

<b>Institutional Animal Care and Use Committee</b>		<b>UNTHSC</b>
Title: Anesthesia in Laboratory Animals		
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**A. BACKGROUND INFORMATION**

- a. The selection of appropriate anesthetics should reflect professional veterinary judgment as to which best meets clinical and humane requirements as well as the needs of the research protocol. (*The Guide*, pg. 121).
- b. The selection of anesthetics depends on many factors, such as species, age, the type and degree of pain and the likely effects of particular agents on specific organ systems, the nature and length of the surgical procedure, and the safety of the agent (*The Guide*, pg. 121).

**B. RESPONSIBILITIES**

- a. It is the responsibility of the Principal Investigator (PI) to consult, if needed, with the Attending Veterinarian to choose the appropriate anesthetic for a specific procedure.
- b. It is the responsibility of the PI to procure the anesthetics that have been approved in the protocol. The PI must have a DEA license, if necessary, to procure controlled substances.
- c. It is the responsibility of the Principal Investigator and other research personnel who will administer anesthetics to have completed the applicable CITI training module.
- d. It is the responsibility of the PI and lab staff to use the anesthetics that have been approved in the protocol and to use them accordingly.

**C. PROCEDURES**

**a. Anesthesia Guidelines**

- i. Fasting:
  - 1. Rodents - generally not fasted before anesthesia.
  - 2. Non-Rodents – Rabbits are generally not fasted before anesthesia. It is recommended that pigs are fasted overnight.
- ii. Use of heat source: Small animals (rats, mice, hamsters) lose body heat rapidly while under anesthesia. It is recommended that a heat source (water circulating heat pad, heating pad, etc.) be used. Monitoring of body temperature with a thermometer can be done for long procedures.
- iii. Administration: Anesthesia agents can be administered by inhalation or injection. Supplemental doses can be administered as needed during the procedure.
- iv. Eye ointment – eye ointment should be used in rodents for to prevent drying of the eyes due to the loss of the blink reflex during anesthesia.
- v. Monitoring anesthesia – Before an incision is made, ensure that the animal is in an adequate plane of anesthesia.
  - 1. For rodents – test the pedal withdrawal reflex by pinching a foot pad on each foot. If the animal pulls back, additional anesthetic may need to be administered. Monitor the animal’s rate and depth of respiration (increase

in depth and decrease in rate signify anesthesia) and re-check reflexes during the procedure. Monitor the color of the animal's ears, tail, mucous membranes and foot pads.

2. For non-rodent mammals – test responsiveness to painful stimuli and rate and depth of respiration (increase in depth and decrease in rate signify anesthesia).
  3. Vital records for USDA-covered species must be turned in to the DLAM Animal Health Technician.
- vi. Post-procedure:
1. Animals should be given a heat source. Be sure the animals do not get too hot or too cold. Animals should not have direct contact with the heat source.
  2. Lab staff must stay with the animals until they have recovered from anesthesia (ambulatory).
  3. Fluids can be administered to speed recovery or to replace fluids lost during the procedure.
  4. The Surgery/Post-op Report must be completed (see SOP 034 Rodent Surgery) for rodent surgeries or procedures.

**b. Classifications of Anesthetics**

- i. Injectable - Effects of these agents cannot be reversed quickly. The drug must be metabolized, excreted or counteracted by another drug to terminate anesthetic action. Examples include sodium pentobarbital, Ketamine/Xylazine cocktail.
- ii. Inhalants - Effects of these agents can be reversed quickly. The agent is eliminated when the administration is discontinued as the animal exhales. The most common inhalant is isoflurane.
- iii. Dissociative - Agents that depress the central nervous system and produce a state of catalepsy (ketamine). These are most effective when combined with tranquilizers and sedatives (e.g., Xylazine, diazepam).

**c. Use of Isoflurane Drop Method**

Due to the occupational health and safety risks of using the drop method for isoflurane, the IACUC does not recommend this method. DLAM is equipped with vaporizer equipment for the use of isoflurane, as well as, many laboratories in various departments. If there is no vaporizer available, and there is a need to use the drop method, please justify this in the IACUC protocol. In addition, please consult with safety and the veterinarian for approval.

**d. Points to Remember**

- i. Always use the anesthetic that is listed in protocol.
- ii. Calculate the dose by body weight if using an injectable.
- iii. Drugs under the control of the Drug Enforcement Agency (DEA) must be stored in a locked cabinet in a secure area.
- iv. A written record is required when controlled drugs under the control of the DEA are used (how much of the drug you have, how much was used and for what purpose).
- v. An inventory list of anesthetics should be kept.

- e. The following listings of anesthetics (and some reversing agents) and the corresponding doses for each species must be considered for use by the Principal Investigator. If another drug not on this list is to be used, the Attending Veterinarian must be consulted.

**D. REFERENCES**

Institute of Laboratory Animal Resources (2011). Guide for the Care and Use of Laboratory Animals. National Academy Press, Washington, D.C.

## Mouse

Drug	Dose/ Route	Frequency	Notes
<b>Inhalation anesthetics</b>			
Recommended: Isoflurane or Sevoflurane	1-3% inhalant to effect (up to 5% for induction). Up to 8% for Sevoflurane	Whenever general anesthesia is required	Survival surgery requires concurrent preemptive analgesia. Must use precision vaporizer
Nitrous oxide (N2O)	Up to 60% with oxygen	Whenever deep sedation or general anesthesia is required	Not acceptable for surgery as sole agent – must be used with inhalant anesthetic to potentiate effect and lower required dose
<b>Ketamine combinations</b>			
Recommended: Ketamine- Xylazine- Acepromazine	70-100 mg/kg (K) +10-20 mg/kg (X) + 2-3 mg/kg (A) (in same syringe)	As needed	May not produce surgical-plane anesthesia for major procedures. If re-dosing, use ketamine alone. May be partially reversed with Atipamezole or Yohimbine
Ketamine- Medetomidine	50-75 mg/kg + 0.5-1 mg/kg IP (in same syringe)	As needed	May not produce surgical-plane anesthesia for major procedures. If re-dosing, use ketamine alone. May be partially reversed with Atipamezole
Ketamine- Xylazine	80-100 mg/kg +5-10 mg/kg IP (in same syringe)	As needed	May not produce surgical-plane anesthesia for major procedures. If re-dosing, use ketamine alone. May be partially reversed with Atipamezole or Yohimbine
Ketamine- Midazolam	80-100 mg/kg + 4-5 mg/kg IP (in same syringe)	As needed	May not produce surgical-plane anesthesia for major procedures, but may be useful for restraint.
Ketamine alone	100-200 mg/kg IP	As needed	Deep sedation, but not surgical anesthesia. Should not often use alone.
<b>Reversal agents</b>			
Atipamezole	0.1-1.0 mg/kg subcutaneous or IP	Any time medetomidine or xylazine had been used	More specific for medetomidine than for xylazine (as a general rule, Atipamezole is dosed at the same volume as Medetomidine, though they are manufactured at different concentrations.)
Yohimbine	1.0-2.0 mg/kg SC or IP	For reversal of xylazine effects	
<b>Other injectable anesthetics</b>			
Sodium pentobarbital (Nembutal)	40-50 mg/kg IP	Recommended for acute/ terminal procedures only, with booster doses as needed	Consider supplemental analgesia (opioid or NSAID) for invasive procedures
Tribromoethanol (Avertin)	250-500 mg/kg IP	May be used once for survival procedure (boosted as necessary during procedure) and once for terminal/acute procedure	Diluted Avertin Solution must be used within 30 days of initial preparation and be properly stored. Lower concentration (1.25%) less likely to cause peritonitis. As this is a non-pharmaceutical substance, scientific justification is needed for use in survival surgeries.

Propofol	12-26 mg/kg IV	As needed	Only useful IV, so therefore limited usefulness in mice. Respiratory depression upon induction is possible.
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## Rat

Drug	Dose/ Route	Frequency	Notes
<b>Inhalation anesthetics</b>			
Isoflurane	1-3% inhalant to effect (up to 5% for induction).	Whenever general anesthesia is required	Survival surgery requires concurrent preemptive analgesia. Must use precision vaporizer
<b>Injectable anesthetics</b>			
Recommended: Ketamine- Xylazine	75-100 mg/kg +5-10 mg/kg IP or IM (in same syringe)	As needed	
Ketamine- Dexmedetomidine	75-100 mg/kg + 0.15 mg/kg IP or IM (in same syringe)	As needed	May not produce surgical-plane anesthesia for major procedures. If re-dosing, use ketamine alone. May be partially reversed with Atipamezole
Sodium Pentobarbital (Nembutal)	40-50 mg/kg IP		Recommended for acute/terminal procedures. If used for survival surgery, should use supplemental analgesia.
<b>Reversal agents</b>			
Atipamezole	0.1-1.0 mg/kg IM or IP	Any time medetomidine or xylazine had been used	More specific for medetomidine than for xylazine (as a general rule, Atipamezole is dosed at the same volume as Medetomidine, though they are manufactured at different concentrations.)

## Hamster

Drug	Dose/ Route	Frequency	Notes
<b>Inhalation anesthetics</b>			
Recommended: Isoflurane or Sevoflurane	1-3% inhalant to effect (up to 5% for induction). Up to 8% for Sevoflurane	Whenever general anesthesia is required	Survival surgery requires concurrent preemptive analgesia. Must use precision vaporizer
<b>Ketamine combinations</b>			
Recommended: Ketamine-Diazepam	6-11 mg/kg + 0.05-0.2 mg/kg IV (in same syringe)	As needed	May not produce surgical-plane anesthesia for major procedures.
Ketamine-Medetomidine	5-10 mg/kg + 0.6 -1 mg/kg IP (in same syringe)	As needed	May not produce surgical-plane anesthesia for major procedures. If re-dosing, use ketamine alone. May be partially reversed with Atipamezole.
Ketamine-Xylazine	50-100 mg/kg +5 mg/kg IM 200 mg/kg + 10 mg/kg IP (in same syringe)	As needed	May not produce surgical-plane anesthesia for major procedures. If re-dosing, use ketamine alone. May be partially reversed with Atipamezole. Note that IM Ketamine combinations often sting upon injection.
Recommended: Ketamine-Midazolam	5-10 mg/kg + 0.1-0.5 mg/kg IM or SC (in same syringe)	As needed	May not produce surgical-plane anesthesia for major procedures, but may be useful for restraint. Note that IM Ketamine combinations often sting upon injection.
Ketamine alone	100 mg/kg IM 200 mg/kg IP	As needed	Deep sedation, but not surgical anesthesia. Not often use alone.
<b>Reversal agents</b>			
Atipamezole	0.1-1.0 mg/kg	Any time medetomidine or xylazine had been used	More specific for medetomidine than for xylazine (as a general rule, Atipamezole is dosed at the same volume as Medetomidine, though they are manufactured at different concentrations.)
<b>Other injectable anesthetics</b>			
Sodium pentobarbital (Nembutal)	20-60 mg/kg IP	Recommended for acute/ terminal procedures only, with booster doses as needed	Consider supplemental analgesia (opioid or NSAID) for invasive procedures

## Rabbit

Drug	Dose/ Route	Frequency	Notes
<b>Inhalation anesthetics</b>			
Recommended: Isoflurane or Sevoflurane	1-3% inhalant to effect (up to 5% for induction). Up to 8% for Sevoflurane	Whenever general anesthesia is required	Survival surgery requires concurrent preemptive analgesia. Must use precision vaporizer. Mask or chamber induction without injected pre-medication may result in breath-holding and injury.
Nitrous oxide (N2O)	Up to 60% with oxygen	Whenever deep sedation or general anesthesia is required	Not acceptable for surgery as sole agent – must be used with inhalant anesthetic to potentiate effect and lower required dose.
<b>Ketamine combinations</b>			
Recommended: Ketamine-Xylazine	35-50 mg/kg + 5-10 mg/kg IM or SC (in same syringe or with xylazine administered 10-20 minutes in advance)	As needed	May not produce surgical-plane anesthesia for major procedures. If redosing, use ketamine alone. May be partially reversed with Atipamezole or Yohimbine. Note that IM Ketamine combinations often sting upon injection.
Ketamine alone	20-60 mg/kg IM or SC	As needed	Deep sedation, but not surgical anesthesia should not be often used alone. Note that IM Ketamine combinations often sting upon injection.
Ketamine-Medetomidine	35-50 mg/kg + 0.5 mg/kg IM or SC (in same syringe, or with medetomidine administered 10-20 minutes in advance)	As needed	May not produce surgical-plane anesthesia for major procedures. If redosing, use ketamine alone. May be partially reversed with Atipamezole. Note that IM Ketamine combinations often sting upon injection.
Ketamine-Xylazine-Acepromazine	35-40 mg/kg + 3-5mg/kg + 0.75-1.0 mg/kg IM or SC (in same syringe)	As needed	May not produce surgical-plane anesthesia for major procedures. If redosing, use ketamine alone. May be partially reversed with Atipamezole or Yohimbine. Note that IM Ketamine combinations often sting upon injection.
Ketamine-Midazolam	35-50 mg/kg + ~2 mg/kg IM or SC (in same syringe)	As needed	May not produce surgical-plane anesthesia for major procedures, but may be useful for restraint. Note that IM Ketamine combinations often sting upon injection.
<b>Reversal agents</b>			
Atipamezole	0.1-1.0 mg/kg subcutaneous or IP	Any time medetomidine or xylazine has been used	More specific for medetomidine than for xylazine (as a general rule, Atipamezole is dosed at the same volume as Medetomidine, though they are manufactured at different concentrations).
Yohimbine	~ 0.2 mg/kg IV or SC	For reversal of xylazine effects	
<b>Other injectable anesthetics</b>			
Sodium pentobarbital (Nembutal)	20-60 mg/kg IV	Recommended for terminal/ acute procedures	Consider supplemental analgesia (opioid or NSAID) for invasive procedures. Apnea is common at anesthetic doses.

		only, with booster doses as needed	
Propofol	12-26 mg/kg IV	As needed	Only useful IV, so therefore limited usefulness. Respiratory depression upon induction is possible.

## Swine

Drug	Dose/ Route	Frequency	Notes
<b>Inhalation anesthetics</b>			
Recommended: Isoflurane or Sevoflurane	1-3% inhalant to effect (up to 5% for induction). Up to 8% for Sevoflurane	Whenever general anesthesia is required	Concurrent preemptive analgesia is recommended for survival surgery. Must use precision vaporizer. Mask induction is possible with very small pigs.
Nitrous oxide (N2O)	Up to 60% with oxygen	Whenever deep sedation or general anesthesia is required	Not acceptable for surgery as sole agent – must be used with inhalant anesthetic to potentiate effect and lower required dose.
<b>Dissociative (Ketamine and/or Telazol®) combinations</b>			
Ketamine alone	11-33 mg/kg IM	Any time sedation is required	Cannot be used as sole agent in swine.
Recommended: Ketamine-Xylazine	15-20 mg/kg + 1.1 – 2.2 mg/kg IM (in same syringe)	Prior to general anesthesia	Can result in large volumes – consider using Telazol ® or Telazol ® combination as alternative.
Recommended: Telazol® alone (a combination of tiletamine and zolazepam – when reconstituted with 5 ml sterile water, a vial contains 50 mg/ml of each drug. Dose listed is based on 100mg/ml of combined active ingredients)	6-8 mg/kg IM ( + .06-.08 ml/kg)	For sedation or pre-anesthesia	Note that Telazol ® must be stored refrigerated once reconstituted.
Telazol®-Ketamine-Xylazine (TKX)	~ 0.025 ml of cocktail per kg IM	For sedation or pre-anesthesia	Note that Telazol® must be stored refrigerated once reconstituted. To mix: reconstitute Telazol® with large animal xylazine (100mg/ml) instead of water; add 5 ml ketamine (concentration of 100mg/ml)
Xylazine – Telazol®	2.2-8.8 mg/kg + 2- 8.8 mg/kg	For sedation or pre-anesthesia	Note that Telazol® must be stored refrigerated once reconstituted. To mix: reconstitute Telazol ® with 5 ml of large animal xylazine (100mg/ml) instead of water.
Ketamine-Diazepam Continuous infusion	~ 0.2 mg/kg + ~ 0.0005 mg/kg/hr	Sedation for imaging or other prolonged procedure – not adequate anesthesia for surgical procedures.	Not adequate anesthesia for surgical procedures.



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## Swine Continued

<b>Reversal agents</b>			
Atipamezole	~1.0 mg/kg subcutaneous or IM	Any time medetomidine or xylazine has been used	More specific for medetomidine than for xylazine (as a general rule, Atipamezole is dosed at the same volume as Medetomidine, though they are manufactured at different concentrations).
<b>Other injectable anesthetics and tranquilizers</b>			
Sodium pentobarbital (Nembutal)	20-60 mg/kg IV single or intermittent bolus, or 2-20 mg/kg/hr IV continuous infusion	Recommended for terminal/acute procedures only, with booster doses as needed	Consider supplemental analgesia (opioid or NSAID) for invasive procedures.
Propofol	16-22 mg/kg IV	As induction agent, prior to general anesthesia with pentobarbital or inhalant	Respiratory depression upon induction is possible.
Acepromazine	0.08 – 0.2 mg/kg IM or SC	May be used whenever ketamine combinations are used	Usually only used in conjunction with anesthetics such as ketamine. Acepromazine is a tranquilizer and does not confer analgesia.