

**PORTLAND VETERANS AFFAIRS MEDICAL CENTER
INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (PVAMC IACUC)
ANIMAL CARE AND USE GUIDELINES**

CHECK ONE:

- I agree to comply with the following guidelines.
- I have attached written justification for deviation from these guidelines, and a description of the methods to be employed.

Principal Investigator

Date

GUIDELINES FOR ANESTHESIA, ANALGESIA AND TRANQUILIZATION

Background. Federal criteria for granting IACUC approval of animal protocols includes the provision that pain and distress must be avoided or discomfort/pain/distress be minimized through appropriate sedation, analgesia or anesthesia. The *Guide for the Care and Use of Laboratory Animals* (Eighth Edition, revised 2011) further states that “If a painful procedure must be conducted without the use of an anesthetic analgesic, or tranquilizer -- because such use would defeat the purpose of the experiment -- the procedure must be justified in writing in the animal protocol approved for the study and **supervised directly by the responsible investigator.**” The Office for Protection from Research Risks (OPRR) *Institutional Animal Care and Use Committee Guidebook (NIH Publication No. 92-3415)* defines analgesia as “a state of insensibility to pain without loss of consciousness,” and anesthesia as “a state of lack of awareness or sensitivity, with or without loss of consciousness.”

Guidelines. For any procedure that will or has the potential to produce pain and distress in laboratory animals,

1. The agent(s) and the dose, route, and frequency of administration of each agent must be listed in the Animal Component of Research Protocol.
2. Principal Investigators must choose a regimen from the attached list of commonly used referenced regimens, or they may propose other anesthetic/analgesic/tranquilizer regimens, provided that either the appropriate published references are provided to the IACUC or the Principal Investigator can otherwise demonstrate the efficacy of the proposed regimen.
3. During the course of the procedure, accurate written documentation of anesthetic/analgesic/tranquilizer administration must be maintained. When requested, such documentation must be made available to the VMO, IACUC, or other appropriate federal and state agencies. The VMU has developed a form to facilitate this documentation (refer to “Post-Procedural Monitoring Record,” with the Guidelines).
4. If analgesic agents will be given on an as needed basis after a potentially painful procedure, accurate written documentation of the assessment of the animals’ well-being by a trained individual must be maintained. When requested, such documentation must

be made available to the VMO, IACUC, or other appropriate federal and state agencies. The VMU has developed a form to facilitate this documentation (refer to "Post-Procedural Monitoring Record," with the Guidelines).

5. If a painful procedure must be conducted without the use of an anesthetic, analgesic, or tranquilizer,
 - a. The Principal Investigator must supply written justification for the omission of anesthetics, analgesics, or tranquilizers,
 - b. the procedure must be approved by the IACUC.

6. After the administration of an anesthetic agent, post-procedural care must include observing and providing supportive care to the animal until it is fully ambulatory, at intervals not to exceed 15 minutes. Supportive care can include:
 - a. Heat sources should not directly come into contact with the animal as this can cause thermal burns. Do not use electrical heating pads because these can cause hyperthermia since they continue to produce heat regardless of skin temperature. Providing adequate insulation of the animal by using a folded towel can help prevent heat loss in the anesthetized patient. By taking steps to reduce heat loss and maintain normal body temperature, recovery from anesthesia is less stressful and often faster. Surgical table padding and warm water circulating pads are useful steps during surgery and those animals receiving fluid support should have warm fluids administered. (*Anesthesia and Analgesia in Laboratory Animals; Kohn DF, Wixson SK, White WJ, Benson, GJ, 1997; p138-139*).
 - b. To prevent dehydration and speed recovery, warm fluids (0.9% saline or equivalent, ~37°C) may be administered subcutaneously or intraperitoneally at 1-2 ml/100 gm body weight.
 - c. To prevent cannibalism, house animals individually until fully ambulatory.
 - d. If recovery from anesthesia will be prolonged (i.e. over 1 hour), the animal should be rotated from side to side every 15 minutes to minimize hydrostatic pulmonary congestion. This practice should be continued until the animal is able to maintain sternal recumbency or sit.

Researchers requiring additional information on the selection of anesthetics, analgesics, and tranquilizers should contact the PVAMC Veterinary Medical Unit, x55032.

Rat Formulary

INHALATION ANESTHETICS:

Drug Name	Dose (mg/kg) & Route	Frequency	Notes
Isflurane	1-3% inhalant to effect; usually 5% for induction	Whenever general anesthesia is required;	Use precision vaporizer. Deliver with 1.0-1.5% oxygen. Survival surgery requires pre-emptive analgesia.
Carbon Dioxide	From a compressed gas cylinder, 20-30% flow rate to effect and for 1 minute past apparent death	Once at time of euthanasia	Must be followed by a secondary means of euthanasia, such as rapid cervical dislocation.

INJECTABLE ANESTHETICS:

Drug Name	Dose (mg/kg) & Route	Frequency	Notes
Recommended: Ketamine (K) + Xylazine (X) (in same syringe)	80-100 (K) + 5-10 (X) IP	0.2 mL/100 grams body weight as needed	May not produce surgical plane of anesthesia; if redosing, use ketamine alone. May be partially reversed with atipamezole or yohimbine.
Ketamine (K)+ Xylazine (X) + Acepromazine (A) (in same syringe)	70-100 (K) + 10-20 (X) + 2-3 (A) IP	0.1 mL/100 grams body weight as needed	May not produce surgical plane of anesthesia; if redosing, use ketamine alone. May be partially reversed with atipamezole or yohimbine.
Ketamine (K) + Medetomidine (M) (in same syringe)	75-100 (K) + 0.5-1 (M) IP	As needed	May not produce surgical plane of anesthesia; if redosing, use ketamine alone. May be partially reversed with atipamezole or yohimbine.

REVERSAL AGENTS:

Drug	Dose (mg/kg) & route	Frequency	Notes
Atipamezole	0.1-1.0 SC or IP	Any time medetomidine or xylazine has been used.	Atipamezole is dosed at the same <u>volume as</u> medetomidine, but they are manufactured at different concentrations.
Yohimbine	1.0-2.0 SC or IP	For the reversal of xylazine	

OTHER INJECTABLE ANESTHETIC AGENTS:

Drug	Dose (mg/kg) & route	Frequency	Notes
Sodium pentobarbital	40-50 IP	Recommended for terminal/acute procedures only; booster doses as needed.	Consider supplemental analgesia (opioid or NSAID) for invasive procedures.

ANALGESIC: OPIOID

Drug	Dose(mg/kg) & route	Frequency	Notes
Buprenorphine	0.01-0.05 SC or IP	Used pre-operatively for preemptive analgesia and post-operatively every 4-12 hours	When used as a sole analgesic agent, this is the typical regimen: once at time of procedure, second dose 4-6 hours later; additional doses every 8-12 hours as needed. Consider multi-modal analgesia with an NSAID and local analgesic agent.

ANALGESIC: NSAID (Non-steroidal anti-inflammatory analgesia) (Note: prolonged use may cause renal or gastro-intestinal problems)

Drug	Dose (mg/kg) & route	Frequency	Notes
Recommended: Carprofen	4-5 SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hours	Depending upon procedure may be used as sole analgesic agent or as multi-modal analgesia with buprenorphine
Recommended: Meloxicam	2.0 PO, IM, or SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hours	Depending upon procedure may be used as sole analgesic agent or as multi-modal analgesia with buprenorphine
Recommended: Ketoprofen	2-5 SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hours	Depending upon procedure may be used as sole analgesic agent or as multi-modal analgesia with buprenorphine
Ketorolac	5-7.5 oral or SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hours	Depending upon procedure may be used as sole analgesic agent or as multi-modal analgesia with buprenorphine
Flunixin meglumine	2 SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hours	Depending upon procedure may be used as sole analgesic agent or as multi-modal analgesia with buprenorphine

ANALGESIC: LOCAL ANESTHETIC/ANALGESIC (lidocaine and bupivacaine may be combined in one syringe for rapid onset and long duration of analgesia)

Drug	Dose (mg/kg) & route	Frequency	Notes
Lidocaine hydrochloride	Dilute to 0.5%, and do not exceed 7 mg/kg total dose. SC or Intra-incisional	For use locally before making a surgical incision or before the skin is sutured.	Faster onset than bupivacaine but < 1 hour of action
Bupivacaine	Dilute to 0.25% and do not exceed 8 mg/kg total dose. SC or Intra-incisional	For use locally before making a surgical incision or before the skin is sutured.	Slower onset than lidocaine but > 4-8 hours of action

REFERENCES:

Lumb and Jones' Veterinary Anesthesia, 3rd edition; Thurmon JC, Tranquilli WJ, Benson GJ; Lippincott, Williams, & Wilkins Publishing; Section VII, Chapter 21, p.686-735.

Formulary for Laboratory Animals, 3rd edition; Hawk CT, Leary SL, Morris, TH; Blackwell Publishing Professional, 2121 State Avenue, Ames, Iowa 50014.

Plumb's Veterinary Drug Handbook, 5th edition; Plumb DC, Blackwell Publishing Professional, 2121 State Avenue, Ames, Iowa 50014.

Mouse Formulary

INHALATION ANESTHETICS:

Drug Name	Dose (mg/kg) & Route	Frequency	Notes
Isoflurane	1-3% inhalant to effect; usually 5% for induction	Whenever general anesthesia is required;	Use precision vaporizer. Deliver with 1.0-1.5% oxygen. Survival surgery requires pre-emptive analgesia.
Carbon Dioxide	From a compressed gas cylinder, 20-30% flow rate to effect and for 1 minute past apparent death	Once at time of euthanasia	Must be followed by a secondary means of euthanasia, such as rapid cervical dislocation.

INJECTABLE ANESTHETICS:

Drug Name	Dose (mg/kg) & Route	Frequency	Notes
Recommended: Ketamine (K)+ Xylazine (X) + Acepromazine (A) (in same syringe)	75 (K) + 7.5 (X) + 1.5 (A) IP	As needed Volume: 0.1 ml/10 grams mouse body weight	May not produce surgical plane of anesthesia; if redosing, use ketamine alone. May be partially reversed with atipamezole or yohimbine.
Ketamine (K)+ Xylazine (X) + Acepromazine (A) (in same syringe)	70-100 (K) + 10-20 (X) + 2-3 (A) IP	As needed	May not produce surgical plane of anesthesia; if redosing, use ketamine alone. May be partially reversed with atipamezole or yohimbine.
Ketamine (K) + Medetomidine (M) (in same syringe)	50-75 (K) + 0.5-1 (M) IP	As needed	May not produce surgical plane of anesthesia; if redosing, use ketamine alone. May be partially reversed with atipamezole or yohimbine.

REVERSAL AGENTS:

Drug	Dose (mg/kg) & route	Frequency	Notes
Atipamezole	0.1-1.0 SC or IP	Any time medetomidine or xylazine has been used.	Atipamezole is dosed at the same <u>volume as</u> medetomidine, but they are manufactured at different concentrations.
Yohimbine	1.0-2.0 SC or IP	For the reversal of xylazine	

OTHER INJECTABLE ANESTHETIC AGENTS:

Drug	Dose (mg/kg) & route	Frequency	Notes
Sodium pentobarbital	40-50 IP	Recommended for terminal/acute procedures only; booster doses as needed.	Consider supplemental analgesia (opioid or NSAID) for invasive procedures.

ANALGESIC: OPIOID

Drug	Dose(mg/kg) & route	Frequency	Notes
Buprenorphine	0.05-0.1 SC or IP	Used pre-operatively for preemptive analgesia and post-operatively every 4-12 hours	When used as a sole analgesic agent, this is the typical regimen: once at time of procedure, second dose 4-6 hours later; additional doses every 8-12 hours as needed. Consider multi-modal analgesia with an NSAID and local analgesic agent.

ANALGESIC: NSAID (Non-steroidal anti-inflammatory analgesia) (Note: prolonged use may cause renal or gastro-intestinal problems)

Drug	Dose (mg/kg) & route	Frequency	Notes
Recommended: Carprofen	5-10 SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hours	Depending upon procedure may be used as sole analgesic agent or as multi-modal analgesia with buprenorphine
Recommended: Meloxicam	5-10 PO, IM, or SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hours	Depending upon procedure may be used as sole analgesic agent or as multi-modal analgesia with buprenorphine
Ketoprofen	2-5 SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hours	Depending upon procedure may be used as sole analgesic agent or as multi-modal analgesia with buprenorphine
Ketorolac	5-7.5 oral or SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hours	Depending upon procedure may be used as sole analgesic agent or as multi-modal analgesia with buprenorphine
Flunixin meglumine	2 SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hours	Depending upon procedure may be used as sole analgesic agent or as multi-modal analgesia with buprenorphine

ANALGESIC: LOCAL ANESTHETIC/ANALGESIC (lidocaine and bupivacaine may be combined in one syringe for rapid onset and long duration of analgesia)

Drug	Dose (mg/kg) & route	Frequency	Notes
Lidocaine hydrochloride	Dilute to 0.5%, and do not exceed 7 mg/kg total dose. SC or Intra-incisional	For use locally before making a surgical incision or before the skin is sutured.	Faster onset than bupivacaine but < 1 hour of action
Bupivacaine	Dilute to 0.25% and do not exceed 8 mg/kg total dose. SC or Intra-incisional	For use locally before making a surgical incision or before the skin is sutured.	Slower onset than lidocaine but > 4-8 hours of action

REFERENCES:

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