

GUIDELINES FOR ANESTHESIA AND ANALGESIA IN LABORATORY ANIMALS

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1. Background

Federal regulations and guidelines mandate that animals undergoing potentially painful procedures be provided with adequate anesthesia and analgesia. In addition, for these procedures, a veterinarian must be consulted regarding the appropriate anesthetic and analgesic agent and dose for the species being used and the procedure being performed. The standard of care is to prevent animal pain whenever possible and to treat animal pain whenever diagnosed. Exceptions to these principles are permitted only if scientific justification is provided in the Animal Use Protocol (AUP) and approved by the Animal Care and Use Committee (ACUC).

2. Training

All personnel who perform anesthesia must be appropriately trained. The Principal Investigator (PI) is responsible for assuring that research personnel receive appropriate training and certification prior to performing any procedure. New anesthetists are trained and supervised by the PI, or appropriate designated personnel, until they are competent to perform the procedure independently (please refer to [ACUC Policy on Training and Education](#) and [ACUC Post-Approval Monitoring Guidelines](#)). All new anesthetists, including PIs, must be observed by OLAC veterinary staff or the OLAC Trainer and their competency certified to the ACUC prior to working independently. The Office of Laboratory Animal Care (OLAC) veterinary staff is available to provide assistance with, or training in, aseptic technique and the proper administration of anesthesia, analgesia, and euthanasia.

3. Anesthetics

- Inhalant anesthetics (e.g., isoflurane) – Delivery of inhaled anesthetics by mask or endotracheal tube via a precision vaporizer is recommended for all non-aquatic species. Adjusting the inhaled percentage of anesthetic gas to deepen anesthesia is far safer than repeated re-dosing of injected drugs. Volatile anesthetics are easier to decrease as well, even compared to drugs for which there is an injectable antagonist or reversal agent. A disadvantage of the inhalant anesthetic agents is the lack of residual analgesia once the vaporizer has been turned off; pre-emptive analgesia is necessary. Contact OLAC veterinary staff at 642-9232 for information regarding vaporizer and scavenger availability and training.
- Injectable anesthetics (e.g., ketamine combinations, dexmedetomidine) – Injectable anesthetics are appropriate for many procedures. There is, however, a great deal of variation in depth and duration of anesthesia among rodent strains and individual animals.
- Immersion anesthetics (i.e., buffered MS-222) – Immersion anesthetics are appropriate for aquatic species, such as amphibians and fish. Different solution strengths may be appropriate for induction and maintenance of anesthesia.
- Local anesthetics (i.e., lidocaine, bupivacaine) – Local anesthetics are considered adjuncts to either inhalant or injectable anesthetics, provide additional analgesic coverage, and aid in preventing “windup phenomenon”.
- Please visit the [OLAC website](#) or consult the [suggested formularies](#) below for appropriate dosages and routes of administration by drug for some common laboratory animals.

4. Analgesics

For the use of any analgesic agent, OLAC veterinarians should be consulted regarding the appropriate agent and dose for the species being used and the procedure being performed.

- Opioids (i.e., buprenorphine, morphine) – Opioids are very effective analgesics for surgical pain but may have effects on cardiovascular and respiratory function, intestinal motility, and can be sedating.
- Non-steroidal anti-inflammatory agents (i.e., meloxicam, carprofen, ketoprofen) – Newer, longer-lasting non-steroidal anti-inflammatory analgesics (NSAIDs) may have longer durations of action than available opioids. These drugs are frequently co-administered with an opioid to combine potency of effect with duration of action.
- Please visit the [OLAC website](#) or consult the [suggested formularies](#) below for appropriate dosages and routes and frequency of administration by drug for some common laboratory animals.

5. Best Practices

The following issues must be considered in developing a protocol for anesthesia and analgesia.

- Multi-modal drug administration – Using a combination of agents of analgesic agents that have different mechanisms of action is recommended. This allows for lower doses of each drug while minimizing the side effects that may occur when using a single agent.
- Pre-emptive analgesia – Pre-emptive analgesia or administration of pain relief *before* the painful stimulus is recommended and is thought to prevent the “wind-up phenomenon¹”:
 - To ensure that pain is being treated as the general anesthetic is wearing off;
 - To lower the overall amount of general anesthetic required;
 - To allow for improved cardiovascular stability
- Frequency of analgesic administration – Scheduling of analgesic doses and frequencies should be carefully planned with consideration of the duration of action required to prevent the need for late night or early morning dosing. For example, many analgesics administered at 5 pm will be ineffective before 8 am the next morning. Multimodal analgesia is recommended to combine potency of effect with duration of action. Animals should be checked when the last dose of analgesic is expected to fall below therapeutic levels for signs of pain or distress. If animals exhibit signs of pain or distress, the OLAC veterinary staff must be consulted and a protocol amendment submitted if necessary.
- Supportive care – Non-pharmaceutical methods to enhance the administration of anesthetic and analgesic agents should be used and include:
 - Keeping the animal warm during and after anesthetic procedures
 - Fluid administration
 - Keeping recovering animals isolated in a quiet area
 - Providing supplemental foods

Contact the veterinary staff for additional information on supportive care.

6. Monitoring

- Euthermic animals (mammals) should never be left alone during anesthesia.

¹ Pain wind-up is a phenomenon of increased central pain sensitization in which repeated painful stimulation of peripheral nerves increases the strength of pain signal reach the brain. The process leads to increase pain in which less stimulation is needed to increase pain response to otherwise nonpainful stimuli and spontaneous pain.

- The depth of anesthesia should be monitored continuously and parameters recorded at least every 15 minutes during all procedures.
- Plans for intra- and post-operative monitoring must be included in the AUP. Monitoring of respiratory rate and character is facilitated by the use of transparent drapes. Monitoring anesthesia includes: assessing the animal's responsiveness to painful stimuli, character of respiration, and color of the ears, tail, mucous membranes, or foot pads, and adjusting anesthetic depth as needed. Pedal withdrawal reflex (toe pinch) is recommended for assuring adequate depth of anesthesia prior to first incision and as a repeated check throughout the procedure.
- Depending on the procedure and animal species, other monitoring may be indicated such as heart rate, blood pressure, body temperature, and tissue oxygenation. Monitoring should be recorded through the post-operative period to complete recovery.
- Dose ranges and titration – All drugs, dose ranges, and routes of administration must be listed in the AUP. Dose ranges are starting points which must be titrated up or down for the individual animal, or for the particular application (procedures conducted, animal age and strain differences). When experience indicates that a recommended dose range is consistently too high or too low for the particular application, the veterinarian should be informed, and a protocol amendment submitted to the ACUC. Anesthetics are always titrated to effect. It is not acceptable to conduct surgical procedures unless the animal is fully anesthetized.

7. Recordkeeping

- Administration of anesthesia and analgesia and peri-operative monitoring should be recorded. Depending on the species, records may be kept in the animal's individual medical record, or in laboratory records and on blue post-operative cage cards provided by OLAC.
- Please refer to ACUC Guidelines on [Recordkeeping for Surgical Procedures on Laboratory Animals](#) for additional information.

8. Controlled Substances

- Several commonly used anesthetics and analgesics (i.e., opioids, ketamine) are controlled substances and require special authorization and procedures to be completed prior to use in animal research.
- More information can be found at the Office of Environment, Health & Safety (EH&S) website (<http://www.ehs.berkeley.edu/controlled-substances>)
- Once they are obtained, controlled substances carry special storage and record keeping requirements.

9. Suggested Formularies

- For mice: <http://www.iacuc.ucsf.edu/Proc/awMouseFrm.asp>
- For rats: <http://www.iacuc.ucsf.edu/Proc/awRatFrm.asp>

10. References

- Carpenter, J.W. (2005). *Exotic Animal Formulary*. (3rd Ed.). Philadelphia, PA: Elsevier Saunders.
- Hawk, C.T., Leary, S., & Morris, T. (2005). *Formulary for Laboratory Animals*. (3rd Ed.). Ames, Iowa: Blackwell Publishing
(http://www3.research.usf.edu/cm/docs/Formulary_for_Lab_Animals_3rd_ed.pdf)
- Principles and Practice of Veterinary Technology, Fourth Edition: Margi Sirois (2017)

**Call 3-VETS if there is an animal emergency
(510-643-8387)**