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**1. PURPOSE**

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This Standard Operating Procedure (SOP) describes methods for anesthetizing non-human primates (NHPs).

**2. RESPONSIBILITY**

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Veterinarian, veterinary care staff

**3. INTRODUCTION**

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- 3.1. Perform a thorough physical exam and obtain an accurate body weight.
- 3.2. Withhold food (not water) for 12 hours prior to anesthesia in order to reduce the risk of aspiration of stomach contents. Juveniles or small species such as marmosets should only be fasted 4 to 6 hours to help avoid hypoglycemia.
- 3.3. Monitor animals closely during induction, maintenance, and recovery from general anesthesia. Monitoring must be documented.
  - 3.3.1. Never leave an anesthetized animal unattended.
  - 3.3.2. Monitor animal every 5 minutes; record the following parameters every 15 minutes:
    - 3.3.2.1. Anesthetic depth: absence of reflexes, e.g., pedal/eyelid/eyelash/palpebral, absence of movement, muscle relaxation (jaw tone).
    - 3.3.2.2. Respiratory function (ventilation): respiratory rate, oxygen saturation (SpO<sub>2</sub>), thoracic wall or rebreathing bag movements, and auscultation. End-tidal carbon dioxide (ETCO<sub>2</sub>) should be included where capnography equipment is available. Blood gas analysis may be indicated for critical patients or procedures.
    - 3.3.2.3. Cardiovascular function (circulation): capillary refill time (CRT), mucous membrane color, pulse quality, heart rate and rhythm, and blood pressure. Electrocardiography (ECG) should be included where equipment is available.
    - 3.3.2.4. Body temperature: rectal or esophageal temperature.
- 3.4. Apply ophthalmic ointment to prevent corneal desiccation. Reapply as needed, every 30 minutes at a minimum.
- 3.5. Keep animals warm by providing a heat source until the animal has recovered from anesthesia. Care should be taken to not overheat or burn the animals.
- 3.6. Maintain records of each anesthesia procedure and include:
  - 3.6.1. Date and time of procedure
  - 3.6.2. Principal investigator and Animal Use Protocol (AUP)
  - 3.6.3. Species and animal's identification
  - 3.6.4. Animals' weight
  - 3.6.5. Name, dose, route, and time of administration of each drug
  - 3.6.6. Description of the procedure
  - 3.6.7. Measurements of the animal's anesthetic depth and vital signs
  - 3.6.8. Time of recovery
  - 3.6.9. Name of the individual monitoring the animal and of the surgeon

#### 4. MATERIALS

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- 4.1. Material or equipment to provide or conserve body heat (e.g. warm-water circulating pad)
- 4.2. Ophthalmic ointment (natural tears)
- 4.3. Animal weighing scale
- 4.4. Gas anesthesia machine (calibrated within the last 12 months) with adequate gas scavenging system or filter
- 4.5. Tight-fitting mask
- 4.6. Monitoring equipment, e.g., stethoscope, thermometer, pulse oximeter, capnograph, ECG
- 4.7. Isoflurane
- 4.8. Glycopyrrolate (0.2 mg/mL)
- 4.9. Intra-venous catheter
- 4.10. Ketamine (100 mg/mL) \*Controlled drug
- 4.11. Diazepam (5 mg/mL) \*Controlled drug
- 4.12. Xylazine (20 mg/mL)
- 4.13. Dexmedetomidine (0.5 mg/mL)
- 4.14. Atipamezole (5 mg/mL)
- 4.15. Midazolam (5 mg/mL) \*Controlled drug
- 4.16. Thiopental sodium (Pentothal) powder \*Controlled drug
- 4.17. Propofol (10 mg/mL)
- 4.18. Alfaxalone (10 mg/ml)
- 4.19. Sterile isotonic saline (0.9% saline) or Lactated Ringer's Solution (LRS)
- 4.20. Xylocaine spray
- 4.21. Sterile lubricant (e.g., water soluble jelly)
- 4.22. Endotracheal tubes, cuffed
- 4.23. Laryngoscope
- 4.24. Plain gauze rolls

#### 5. PROCEDURES

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- 5.1. Premedication:
  - 5.1.1. Can be used for longer procedures to control salivation.
  - 5.1.2. Administer glycopyrrolate, intramuscularly
    - 5.1.2.5. Macaque: 0.004 to 0.008 mg/kg
    - 5.1.2.6. Marmoset: 0.005 to 0.01 mg/kg
  - 5.1.3. Glycopyrrolate should not be administered in conjunction with Alpha-2 agonists, e.g., xylazine and dexmedetomidine.
- 5.2. Injectable anesthesia:
  - 5.2.1. Can be used alone for short, non-invasive procedures.
  - 5.2.2. Used for induction prior to use of isoflurane anesthesia for smooth and rapid induction and to facilitate intubation.

Drug	Dose		Route	Duration of Effect	Notes
	Macaque	Marmoset			
Ketamine	10 to 15 mg/kg	15 to 20 mg/kg	IM	15 to 30 minutes	
Ketamine Diazepam	15 mg/kg 1 mg/kg	15 to 20 mg/kg 1 mg/kg	IM	30 minutes to 1 hour	Can be mixed in the same syringe.
Ketamine Xylazine	7 mg/kg 0.6 mg/kg	10 to 20 mg/kg 3 mg/kg	IM	30 minutes to 2 hours	Can be mixed in the same syringe. Can be reversed with atipamezole by administering the same volume of xylazine used.
Ketamine Dexmedetomidine	5 to 10 mg/kg 0.05 mg/kg	10 to 20 mg/kg 1 mg/kg	IM	30 minutes to 2 hours	Can be mixed in the same syringe. Can be reversed with atipamezole by administering the same volume of Dexmedetomidine used.
Ketamine Midazolam	8 mg/kg 0.2 mg/kg	10 to 15 mg/kg 1 mg/kg	IM	30 to 45 minutes	Can be mixed in the same syringe.
Propofol	Loading dose: 2 to 5 mg/kg Infusion: 0.3 to 0.4 mg/kg/min	Loading dose: 7 to 8 mg/kg Infusion: 0.9mg/kg/min	IV, slowly	Until discontinued	May produce apnea.
Alfaxalone		7-10 mg/kg	IM	30-45 minutes	May cause respiratory depression.

5.3. Intravenous (IV) catheter placement:

5.3.1. To provide IV fluid therapy and venous access during surgery.

5.3.2. Insert IV catheter in either the cephalic, saphenous, or tail vein and secure.

5.4. IV fluid administration:

5.4.1. Administer isotonic saline (0.9% saline) or Lactated Ringer's Solution at a rate of 5-10 mL/kg/hour.

5.5. Endotracheal intubation:

5.5.1. Placement of an endotracheal tube is recommended for maintaining open airways for delivery of isoflurane anesthesia when:

5.5.1.1. Profound sedation, preventing protective airway reflexes, is required. As a guide, light sedation should last under 30 minutes and is performed for less invasive procedures.

5.5.1.2. Surgical level anesthesia is required.

5.5.1.3. Head or airway cannot be accessed readily due to position, equipment, etc.

5.5.2. Cuffed endotracheal tubes are preferred as they reduce the possibility of aspiration of saliva or stomach contents.

5.5.3. Intubation:

5.5.3.1. Lubricate endotracheal tube with sterile lubricant.

5.5.3.2. With the animal in sternal recumbency, extend the neck and head so that they are in a straight line.

5.5.3.3. While holding the upper jaw, pull the tongue forward and down so that the epiglottis is visible.

- 5.5.3.4. Use the laryngoscope to disengage the epiglottis from the soft palate, exposing the glottis and vocal chords.
  - 5.5.3.5. The laryngeal folds may be sprayed with 2% xylocaine to help decrease laryngospasm (spasmodic closing and opening of the glottis).
  - 5.5.3.6. Insert the endotracheal tube (with the convex side facing upwards) gently into the proximal larynx.
  - 5.5.3.7. Gently rotate the endotracheal tube 180° and apply gentle pressure to insert into the trachea. Confirm proper placement by checking for the animal's breath as it exits the endotracheal tube during exhalation.
  - 5.5.3.8. Secure the endotracheal tube by tying a piece of gauze around the tube then behind the animal's head.
  - 5.5.3.9. Inflate the cuff of the endotracheal tube.
  - 5.5.3.10. Verify adequate ventilation of both lungs by auscultation.
- 5.6. Isoflurane anesthesia:
- 5.6.1. Induction (if injectable anesthetics cannot be used; the animal needs to be premedicated to reduce stress of induction):
    - 5.6.1.1. Use a tight-fitting mask.
    - 5.6.1.2. Adjust the oxygen flowmeter to 0.8 to 1.5 L/min.
    - 5.6.1.3. Adjust the isoflurane vaporizer to 3%, increase as needed to effect.
  - 5.6.2. Maintenance:
    - 5.6.2.1. Use the endotracheal tube or mask connected to the Bain circuit.
    - 5.6.2.1. Adjust the flowmeter to 0.8 to 1.5 L/min.
    - 5.6.2.2. Adjust the isoflurane vaporizer to 1.0 to 2.0% (dose to effect).
    - 5.6.2.3. Apply ophthalmic ointment (natural tears) to both eyes.
    - 5.6.2.4. When not under assisted ventilation, animal should be manually ventilated or "bagged" every 5-10 minutes to ensure proper air exchanges.
  - 5.6.3. Recovery:
    - 5.6.3.1. Turn off the isoflurane vaporizer but keep the animal on oxygen for 2 to 5 minutes or longer if oxygen saturation levels are low.
    - 5.6.3.2. Remove the endotracheal tube as soon as the animal shows signs of impending arousal, i.e., when the animal starts swallowing on its own and reflexes begin to return.
    - 5.6.3.3. Monitor the animal in his home cage until it is ambulatory to ensure it regains full consciousness.

## 6. REFERENCES

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- 6.1. Carpenter, J. W., & Marion, C. J. (2013). Exotic animal Formulary. Saunders.
- 6.2. Marini, R. P., Wachtman, L. M., Tardif, S. D., Mansfield, K., & Fox, J. G. (2018). The Common Marmoset in Captivity and Biomedical Research. Academic Press.
- 6.3. Goodroe, A., Fitz, C., & Bakker, J. (2020). Current Topics in Marmoset Anesthesia and Analgesia. ILAR journal, 61(2-3), 218–229. <https://doi.org/10.1093/ilar/ilab001>

## SOP REVISION HISTORY

DATE	NEW VERSION
2024.01.12	2. RESPONSIBILITY Veterinarian, veterinary care staff
2024.01.12	<b>3.3. Monitor animals closely during induction, maintenance, and recovery from general anesthesia. Monitoring must be documented.</b> 3.3.1. Never leave an anesthetized animal unattended. <b>3.3.2. Monitor animal every 5 minutes; record the following parameters every 15 minutes:</b> 3.3.2.1. Anesthetic depth: absence of reflexes, e.g., pedal/eyelid/eyelash/palpebral, absence of movement, muscle relaxation (jaw tone). 3.3.2.2. Respiratory function (ventilation): respiratory rate, oxygen saturation (SpO <sub>2</sub> ), thoracic wall or rebreathing bag movements, and auscultation. End-tidal carbon dioxide (ETCO <sub>2</sub> ) should be included where capnography equipment is available. Blood gas analysis may be indicated for critical patients or procedures. 3.3.2.3. Cardiovascular function (circulation): capillary refill time (CRT), mucous membrane color, pulse quality, heart rate and rhythm, and blood pressure. Electrocardiography (ECG) should be included where equipment is available. 3.3.2.4. Body temperature: rectal or esophageal temperature.
2024.01.12	<b>3.4. Apply ophthalmic ointment to prevent corneal desiccation. Reapply as needed, every 30 minutes at a minimum.</b>
2024.01.12	<b>3.6. Maintain records of each anesthesia procedure and include:</b> 3.6.1. Date and time of procedure 3.6.2. Principal investigator and Animal Use Protocol (AUP) 3.6.3. Species and animal's identification 3.6.4. Animals' weight 3.6.5. Name, dose, route, and time of administration of each drug 3.6.6. Description of the procedure 3.6.7. Measurements of the animal's anesthetic depth and vital signs 3.6.8. Time of recovery 3.6.9. Name of the individual monitoring the animal and of the surgeon
2024.01.12	<b>4.3. Animal weighing scale</b>
2024.01.12	<b>4.5. Monitoring equipment, e.g., stethoscope, thermometer, pulse oximeter, capnograph, ECG</b>
2024.01.12	<del>4.9. Sevoflurane</del>
2024.01.12	<del>5.2.3. Anesthesia protocols:</del>
2024.01.12	5.2. Drug: Ketamine - Xylazine, Dose Macaque: 7 mg/kg - 0.6 mg/kg, Dose Marmoset: 10 to 20 mg/kg - 3 mg/kg, Route: IM, Duration of Effect: 30 minutes to 2 hours, Notes: Can be mixed in the same syringe. <b>Can be reversed with atipamezole by administering the same volume of xylazine used.</b>
2024.01.12	5.2. Drug: Ketamine – Midazolam, Dose Macaque: 8 mg/kg - 0.2 mg/kg, Dose Marmoset: <b>10 to 15 mg/kg - 1 mg/kg</b> , Route: IM, Duration of Effect: 30 to 45 minutes, Notes: Can be mixed in the same syringe.
2024.01.12	<del>5.2. Drug: Pentothal, Dose Macaque and Marmoset: 5 mg/kg, Route: IV, slowly, Duration of Effect: 15 minutes, Notes: May produce apnea. Administer slowly to effect.</del>
2024.01.12	5.3.2. Insert IV catheter in either the cephalic, <del>or</del> saphenous, <b>or tail vein</b> and secure.
2024.01.12	5.4.1. Administer isotonic saline (0.9% saline) or Lactated Ringer's Solution at a rate of 5-10 mL/kg//hour.
2024.01.12	5.5.1. Placement of an endotracheal tube is recommended <del>for maintaining open airways for delivery of isoflurane anesthesia when:</del> <b>5.5.1.1. Profound sedation, preventing protective airway reflexes, is required. As a guide, light sedation should last under 30 minutes and is performed for less invasive procedures.</b> <b>5.5.1.2. Surgical level anesthesia is required.</b> <b>5.5.1.3. Head or airway cannot be accessed readily due to position, equipment, etc.</b>
2024.01.12	<b>5.5.3.5. Spray</b> The laryngeal folds <b>may be sprayed</b> with 2% xylocaine to help decrease laryngospasm (spasmodic closing and opening of the glottis).
2024.01.12	5.6.1. Induction (if injectable anesthetics <del>not previously administered</del> <b>cannot be used; the animal needs to be premedicated to reduce stress of induction</b> ):
2024.01.12	5.6.1.3. Adjust the isoflurane vaporizer to 3% <del>to 5%</del> , <b>increase as needed to effect.</b>
2024.01.12	5.6.2.3. Apply ophthalmic ointment (natural tears) to both eyes <del>to prevent dryness and damage to the cornea.</del>
2024.01.12	5.6.3.2. Remove the endotracheal tube as soon as the animal shows signs of impending arousal, i.e., when <b>the animal starts swallowing on its own</b> and reflexes begin to return.
2024.01.12	5.6.3.3. Monitor the animal in his home cage <del>to ensure it regains full consciousness and able to stand in a sternal position until it is ambulatory to ensure it regains full consciousness.</del>

2024.01.12	<p>5.7. Sevoflurane anesthesia:</p> <p>5.7.1. Induction (if injectable anesthetics not previously administered):</p> <p>5.7.1.1. Use a tight fitting mask.</p> <p>5.7.1.2. Adjust the oxygen flowmeter to 0.8 to 1.5 L/min.</p> <p>5.7.1.3. Adjust the vaporizer to 5% to 8%.</p> <p>5.7.2. Maintenance:</p> <p>5.7.2.1. Use the endotracheal tube or mask connected to the Bain circuit.</p> <p>5.7.2.2. Adjust the flowmeter to 0.8 to 1.5 L/min.</p> <p>5.7.2.3. Adjust the vaporizer to 1.0 to 3.0% (dose to effect).</p> <p>5.7.2.4. Apply ophthalmic ointment (natural tears) to both eyes to prevent dryness and damage to the cornea.</p> <p>5.7.2.5. When not under assisted ventilation, animal should be manually ventilated or “bagged” every 5-10 minutes to ensure proper air exchanges.</p> <p>5.7.3. Recovery:</p> <p>5.7.3.1. Turn off the vaporizer but keep the animal on oxygen for 2 to 5 minutes or longer if oxygen saturation levels are low.</p> <p>5.7.3.1. Remove the endotracheal tube as soon as the animal shows signs of impending arousal, i.e., when reflexes begin to return.</p> <p>5.7.3.1. Monitor the animal in his home cage to ensure it regains full consciousness and able to stand in a sternal position.</p>
2024.01.12	<p>6.2. Marini, R. P., Wachtman, L. M., Tardif, S. D., Mansfield, K., &amp; Fox, J. G. (2018). The Common Marmoset in Captivity and Biomedical Research. Academic Press.</p> <p>6.3. Goodroe, A., Fitz, C., &amp; Bakker, J. (2020). Current Topics in Marmoset Anesthesia and Analgesia. ILAR journal, 61(2-3), 218–229.  <a href="https://doi.org/10.1093/ilar/ilab001">https://doi.org/10.1093/ilar/ilab001</a></p>