Animal Facility SOP
Anesthesia and Analgesia SOP 3.2

Date Adopted	8/21/20
Date Last Updated	6/17/20; 8/3/2022
Prepared by	Michelle Dennis and Ingrid Tulloch
Reviewed by	Terzi, added resources/dosing info, clarified some definitions Julie Watson 8/21/20, Reviewed and updated sedatives: Julie Watson and Ingrid Tulloch 8/3/2022

I. Purpose

This document will outline the guidelines for the use of anesthetics and tranquilizers for non-survival and survival surgeries; and analgesia for pain relief and animal care needs following survival surgeries.

II. Scope

Anyone who performs procedures in animals requiring anesthesia and/or analgesia.

III. Definitions

Preanesthetic medication with **sedative, tranquilizers, and analgesics** are generally administered to reduce apprehension, favor stress-free induction and recovery, to reduce doses and side effects of other anesthetic agents, and achieve pre-emptive analgesia. However, in mice a “single shot” anesthetic protocol is advisable to minimize the stress caused by multiple injections.

General anesthesia produces loss of consciousness, so the animal cannot consciously perceive pain, but in unconscious animals, painful stimuli will still be transmitted and processed by the central nervous system. Although the animal does not perceive pain during the surgery, central hypersensitivity can still develop in the spinal cord and brain causing perception of postoperative pain to be heightened. Some anesthetics, such as the alpha-2 adrenoreceptor agonists (i.e. Xylazine, Dexmedetomidine), do have some analgesic properties. In addition, additional analgesics can be used as part of the anesthetic regimen (i.e. opioids, non-steroidal anti-inflammatories).

Analgesia - loss of pain sensation over a specific area, caused by local administration of a drug that blocks nerve conduction (e.g. lidocaine, bupivicaine), or throughout the whole organism by the administration of systemic analgesic agents (e.g. carprofen, buprenorphine).

Tranquilizers- Substances that reduce the anxiety and stress that an animal may experience when it is handled. (e.g. Midazolam and Diazepam)

Sedatives - Substances that also relieve anxiety, but also promote semi- or full-unconsciousness. Sedatives, used appropriately and in some cases with other drugs, may also be used as part of a general anesthesia regime for rodents. (e.g. ketamine)

IP vs SC - When administering drugs, the route of administration will determine, in some part, how the drug affects the animal. In the case of sedatives/anesthetics, an intraperitoneal (IP) injection will generally have a faster onset, and also faster recovery, than the same dose delivered as a subcutaneous (SC) injection. Please only administer the following drugs via the routes listed below.

IV. Guidelines

Survival Surgery Guidelines All species are at risk for hypothermia while under anesthesia. Rats are particularly susceptible due to their high body surface area to body mass ratio. Hypothermia induces a significant physiological stress on animals that can prolong recovery and potentially be fatal.

1. **Temperature regulation**. **Supplemental heat is required during all anesthetic events**. Supplemental heat sources include circulating water blankets, and commercial products that can be warmed in a microwave. Electric heating pads are less desirable because of the possibility of overheating or burns. Hotplates should never be used.

2. **Fluid supplementation is recommended.** Consider providing warm subcutaneous (SQ) or intraperitoneal (IP) fluids, particularly for prolonged anesthetic events or animals that are ill, aged, or debilitated.

3. **Eyes must be protected** with ophthalmic ointment to avoid drying out and subsequent corneal damage.

4. **Surgical Plane of Anesthesia.** After properly dosing an animal, always check that the animal is at a surgical plane of anesthesia before performing any surgical manipulation. For rodents, this is easily accomplished by firmly pinching

the animal's toe/foot. If the animal reflexively pulls the limb toward the body, the animal is not yet at the appropriate plane of anesthesia. Special attention should be paid to what stage and plane or anesthesia the animal is in during surgical procedures.

5. **Recovery and monitoring.** Animals should be monitored continuously while under anesthesia. After anesthesia is discontinued, continue to monitor the animals periodically until they are capable of making normal postural adjustments and protecting their airway. Recover animals on paper towels (without bedding) in a clean cage. This minimizes the risk of tracheal obstruction or pneumonia. Recovering anesthetized animals should be alone in a cage with supplemental heat during recovery. When the animal is ambulatory, return it to the home cage with immediate access to food and water.

6. **Anesthetic records** should be maintained according to the study protocol.

General Information

Stages of Anesthesia. There are four stages of anesthesia and four planes within stage III. The stages range from induction to maintenance to recovery.

Stages 1. Disorientation. The animal is not anesthetized. Respiration and heart rate might be normal but the animal shows disorientation, panting, and struggle in response to surgical procedures. Pupils begin to dilate

Stage 2. Excitement or delirium. The animal is not anesthetized and might show irregular heartbeat, breath holding or hyperventilation, involuntary movement and exaggerated reflexes. Pupils are dilated and muscle tone is normal.

Stage 3. Anesthesia. The animal is anesthetized at this stage. Muscles are relaxed and swallowing reflex is diminished or absent. However there are four planes of anesthesia and surgeries should be conducted at plane III.

a. **Plane 1.** *Lightly anesthetized***,** no eyeball movement, regular breathing rate, strong pulse and might move around. Pupil and muscle tone are normal diminished or absent swallowing reflexes

b. **Plane 2.** Laryngeal and corneal reflexes are lost, low muscle tone and no toe-pinch withdrawal reflex.

c. **Plane 3**. *Deep Anesthesia* (Surgical plane). Weak corneal reflex dilated pupils that are centered, low blood pressure

d. **Plane 4**. *Danger*, the animal is overdosed and shows cyanosis/bluish color around mouth, loss of sphincter control, low heart rate and extreme pupil dilation.

Stage 4. Impending death. There is complete paralysis of both the intercostal muscles and the diaphragm, which causes respiratory arrest paralysis, and finally death. The pupils dilate, remaining fixed in dilation while the muscles relax.

Anesthetic Dosing Chart

Local Anesthetic and Analgesics			
Lidocaine hydrochloride (2%)	***Dilute to 0.5%, do not exceed 10 mg/kg total dose, SC or intra incisional***	***Use locally before making surgical incision***	***Faster onset than bupivacaine but short (<1 hour) duration of action***
Bupivacaine (0.5%) (Marcaine) (Recommended)	***Dilute to 0.25%, do not exceed 4 mg/kg total dose, SC or intraincisional***	***Use locally before making surgical incision***	***Slower onset than lidocaine but longer (~ 4-8 hour) duration of action***
Ketamine combinations			
Ketamine-Dexmedetomidine (Recommended)	***K:75 mg/kg + D:0.5 mg/kg IP or SQ (in same syringe)***	***May not produce surgical-plane anesthesia for major procedures. If redosing, use 1/3 dose of ketamine alone-may lose surgical anesthesia. Dexmedetomidine may be reversed with Atipamezole.***	
Ketamine-Xylazine	***K: 80-100 mg/kg + X: 10 mg/kg IP or SQ***	***May not produce surgical-plane anesthesia for major procedures. If redosing, use 1/3 dose of ketamine alone-may lose surgical anesthesia.***	

	(in same syringe)	*Xylazine may be reversed with Atipamezole or Yohimbine.*	
Ketamine-Xylazine-Acepromazine (Recommended)	*K: 80-100 mg/kg + X:10 mg/kg +A: 3 mg/kg IP or SQ (in same syringe)*	*May not produce surgical-plane anesthesia for major procedures. If redosing, use 1/3 dose of ketamine alone. Overdose for Xylazine may be partially relieved with Atipamezole or Yohimbine.*	
Ketamine-Midazolam	*K: 80-100 mg/kg + M: 5 mg/kg IP or SQ (in same syringe)*	*Will not produce surgical-plane anesthesia for surgical procedures, but may be useful for restraint.*	
Other injectable anesthetics			
Sodium pentobarbital (Nembutal)	*40-50 mg/kg IP*	*Recommended for terminal/acute procedures only, with redosing as needed. May occasionally be appropriate for survival procedures. Dilute to 9.1 mg/ml for use (do not use the euthanasia solution).*	*Consider supplemental analgesia (opioid or NSAID) for invasive procedures, especially when used on a survival basis. For surgery, do not use the euthanasia solution which is typically 240 mg/ml*
Opioid analgesia			
Buprenorphine (Recommended)	*0.05-0.1 mg/kg SC*	*Used pre-operatively for preemptive analgesia and postoperatively every 8-12 hours*	*For major procedures, require more frequent dosing than 12 hour intervals. Consider multimodal analgesia with a NSAID. High doses of buprenorphine may lead to pica behavior in rats.*
Non-steroidal anti-inflammatory analgesia (NSAID) Note that prolonged use may cause renal, gastrointestinal, or other problems. Avoid using longer than 2 to 3 days.			
Carprofen	*5 mg/kg SC or orally*	*Used pre-operatively for preemptive analgesia and*	*Depending on the procedure, may be used as sole analgesic, or as multi-modal*

		postoperatively every 24 hours for 3 days	*analgesia with buprenorphine.*
Meloxicam (Recommended)	*5 mg/kg SC or orally*	*Used pre-operatively for preemptive analgesia and postoperatively every 24 hours for 3 days*	*Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine. Recommended to give concurrent SQ fluids.*
Ketoprofen (Recommended)	*5 mg/kg SC*	*Used pre-operatively for preemptive analgesia and postoperatively every 24 hours for 3 days*	*Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine. Recommended to give concurrent SQ fluids.*
Inhalation anesthetics			
Isoflurane (Recommended)	*1-3% inhalant to effect (up to 5% for induction).*	*Survival surgery with preemptive analgesia. calibrated precision vaporizer use determined according to the pain expected as part of the IACUC protocol*	

Contact the veterinarian with questions or for additional information.

Formularies and definitions adapted from

http://ors.ubc.ca/contents/animal-care-sops-guidelines

Laboratory Animal Anaesthesia, 4th Edition, Flecknell, 2016

Formulary for Laboratory Animals, Second Edition