for immobilization.

[#]Reversal of α2agonists such as xylazine and dexmedetomidine can be accomplished by giving atipamazole (Antisedan®) 1-2.5 mg/kg IM, IP, SC or IV

Analgesics	**Dose**	**Duration**
Opioid		
Buprenorphine **Recommended**	0.05-0.1 mg/kg SC, IP	6-12 hr
NSAID		
Meloxicam **Recommended**	5 mg/kg SC, PO	24 hr
Carprofen	5 mg/kg SC or 10 mg/kg PO	24 hr
Ketoprofen	2-5 mg/kg SC	24 hr
Flunixin meglumine	2.5 mg/kg SC	12 hr (not commonly used)

Subcutaneous (SC), Intraperitoneal (IP), Intravenous (IV), oral (PO)

Anesthesia and Analgesia in Mice

Mouse Neonatal Anesthesia (mouse < 10 days of age)

Hypothermia- can only be performed in neonatal rodents < 6 days old and should not be used for procedures lasting longer than 30 minutes.

1. Place neonates either on a latex covered bed of crushed ice, in a cut off finger of a latex glove and place in ice water (animal's head must be held above water to prevent water aspiration and death) or a paper lined test tube and placing in crushed ice/ice water.
2. Animals have reached proper plane of anesthesia when pedal reflex is lost (animal does not respond to toe pinch).
3. Once proper plane is reached, remove pups from ice bath and placed on a chilled cold pack or bed of ice.
4. Use fiber optic light during procedure because incandescent bulbs can warm surgical field.
5. Following anesthesia, pups should be rewarmed slowly. Rapid warming can cause tissue damage. Pups can be rewarmed on a circulating water heating pad (40°C) or in an incubator (33°C).
6. Pups can be returned to dam once they are able to crawl.

Inhalant Anesthetics

Stage of Anesthesia	Route	Oxygen (L/min.)	Isoflurane (%)
Induction	Mask or Chamber	0.5-1	4-5
Maintenance	Mask or intubation	0.5-1	1-2

Recommended Injectable Anesthetics for neonates

Ketamine + Xylazine- Mice >7 days, 50-150 mg/kg Ketamine + 5-10 mg/kg xylazine

1. Intraperitoneal (IP)- 27 g needle, 1 ml syringe; maximum volume- 0.5 ml
2. Subcutaneous (SC)- 27 g needle, 1 ml syringe; maximum volume- 1 ml

Ketamine/Xylazine Dilution for Rodents

Ketamine (Ketaset®) 100 mg/ml
Xylazine (Rompun®, Anased®) 20 mg/ml *Be careful to verify that it is 20 mg/ml & not 100 mg/ml.
Diluent: 5% Dextrose (D5W) or normal saline (0.9% NaCl)
Stability: stable for 28 days stored under ambient conditions and at 4°C, protected from light (amber bottle).

Mouse Anesthetic Dose

Ketamine 100 mg/kg + Xylazine 10 mg/kg

1.0 ml Ketamine (100 mg/ml) + 0.5 ml xylazine (20 mg/ml) + 8.5 ml D5W or normal saline for injection

Mice receive 0.1 ml/10 g body weight

Ketamine and xylazine diluted as above with D5W (5% dextrose) or normal saline are chemically and physically stable after storage for 28 days under ambient conditions of 4°C protected from light.

Ketamine + Xylazine + Acepromazine

Ketamine 100 mg/kg **+** Xylazine 10mg/kg **+** Acepromazine 3mg/kg

The following regimen will provide a surgical plane of anesthesia for 30-40 minutes and sedation for 1-3 hours:
1.0 ml Ketamine (100 mg/ml) + 0.5 ml Xylazine (20 mg/ml) + 0.3 ml Acepromazine (10 mg/ml) + 8.2ml normal saline 0.9% or sterile PBS

Mice receive 0.1 ml/10 g body weight

Anesthesia and Analgesia in Mice

Buprenorphine Dilution and Dosage Chart

Buprenorphine (Buprenex®) 0.3 mg/ml in boxes of 5 1 ml vials

Dilution for Mice: 1.0 ml Buprenorphine (0.3 mg buprenorphine/ml) + 9.0 D5W (5% dextrose in water) for injection to make a final concentration of 0.03 mg/ml. Using this dilution, dose mice according to the following chart. Buprenorphine is **light sensitive** so prepare dilution in an **amber bottle** or cover bottle with **foil**.

Mouse	**Dosage**		
Weight	**0.05 mg/kg**	**0.075 mg/kg**	**0.1 mg/kg**
15 g	0.025 ml	0.04 ml	0.05 ml
20 g	0.03 ml	0.05 ml	0.07 ml
25 g	0.04 ml	0.06 ml	0.08 ml
30 g	0.05 ml	0.08 ml	0.1 ml
35 g	0.06 ml	0.09 ml	0.12 ml
40 g	0.07 ml	0.1 ml	0.13 ml
45 g	0.08 ml	0.11 ml	0.15 ml
50 g	0.08 ml	0.12 ml	0.17 ml

Stable for up to 30 d at 21°C or 4°C- Jappinen A, Kokki H, Naaranlahti TJ, Rasi AS. Stability of buprenorphine, haloperidol and glycopyrrolate mixture in 0.9% sodium chloride solution. Pharm World Sci. 1999: 21(6): 272-4.

NSAID DILUTIONS FOR MICE

Meloxicam dilution based on dose of 5 mg/kg for stock solution 50 mg/ml
1.0 ml Meloxicam (50 mg/ml) + 9.0 ml sterile water or 0.9% sterile saline

Carprofen dilution based on dose of 5 mg/kg for stock solution 50 mg/ml
1.0 ml Carprofen (50 mg/ml) + 9.0 ml sterile water or 0.9% sterile saline

Mouse	**Dosage 5mg/kg**	
Weight	**Meloxicam**	**Carprofen**
15 g	0.15 ml	0.15 ml
20 g	0.2 ml	0.2 ml
25 g	0.25ml	0.25ml
30 g	0.3 ml	0.3 ml
35 g	0.35 ml	0.35 ml

Please refer to **IACUC Policy 035 Use of Non-Pharmaceutical Grade Compounds in Animal Research**
Non-pharmaceutical grade chemical compounds may be used for scientific investigation when scientific justification is provided. Acceptable reasons for use of non-pharmaceutical or chemical grade agents may be:

1. Scientific necessity.
2. Non-availability of an acceptable veterinary or human pharmaceutical-grade product.

Examples of non-pharmaceutical grade compounds are: tribromoethanol, urethane, and alphachloralose.

Tribromoethanol was once manufactured specifically for use as an anesthetic under the trade name Avertin, but is no longer available commercially. Tribromoethanol may be appropriate for short procedures in mice, especially surgical procedures, where it will be given only on a single occasion. A repeat anesthetic episode can be associated with an increase in morbidity and mortality.

Anesthesia and Analgesia in Mice

Disadvantages of Avertin: • Tribromoethanol is an irritant, especially at high doses, high concentrations, or with repeated use. Adhesions are sometimes seen in the abdominal cavity after IP injections. • Tribromoethanol degrades in the presence of heat or light to produce toxic byproducts. Degraded solutions can be both nephrotoxic and hepatotoxic. Administration of degraded Tribromoethanol solutions has been associated with death, often 24 hours after surgery. • Tribromoethanol can cause intestinal ileus (stopping of the gut motility and subsequent death of the animal) several weeks after injection. This is more common with Avertin stored in the presence of light or heat, stored at higher than recommended doses, or given at higher than recommended concentrations. • The effects of Tribromoethanol are also somewhat unpredictable in mice younger than 16 days, or in animals with altered carbohydrate metabolism, such as various mouse strains used for diabetes or obesity models (db/db mice or ob/ob mice).

Alphachloralose provides very little analgesia and should not be used as a surgical anesthetic unless scientifically justified, e.g. in certain physiological recording experiments. It may be combined with Urethane and used in non-recovery procedures of long duration where preservation of autonomic reflexes is essential.

Urethane may be used for non-recovery procedures of exceptionally long duration where preservation of autonomic reflexes is essential. It is often combined with Alphachloralose as an adjunct in long, non-recovery recording procedures.