GUIDELINES ON ANESTHESIA AND ANALGESIA IN LABORATORY ANIMALS

University of South Florida provides the following guidelines for use by IACUC-certified faculty and staff.

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A. Background

1. A fundamental responsibility of individuals that use animals in research, teaching or testing is to anticipate and eliminate or minimize any potential that procedures may cause animal pain, distress, or discomfort.

2. Although animals that are in pain may not behave like humans, (e.g., pain in animals may be accompanied by immobility and silence, in contrast to the groans and cries of human patients), it is assumed that **procedures that cause pain in humans cause pain in animals**.

3. The presence of pain in animals can be recognized by alterations in animal behavior (e.g., reduced activity, reduced grooming, hunched-up posture, altered gait, changes in temperament, vocalizations, reduced food and water intake, reduced urinary and fecal output), and in physiological variables, (e.g., reduced depth of respiration, increased heart rate, and reduced hydration status) (refer to Table I).

4. Animal pain, distress, and discomfort can **produce a range of undesirable physiological changes, which may radically alter measured responses to experimental stimuli**, as well as the rate of recovery from surgical procedures, hence, its avoidance and alleviation are in the best interest of both the animal and researcher.

5. Reducing post-procedural/post-operative pain, distress, and discomfort is accomplished by **good nursing care**, (e.g., keeping the animal warm, clean, dry and well padded), and by the administration of **analgesic drugs**.

6. The selection of an appropriate analgesic involves consideration of the level of animal pain anticipated or presumed, the species involved, and the experimental protocol. Severe pain, such as may occur during the post-operative period, can be alleviated by the administration of narcotic analgesics, (e.g., buprenorphine, an opioid partial agonist). Non-steroidal anti-inflammatory drugs, with or without the infusion of local anesthetics, can control mild to moderate pain, in some species, though is contra-indicated in others. Selection of an appropriate route of administration also involves consideration of the

recipient species. For example, oral analgesic drug delivery to rodents (e.g., acetaminophen elixir added to the drinking water of rats) may not afford detectable analgesia.

7. In addition to the avoidance and alleviation of pain and discomfort, adequate post-procedural /post-operative animal care also includes efforts to prevent and/or treat post-anesthetic complications, (e.g., aspiration, hypostatic pneumonia, cardiovascular and respiratory depression, dehydration, and infection).

8. Reducing the potential for laboratory animal pain, distress, or discomfort is required by the *U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training,* the *Guide for the Care and Use of Laboratory Animals (1996 ed.),* and the *Animal Welfare Act (Public Law 89-544)*.

9. The prevention or minimization of animal pain, distress, or discomfort by the proper use of tranquilizers, anesthetics, and analgesics is scientifically and ethically essential to the humane care, use, and treatment of research animals. The use of these classes of drugs must effectively prevent or minimize suffering and discomfort of animals during potentially painful procedures.

10. The use of these three classes of drugs must be in accordance with currently accepted veterinary medical practice and produce in the subject animal an appropriate level of tranquilization, anesthesia, or analgesia consistent with the protocol or design of the experiment.

11. These guidelines are provided as a resource for the use of IACUC-certified University of South Florida research faculty using animals in research, teaching, or testing.

12. Always **consult University laboratory animal veterinarians** whenever designing a research, teaching or testing protocol that involves animals.

B. Definitions

- Neuroleptic - produces central nervous depression, depression of excitability of the autonomic nervous system, a dulling of consciousness and a reduction of spontaneous motor activity (e.g., tranquilizers/sedatives).

- Analgesia - relief from pain.

- Preemptive analgesia - managing pain before it begins.

- Tranquilization - a state of behavioral change in which the patient is relaxed, unconcerned by its surroundings, and often, indifferent to minor pain.

- Sedation - a mild degree of central depression in which the patient is awake but calm; larger doses of sedative may lead to narcosis.

- Narcosis - a drug-induced state of sedation in which the patient is oblivious to pain.

- Local anesthesia - loss of sensation in a limited body area.

- Regional anesthesia – loss of sensation in a larger, though limited, body area.

- Basal anesthesia - a light level of general anesthesia usually produced by preanesthetic agents; serves as a basis for deeper anesthesia following the administration of other agents.

- General anesthesia - complete unconsciousness

- Surgical anesthesia - unconsciousness, accompanied by muscular relaxation to such a degree that surgery can be performed painlessly.

- Neuroleptanalgesia - a state of central nervous system depression and analgesia usually produced by a combination of a neuroleptic and a narcotic analgesic.

C. General Considerations

1. In order to reduce anesthetic risk and prevent post-anesthetic complications, animals must first be examined for signs of disease or distress including, but not limited to, ruffled, matted or dull hair coat, labored breathing, lack of inquisitiveness, failure to respond to stimuli, abnormal posture/positioning, dehydration, or impaired locomotion.

2. Acclimatizing animals allows them to adjust physiologically and psychologically to their new environment and provides the opportunity to carefully monitor for any abnormalities. Animals should be acclimatized for a minimum of 7 days.

3. When planning to administer drugs, recall that **dosage charts** for anesthetic and analgesic agents state only the **average amount of drug** that would be expected to produce a desired level of anesthesia or analgesia under standard conditions. Consequently, animals must be monitored carefully and the dosages tailored to meet each clinical and research situation.

4. The duration of anesthesia produced by the anesthetic should coincide with the expected duration of the operative procedure. The duration of analgesia produced by the analgesic should coincide with the expected duration and intensity of post-operative pain generated by the procedure. The time required for post-surgical recovery from anesthesia, as well as the frequency of administration of analgesics should be based on the species, anesthetics used, and the procedure performed. Knowledge, experience and skill with available agents and equipment are essential to the successful use of anesthetics and analgesics.

D. Controlled Substances

1. Many of the drugs described in this guide have the potential for human abuse, and must be maintained in a manner consistent with *Public Law 91-513* and IACUC Principle and Procedure XIV.

2. Faculty members requesting, possessing, or using any controlled substance in research or teaching must be registered with the Division of Comparative Medicine by the Surgical Core Manager.

3. Controlled Substances must be ordered through the Surgical Core Manager in writing using a *Comparative Medicine Order Form* at least 24 hours prior to being dispensed.

4. The following is a partial list of controlled substances that are used in laboratory animals.

   - **Schedule I** – A drug or other substance that has a high potential for abuse, and no currently accepted medical use in treatment in the United States.

   - **Schedule II** – A drug or other substance that has a high potential for abuse, and a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions. Abuse of these drugs or other substances may lead to severe psychological or physical dependence (e.g., Codeine, Fentanyl, Meperidine, Morphine, Pentobarbital).

   - **Schedule III** – A drug or other substance that has a potential for abuse less than those drugs or substances in schedules I and II, and has a currently accepted medical use in treatment in the United States. Abuse of these drugs or substances may lead to moderate or low physical dependence or high psychological dependence (e.g., Ketamine, Thiopental, Telazol or Tiletamine + Zolazepam, Buprenorphine).

   - **Schedule IV** – A drug or other substance that has a low potential for abuse relative to the drugs or substances in schedules I-III, and has a currently accepted medical use in treatment in the United States. Abuse of the drug or other substance may lead to limited physical dependence or psychological dependence (e.g., Butorphenol, Diazepam, Pentazocine).

   - **Schedule V** - A drug or other substance that has a low potential for abuse relative to the drugs or substances in schedule IV, and has a currently accepted medical use in treatment in the United States. Abuse of the drug or other substance may lead to limited physical dependence or psychological dependence relative to the drug or other substance in schedule IV.

E. Pre-Anesthetic Treatments

1. Pigs, cats, dogs, and primates should be fasted for 8-12 hours to minimize the risk of vomiting and aspiration of vomit during induction of anesthesia and during recovery. Since rabbits and rodents do not vomit, they do not require fasting. Fasting ruminants has little effect on the volume of ingesta in the rumen.

2. All animals should have access to drinking water until one hour prior to induction of anesthesia.

3. Animals should be weighed to ensure accurate drug dosage calculations.

4. Drugs such as anticholinergics, tranquilizers, or sedatives are given as anesthetic pre-treatments to minimize stress, anxiety or excitement of the patient, to ease the transition to the first plane(s) of general anesthesia, to decrease the amount of anesthetic agent, to prevent vomiting, and to control salivary and bronchial secretions.

5. Administering a sedative or tranquilizer when the animal is still in its pen or cage and allowing the drug to take effect before moving the animal to the prep area or operating room may significantly reduce the animal's stress.

6. **Anticholinergics** (e.g., atropine sulfate, glycopyrrolate) block parasympathetic impulses to the cardiopulmonary system, glands, and smooth muscle. Consequently, they prevent vaso-vagal reflexes, slow the heart (bradycardia), and reduce salivary gland and bronchial secretions. The effectiveness of atropine varies among species, especially rabbits. Some rabbits (up to 50%) may produce **atropinesterase** that rapidly degrades atropine. Glycopyrrolate, which is less affected by atropinesterase, is recommended for use in rabbits.

7. **Tranquilizers** and **sedatives** (e.g., the phenothiazine tranquilizer acepromazine, the butyrophenone tranquillizers droperidol, or azaperone, and the benzodiazepine sedatives diazepam, or zolazepam) **do not produce analgesia**. Tranquilizers produce a calming effect, facilitate handling, and reduce the amount of anesthetic required for induction and maintenance of anesthesia without producing a loss of consciousness. Tranquilizers may enhance anesthetic recovery when used with analgesics. Tranquilizers can provide additional skeletal muscle relaxation when that which is produced by the anesthetic is not adequate. Combining acepromazine and ketamine produces muscle relaxation in cats and rabbits, but not surgical anesthesia. Sedatives produce mild central nervous system depression and reduce fear and apprehension without loss of consciousness. They produce good muscle relaxation. Like tranquilizers, sedatives reduce the amount of anesthetic required and enhance anesthetic recovery when used with analgesics. Loud noises can counteract the calming effect of these drugs. Sufficient time should be allowed for these drugs to attain their maximum effect before inducing anesthesia.

8. **Alpha$_2$-adrenergic agonists** (e.g., xylazine, detomidine, medetomidine) mediate analgesia, anxiolysis, sedation, sympatholysis, and control of hypertension. These drugs are usually classified as sedative-analgesics and skeletal muscle relaxants. There is wide species variation in the reaction to these drugs. Xylazine sedation may be reversed using yohimbine, tolazoline, or idazoxan. Atipamezole is a highly selective and potent α_2-antagonist that rapidly reverses sedation as well as other behavioral and physiologic effects of medetomidine. Xylazine is often used in combination with ketamine to produce anesthesia in laboratory animals.

F. General Anesthetics

1. Anesthesia is the act of providing sensation-free relief from pain or pain-producing procedures. Anesthesia must be performed by a person with knowledge of and familiarity with the drugs to be used in the animal species under consideration. The Principal Investigator must ensure adherence to IACUC-approved procedures during performance of the protocol, and is responsible for ensuring that they and their staff are trained in the proper use of tranquilizers, anesthetics, and analgesics appropriate for the species and planned procedures.

2. Many factors can affect the activity of anesthetics. The species, strain, sex, age, nutritional and disease status, relative body size, disposition/demeanor, presence of concurrent pain or distress, or medication are known to cause a variation in the amount of drug needed to produce a desired effect in an individual animal.

3. Although the mechanisms of action vary, anesthetics produce, in a controllable manner, both loss of consciousness and an absence of motor response to noxious stimuli. This unconsciousness, analgesia, and muscle relaxation should be sufficient to allow the performance of procedures without the subject experiencing pain. In addition to these effects, anesthetics also produce a depressant effect on the cardiovascular, respiratory, and thermo-regulatory systems. Their use must be monitored closely.

4. The level of anesthesia should be limited to the induction of the minimal degree of CNS depression necessary for performing the procedure. When an injected anesthetic agent is used, drug dose calculation should be based on body weight and age. General anesthesia must be given "to effect," as noted in physiologic responses and in response to noxious stimuli. It is important to realize that some drugs take time to take effect. Anesthetic death can be attributed to giving the anesthetic insufficient time to work. This is especially true of parentally administered drugs (e.g., barbiturates). Once they are injected, there is little the anesthetist can do to control the outcome.

5. **Inhaled Anesthetics** (e.g., halothane, enflurane, isoflurane, sevoflurane, desflurane) have a greater margin of safety and produce a more stable plane of surgical anesthesia, when used with a calibrated vaporizer, than injectable anesthetics. Since these anesthetics enter and leave the body via the respiratory system, the concentration of the anesthetic in the blood and brain can be changed rapidly, thus readily altering the depth of anesthesia. Elimination of these anesthetics is primarily by the lungs, allowing rapid induction and smooth recovery.

6. Intubation is the recommended method for administering inhalant agents, although inhaled anesthetics can be administered by mask. Both provide a constant, high concentration of O_2 to the patient. Intubation allows rapid response to hypoventilation or respiratory arrest through mechanical ventilation using the anesthetic machine.

7. Safety precautions should include the protection of humans from vapors of inhalant anesthetics, which can cause reproductive and other health problems. This is best accomplished by the use of an approved gas scavenging system or by using the inhalant anesthetic agent inside an approved fume hood. Intubation eliminates the release of gas into the room air that occurs when a mask is used.

8. **Injected Anesthetics** (e.g., the barbiturates pentobarbital or thiopental, or the dissociative anesthetics ketamine or tiletamine) produce a depth of anesthesia that cannot be readily altered. Injectable agents are eliminated by redistribution in the body, liver metabolism, and renal excretion. Recovery from these agents is more dependent on hepatic and renal function as well as body mass and fat than inhaled anesthetics. Animals under injectable anesthesia usually are not intubated and breath room air that is approximately 20% O_2**.** Hence, patient animal responses to respiratory emergencies are delayed. Despite these drawbacks injectable anesthetics are safe and effective to use in many situations. (Note: Ketamine should be used in combination with xylazine or diazepam to produce surgical anesthesia.)

G. Neuromuscular Blocking Agents

1. Neuromuscular blocking agents (immobilizing drugs or paralytics) inhibit the transmission of nerve impulses at the neuromuscular junction (e.g., succinylcholine) or at spinal synapses (e.g., mephenesin, guaifenesin) resulting in skeletal muscle paralysis and profound muscular relaxation without loss of consciousness. These agents are used as an adjunct in surgical anesthesia to obtain more complete muscle relaxation for specific procedures (e.g., bone fracture repair in heavily muscled animals such as horses).

2. Depolarizing neuromuscular blocking drugs (e.g., succinylcholine) cannot be reversed. Competitive neuromuscular blocking agents (e.g., d-tubocurarie, pancuronium) can be reversed by administering anticholinesterases (e.g., neostigmine, pyridostigmine). These agents produce muscle paralysis only. They **do not produce sedation or analgesia**, and must never be used as an anesthetic or analgesic agent (*9 CFR 2.31: NRC. 1996: PHS. 1996*). Since these agents paralyze the muscles of respiration, endotracheal intubation and mechanical ventilation are necessary. Neuromuscular blocking agents, when used in surgical procedures, are restricted to anesthetized animals.

H. Monitoring Anesthesia

1. General anesthesia always carries the risk of compromising the patient's vital functions and even death. Animals should be closely monitored during induction, maintenance, and recovery from general anesthesia. Cardiovascular, respiratory, thermo-regulatory functions, and depth of anesthesia must be frequently assessed. This requires observation of both **vital signs** (e.g., heart rate, respiratory rate and depth, color of mucous membranes, capillary refill time, body temperature) and **reflexes** (e.g., toe pinch, tail pinch, eyelid/eyelash, palpebral). Vital signs are indicators of basic homeostatic functions and reflexes help to assess depth of anesthesia. No one parameter is sufficient to assess the effect of anesthesia on a patient. All parameters must be considered in combination to determine the animal's response to anesthesia.

2. Reflexes are absent and muscle tone is relaxed during surgical anesthesia. The pedal withdrawal reflex (i.e., toe pinch), eyelid/eyelash reflex, palpebral reflex, and the tone of jaw and anal sphincter muscles can be readily evaluated in larger mammals such as dogs, cats, and pigs. The pedal withdrawal reflex can be used in all species. In rodents pinching the tail may be used as an alternate if the limbs are inaccessible. Ocular position and pupillary size are unreliable indicators of depth of anesthesia. However, a widely dilated pupil, with little or no iris visible, should always cause concern, since it may be the result of an excessively deep plane of anesthesia, or hypoxia.

3. Respiratory Signs – Anesthetists should monitor the rate, rhythm, and depth of respiration and mucous membrane color. An increase in respiratory depth, regular rhythm, and decrease in respiratory rate signifies surgical anesthesia. Cyanotic mucous membranes indicate hypoxemia from inadequate lung ventilation. Opioids can cause severe respiratory depression, which can be reversed by the administration of naloxone. Respiratory arrest usually precedes cardiovascular collapse.

4. Cardiovascular Signs – A slowing heart rate indicates surgical anesthesia. An increase in rate (tachycardia) during the performance of a surgical procedure often indicates that the depth of anesthesia is not adequate. A decrease of rate (bradycardia) during surgery may signify an excessive dose of anesthetic. Opioids, xylazine, and vagal reflex activity can cause bradycardia. If the depth of anesthesia can be determined to be appropriate using other parameters, the use of anticholinergics can counteract these effects. Pulse strength, rhythm, and rate are readily determined in larger mammals by digital pressure over an accessible site (e.g., femoral artery, tail artery, auricular artery, lingual artery). Capillary refill time (CRT) is an indicator of peripheral perfusion and is normally less than 2 seconds. During lengthy procedures, anesthetized animals may become dehydrated. To help maintain normal hemodynamics, warm, balanced electrolyte solutions should be administered, by continuous intravenous drip, throughout the surgical procedure. Rodents may be administered fluids via the subcutaneous route.

5. Body Temperature – Anesthetics usually cause a depression of body temperature. Body temperature can be measured rectally in most species. Maintaining body temperature at normal levels, usually 37°-39° C (98.6°-102.2° F) allows more rapid metabolism of anesthetic agents. To avoid hypothermia, body temperature should be monitored and maintained throughout the anesthetic process and post-operative period. Conservation of body heat is an integral part of anesthetic management. Core body temperature can fall precipitously during general anesthesia, especially in small animals, and when combined with other factors, can lead to death. To avoid thermal burns, water heating pads rather than electrical pads, should be used.

6. Post-operatively – The anesthetist's responsibility for the animal's welfare extends beyond the completion of the surgical procedure. Monitoring should continue until the animal attains sternal recumbency and exhibits purposeful movement. Some anesthetics and analgesics can affect animals for days after administration. Therefore, it is important to check animals for signs of anorexia, fever, vomiting, or abnormal respiration or heart rate.

7. Indications of Anesthetic Overdose – Monitoring vital signs continuously during anesthesia will provide early warning of potential problems and emergencies that may be averted by appropriate and quick corrective actions. Do not rely on a single parameter to assess the animal's condition. All parameters should be evaluated prior to initiating any corrective actions. The following indicators of anesthetic overdose, which may lead to cardiac or respiratory failure, are helpful in assessing the animal's status during anesthesia. Heart rate may be rapid or slow, depending on the animal's state of physiological decompensation. Remember that anticholinergics cause the heart rate to increase. Pulses may be

weak, slow, irregular, or even imperceptible. Blood pressure requires electronic or mechanical monitors to measure. It will be reduced if blood loss is significant, in shock, or pending cardiac arrest. Cardiac arrhythmias may be noted if electronic monitors are used. Capillary refill time progressively slows to 3 or more seconds indicating blood pressure is inadequate to perfuse peripheral tissues (blood loss, shock, pending cardiac arrest). Respirations may be slow, irregular, shallow, often become diaphragmatic, and may eventually cease. Paradoxically respirations may increase in response to low blood O_2 and high blood $C0_2$ during deep anesthesia. Mucous membrane and skin color (depending on the animal's pigmentation) may be pale to cyanotic from poor perfusion of capillary beds and low blood O_2. Blood loss, decreased blood pressure, shock, and hypothermia reduce blood flow to tissues. Low blood O_2 from hypoventilation causes cyanosis, although tissue perfusion may be normal. Gastrointestinal, ocular, musculoskeletal, and nervous system reflexes may be greatly diminished or cease. Hypothermia equal to or lower than 35° C (95° F).

8. The following corrective actions should be taken when signs of anesthetic overdose are apparent. Turn off gas anesthetics. If reversible anesthetics are on board, administer a reversal agent. Mechanically ventilate with 100% oxygen. If the animal is not already intubated, insert an endotracheal tube immediately. Administer warm isotonic fluids, intravenously or intraperitoneally (rodents). Administration of fluids to larger mammals is facilitated if an IV line is already in place. Warm the animal to increase body temperature. If available, administer appropriate antidote/reversal agent.

I. Analgesics

1. Analgesia must be provided for every animal undergoing a potentially painful procedure including post-operative periods. Analgesics allow a smoother post-operative recovery period. Pain can cause alterations in physiological parameters that may influence research results. The lack of use of analgesics during painful procedures or post-operatively must be scientifically justified in writing to, and approved by the IACUC.

2. **Preemptive analgesia**, managing pain before it begins, holds significant benefits for the animal. If the selected analgesic does not interfere with the research parameters, the data produced can be improved when the stress secondary to pain is removed. Analgesia is always more effective when given before the painful stimulus is introduced, and preemptive analgesia should be used whenever possible. Analgesics are broadly classified into two groups, the opioids, and non-steroidal anti-inflammatory drugs (NSAIDS).

3. **NSAIDS** (e.g., aspirin, carprofen, ketoprofen) are effective in ameliorating low to moderate pain. These drugs act by inhibiting the enzymatic production of protaglandins that are released following tissue damage, and affect nociceptors. In addition to analgesia, NSAIDS have varying degrees of anti-inflammatory and anti-pyretic activity. Prolonged use (>3 days) of NSAIDS can cause stomach and intestinal ulcers and bleeding as well as nephrotoxicity. NSAIDS are metabolized in the liver and excreted by the kidneys.

4. **Opioids** (e.g., morphine, oxymorphone, meperidine, butorphanol, buprenorphine, pentazocine, fentanyl) act by binding to receptors in the cortex and spinal cord. This group of drugs is most effective at relieving continuous dull pain such as that experienced post-operatively. Opioids also cause drowsiness, decreased gastrointestinal motility, nausea, vomiting, and alterations of the endocrine and autonomic nervous system. These drugs can produce significant respiratory depression if used incorrectly. The effects of opioids can be reversed or prevented by the administration of naloxone. Fentanyl is administered as a transdermal patch in dogs and cats. Opioids are metabolized in the liver and excreted by the kidneys.

J. Comments regarding Anesthetics and Analgesics

1. Several commonly used or historically used anesthetics and analgesic medications are described briefly below. However, numerous additional agents are available for use in a variety of species. Contact a University of South Florida laboratory animal veterinarian for additional information on drugs not listed here. A veterinary drug formulary and a number of veterinary anesthesia textbooks are available in the Comparative Medicine library.

2. Acepromazine Maleate (formerly acetylpromazine), a phenothiazine derivative, is a potent neuroleptic agent with relatively low toxicity. Acepromazine induces tranquilization, muscle relaxation, and a

decrease in spontaneous activity. At high doses, sedation occurs. Preanesthetic administration decreases the amount of general anesthetic required. Acepromazine possesses antiemetic, anticonvulsant, antispasmodic, hypotensive, and hypothermic properties. Acepromazine will prevent or decrease severity of the malignant hyperthermia syndrome in susceptible swine exposed to halothane. Acepromazine potentiates opiates such as butorphanol and buprenorphine, which if used in combination as a pre-anesthetic, will provide sedation as well as preemptive analgesia.

3. Equi-Thesin, although no longer commercially available, can be prepared in the following manner. Dissolve 8.5 mg of chloral hydrate in 20 ml 95-100% ethanol. Then add 1.96 g pentobarbital (Nembutal @ 50 mg/ml) and 4.25 g MgS04. After everything else is in solution, add 60 ml propylene glycol. Bring up to a total volume of 200 ml with water (water can be added at any stage). Dose for rats is 1 ml/300 g IP.

4. Ether: Because of the serious hazard created by the highly flammable and explosive properties of ether, together with the fact that satisfactory alternative inhalation anesthetics are available (e.g., isoflurane or halothane), **use of ether as an anesthetic agent is prohibited**. In addition, the use of ether as a euthanasia agent is prohibited.

5. Fentanyl citrate patch is a very potent opiate agonist. The patch is a transdermal delivery system for the fentanyl, and is used primarily in dogs and cats to alleviate postoperative pain, and to control chronic pain (e.g. associated with cancer). Therapeutic levels are achieved within 6-8 hours of application in the cat, while it takes at least 12 hours to reach therapeutic levels in the dog, so patch application should be performed prior to the procedure keeping these times in mind. Small dogs and cats may be dosed with 2 patches, but the patch should not be cut in half. Instead, cover ½ of the gel membrane with tape. The patch is generally placed on the dorsal cervical area, or over the shoulders. The hair at the site should be closely clipped with at least a 1-cm margin around the patch. Do not shave, as cuts, abrasions or wounds can alter the absorption of fentanyl. After clipping, wipe the skin with a damp cloth to remove small hairs and skin debris, do not scrub or surgically prepare the site. Allow to completely dry. Place the patch over the clipped area and hold it in place for 2-3 minutes to maximize adherence. Use a slightly padded bandage or transparent dressing used with medical adhesive spray to assure adherence and to keep it dry. Increased temperatures can stimulate an excessive release of fentanyl from the patch, so avoid placing the patch on a heating pad.

6. Ketamine is a dissociative anesthetic, produces sedation and immobility, increased blood pressure, increased muscle tone, increased salivary secretions, only slight respiratory depression in most species (severe in rodents), variable analgesia, and may cause apnea. Ketamine should be administered in combination with xylazine or diazepam to induce surgical anesthesia.

7. Local anesthetics: A variety of local anesthetic agents are available and may be valuable in several types of experimental procedures. For example, local infusion of an incision site with lidocaine may reduce the amount of general anesthetic that is required. Application of lidocaine gel to a suture line or a cranial implant or the use of bupivicaine to block intercostal nerves following thoracotomy may provide considerable pain relief.

8. Pentobarbital can induce severe cardiovascular and respiratory depression at doses close to those needed to obtain a surgical level of anesthesia, and can result in death. To reduce the likelihood of this occurrence, pentobarbital can be administered intravenously. Calculate the required pentobarbital volume based on a mg/kg dose and draw this volume into a syringe; administer approximately half of the volume by rapid IV injection to achieve basal narcosis, and then slowly inject additional incremental volumes until surgical anesthesia is achieved. The IP route of administration should be used in rodents only.

9. Telazol is a commercially available preparation of tiletamine (50 mg/ml) and zolezapam (50 mg/ml). It is not recommended for use in rabbits (potentially nephrotoxic).

10. Urethane can be mutagenic and carcinogenic, and its use is strongly discouraged unless strict precautions are taken to protect personnel, its use is limited to non-survival procedures, and its use is justified in writing to, and approved by the IACUC.

11. Volatile anesthetics include halothane, enflurane, isoflurane, sevoflurane, and desflurane. These agents should be used only with adequate ventilation or scavenging systems. Precision vaporizers should be

used for these anesthetic agents because lethal concentrations can easily be reached using the open drop method, or using a bell jar as an anesthetic chamber.

12. Xylazine (i.e., Rompun®) is a centrally acting alpha-2 adrenergic receptor agonist with analgesic and sedative effects. Xylazine can induce profound bradycardia, decreased cardiac output, emesis and depressed thermoregulation. Ruminants are extremely sensitive to xylazine. Yohimbine or 4-aminopyridine can be used to reverse the effects of xylazine.

- The following tables of drugs commonly used for pre-anesthesia, anesthesia, analgesia, sedation, tranquilization, and restraint of laboratory animal species are provided as a reference only, for use by University of South Florida, IACUC-certified faculty and staff.

- Variations in dose and duration of action will probably be observed due to factors such as animal strain, route of administration, weight, temperament, presence of other drugs, and state of health. Because of these considerations, animal users must be able to judge depth of anesthesia in the individual animal to avoid administration of a lethal dose, or a dose that inadequately controls pain.

Table I. Signs of Pain and Distress in Laboratory Animals*

Species	Signs of mild to moderate pain of distress	Signs of severe or chronic pain or distress
Mouse	Eyelids partially closed; changes in respiration; rough hair coat; increased vibrissae movement; unusually apprehensive or aggressive; possible writhing, scratching, biting, self-mutilation; hunched posture; sudden running; aggressive vocalization; guarding.	Weight loss; dehydration; incontinence; soiled hair coat; eyes sunken, lids closed; wasting of muscles on back; sunken or distended abdomen; decreased vibrissae movement; unresponsive; separates from group; hunched posture; ataxia; circling; hypothermia; decreased vocalization.
Rat	Eyelids partially closed; porphyrin staining around eyes, nose; rough hair coat ± hair loss; increased aggression; reduced exploratory behavior; aggressive vocalization; licking, biting, scratching; guarding.	Eyes closed; poor skin tone; muscle wasting along back; dehydration; weight loss; incontinence; soiled hair coat; depressed/ unresponsive; sunken or distended abdomen; self-mutilation; recumbent position with head tucked into abdomen; decreased vocalization; hypothermia.
Syrian hamster	Ocular discharge; increased aggression; hunched posture; reluctance to move.	Loss of coat and body condition; increasing depression; extended daytime sleep periods; lateral recumbency; hypothermia; sores on lips, paws.
Gerbil	Ocular discharge; eyelids partially closed and matted with dry material; may "faint" when handled; changes in activity and burrowing behavior; arched back; hunched posture	Loss of weight and condition; sores on face; hair loss on tail.
Guinea Pig	Eyes sunken and dull; changes in respiration; increased timidity; increased sleepiness; arched back; increased vocalization.	Weight loss; hair loss; scaly skin; dehydration; decreased timidity; unresponsive; excessive salivation (oral problems); increased barbering; loss of righting reflex; decreased vocalization; hypothermia
Rabbit	Ocular discharge; protruding nictitans; photophobia; constipation or diarrhea; depression; facing back of cage; excessive self-grooming; stretched posture; early failure to eat and drink; dull attitude or increased aggression when handled; possible vocalization when handled; tooth grinding	Tooth grinding; apparent sleepiness; dehydration; weight loss; fecal staining, wasting of lower back muscles; decreased production of night feces; unresponsive.
Non-human primates	Generally very few signs, especially in the presence of humans; decreased activity; decreased food and water intake.	Huddled or crouching posture, with hand folded over abdomen; clenching or grinding teeth; depression or increased restlessness; withdrawal from cage mates; increased (generally aggressive) attention from cage mates; anorexia; weight loss; decreased grooming.
Dog	Decreased alertness; stiff posture; panting; biting, licking or scratching; increased aggression; increased vocalization.	Unwillingness to move; crouching posture; depression or increased aggression; crying when handled or moved; increased restlessness.
Cat	Increased aggression when approached; decreased food intake; licking.	Hunched, crouching or stretched posture; increased aggression; anorexia; weight loss; vocalizing; wild escape behavior; unkempt appearance; pupillary dilation; stiff gait.
Pig	Changes in gait or posture; increased efforts to avoid handling; increased squealing when approached or handled.	Depression; unwillingness to move; attempts to hide; withdrawal from pen mates; anorexia.
Sheep, Goat	Sheep are more stoic than goats; lying with legs extended; stamping feet; swaying stance; mild ataxia; restlessness or depression; depressed food intake; increased aggression on handling; guarding; tooth grinding.	Rolling; frequently looking or kicking at abdomen; falling over; walking backward; rapid, shallow respiration; weight loss; tooth grinding; grunting; vocalization on handling (goats especially); rigidity; unwillingness to move.
Bird	Increased escape behavior and vocalization when approached or handled.	Eyelids partially closed; anorexia; ruffled, drooping, unkempt appearance; immobility when approached.

*Adapteded from the University of Nebraska Medical Center “IACUC Guidelines for the Humane Care and Use of Live Vertebrate Animals,” 4th Edition, Appendix E: “Guidelines on the Recognition of Pain”.

Table II. Commonly Used Anesthetics and Analgesics for Mice

University of South Florida provides the following table as a reference only, for use by IACUC-certified faculty and staff only.

Anesthesia in Mice	**Dose & Route**	**Comments**
Isoflurane (Forane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer, adequate ventilation or scavenging essential
Ketamine + Xylazine	100 mg/kg (K) + 10 mg/kg (X) IP	
Ketamine + Xylazine + Acepromazine	100 mg/kg (K) + 20 mg/kg (X) + 3 mg/kg (A) IP	
Ketamine + Dexmedetomidine	75 mg/kg (K) + 0.5 mg/kg (D) IP	
Hypothermia (Neonates <4 days old undergoing minor surgical procedures only)	Submerge for 3 – 4 minutes in ice water	Pup placed in rubber sleeve, submerged to cervical area with resultant 10 minutes of anesthesia
Pentobarbital	35 mg/kg IV 40 – 70 mg/kg IP	Caution! Potentially significant cardiovascular and respiratory depression, variable response
Tribromoethanol (formerly known as Avertin)	125-250 mg/kg IP	Store at 4°C; dark conditions, not available as a pharmaceutical preparation
Analgesia in Mice*		
Carprofen	5 – 10 mg/kg SC, PO	Up to 12-24 hours of analgesia
Ketoprofen	10 mg/kg SC	Up to 12-24 hours of analgesia
Meloxicam	5.0 mg/kg SC, PO	Up to 12-24 hours of analgesia
Buprenorphine (Buprenex®)	2.0 mg/kg SC	5-8 hours of analgesia; do not use with tribromoethanol
Bupivicaine +/- epinephrine	< 2 mg/kg SC infiltration at incision site or nerve block	Up to 8-12 hours of analgesia
Alternative Drugs with Analgesic Potential		
Imipramine	2 – 3 mg/kg SC	Up to 12 hours of analgesia
Analgesic Recommendations by Procedure		
Minor surgery (tail biopsy in adults, subcutaneous pump placement, vascular cut down)	At least 24 hours of analgesia	Carprofen 5-10 mg/kg once OR Ketoprofen 10 mg/kg once
Major surgery (laparotomy, thoracotomy, orthopedic, burns, vascular cut down with extensive tissue dissection)	At least 48 hours of analgesia	
Major surgery option 1 – dosing interval up to 12 hours	Carprofen 5-10 mg/kg OR ketoprofen 10 mg/kg SQ every 12 hours +/- bupivacaine +/- epinephrine	Option 1. NSAID +/- local (always for thoracotomy)
Major surgery option 2 – dosing interval up to 24 hours	Carprofen 5-10 mg/kg OR ketoprofen 10 mg/kg every 12-24 hours Buprenorphine 0.1-2.0 mg/kg once +/- bupivacaine +/- epinephrine SQ	Option 2. NSAID and Opioid +/- local (always for thoracotomy)

*Note: Analgesic drug selections and the frequency and interval of their administration should consider that the degree and extent of analgesic pain relief will vary depending on the procedure(s) and the anticipated degree and extent of associated discomfort and pain. Mild discomfort/pain (e.g., superficial subcutaneous tumor cell implantations) may be alleviated by a NSAID (e.g., carprofen) or opioid (e.g., buprenorphine) alone. Moderate to severe pain (e.g., laporotomy, thoracotomy, cannulae implantation) may be better alleviated by a multimodal approach (i.e., combination of a NSAID

and an opioid drug), which allows for additive or synergistic analgesic actions at multiple points of the afferent pain pathway.

Note: All animals should be monitored at regular intervals during the perioperative period including after termination of analgesic treatment. If animals exhibit signs of pain or discomfort, analgesic therapy should be continued as needed and monitoring should be continued until recovery.

Note: Mice have a relatively small total muscle mass and are prone to develop muscular atrophy or nerve damage following IM injections. The IM route should be avoided in mice. If drugs must be administered via the IM route, minimal injection volumes (≤0.05 ml), and a 27-30-gauge needle should be used.

Table III. Commonly Used Anesthetics and Analgesics for Rats

University of South Florida provides the following table as a reference only, for use by IACUC-certified faculty and staff only.

Anesthesia in Rats	**Dose & Route**	**Comments**
Isoflurane (Forane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer, adequate ventilation or scavenging essential
Ketamine + Xylazine	60 – 90 mg/kg (K)+ 6 – 9 mg/kg (X) IP	30 – 45 minute duration; may supplement with ketamine only @ 1/3 dose. Reverse xylazine w/IP yohimbine, 2.1 mg/kg BW
Ketamine + Dexmedetomidine	75 mg/kg (K) + 0.5 mg/kg (D) IP or SC	
Pentobarbital	30 – 40 mg/kg IV 40 – 60 mg/kg IP	Caution! Potentially significant cardiovascular and respiratory depression, variable response
Analgesia in Rats*		
Carprofen	5.0 mg/kg SC	Up to 12-24 hours of analgesia
Meloxicam	2.0 mg/kg SC, PO	Up to 12-24 hours of analgesia
Buprenorpine (Buprenex®)	0.01 – 0.5 mg/kg SC	From 6 – 8 hours of analgesia
Bupivicaine +/- epinephrine	< 2 mg/kg SC infiltration at incision site or nerve block	Up to 8-12 hours of analgesia
Analgesic Recommendations by Procedure		
Minor surgery (subcutaneous pump placement, vascular cut down)	At least 24 hours of analgesia	Carprofen 5.0 mg/kg once
Major surgery (laparotomy, thoracotomy, orthopedic, burns, vascular cut down with extensive tissue dissection)	At least 48 hours of analgesia	
Major surgery option 1 – dosing interval up to 12 hours	Carprofen 5 mg/kg SQ every 12 hours +/- bupivacaine +/- epinephrine	Option 1. NSAID +/- local (always for thoracotomy)
Major surgery option 2 – dosing interval up to 24 hours	Carprofen 5 mg/kg every 12-24 hours Buprenorphine 0.1-2.0 mg/kg once +/- bupivicaine +/- epinephrine SQ	Option 2. NSAID and Opioid +/- local (always for thoracotomy)

*Note: Analgesic drug selections and the frequency and interval of their administration should consider that the degree and extent of analgesic pain relief will vary depending on the procedure(s) and the anticipated degree and extent of associated discomfort and pain. Mild discomfort/pain (e.g., superficial subcutaneous tumor cell implantations) may be alleviated by a NSAID (e.g., carprofen) or opioid (e.g., buprenorphine) alone. Moderate to severe pain (e.g., laporotomy, thoracotomy, cannulae implantation) may be better alleviated by a multimodal approach (i.e., combination of a NSAID and an opioid drug), which allows for additive or synergistic analgesic actions at multiple points of the afferent pain pathway.

Note: All animals should be monitored at regular intervals during the perioperative period including after termination of analgesic treatment. If animals exhibit signs of pain or discomfort, analgesic therapy should be continued as needed and monitoring should be continued until recovery.

Note: Rats have a relatively small total muscle mass and are prone to develop muscular atrophy or nerve damage following IM injections. The IM route should be used with caution in rats. If drugs must be administered via the IM route, minimal injection volumes (≤0.3 ml), and a 25-gauge needle or smaller should be used.

Table IV. Commonly Used Anesthetics and Analgesics for Hamsters

University of South Florida provides the following table as a reference only, for use by IACUC-certified faculty and staff only.

Anesthesia in Hamsters	**Dose & Route**	**Comments**
Isoflurane (Forane®) Halothane (Fluothane®) Enflurane (Ethrane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer, adequate ventilation or scavenging essential
Pentobarbital	70 – 90 mg/kg IP	Caution! Potentially significant cardiovascular and respiratory depression, variable response
Ketamine+Xylazine	80 – 100 mg/kg (K) + 7 – 10 mg/kg (X) IP	
Ketamine + Medetomidine	100 mg/kg (K) + 0.25 mg/kg (M) IP	
Tiletamine - Zolazepam (Telazole®)	20 – 40 mg/kg IP for sedation 50 – 80 mg/kg IP for anesthesia	
Telazole® + Xylazine	30 mg/kg (T) + 10 mg/kg (X) IP	
Urethane	1500 mg/kg IP	Caution! Prolonged anesthesia; terminal procedures only; carcinogenic and mutagenic
Urethane (50%) + α-Chloralose (10%) + Pentobarbital	380 mg/kg (U) + 38 mg/kg (C) + 26 mg/kg (P) IP	Anesthesia extended with 135 mg (U) + 14 mg (C) IP
Analgesia in Hamsters		
Morphine	10 mg/kg SC	Up to 3 hours of analgesia
Meperidine	20 mg/kg SC	Up to 3 hours of analgesia
Buprenorphine (Buprenex®)	0.05 – 0.5 mg/kg SC	Between 8 – 12 hours of analgesia
Sedation in Hamsters		
Chlorpromazine	0.5 mg/kg IM	
Ketamine	40 - 80 mg/kg IP	

Table V. Commonly Used Anesthetics and Analgesics for Guinea Pigs

University of South Florida provides the following table as a reference only, for use by IACUC-certified faculty and staff only.

Anesthesia in Guinea Pigs	**Dose & Route**	**Comments**
Isoflurane (Forane®) Enflurane (Ethrane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer required, scavenging required
Ketamine + Xylazine	40 mg/kg (K) + 5 mg/kg (X) IP	Up to 60 minutes of anesthesia
Ketamine + Diazepam	100 mg/kg (K) + 5 mg/kg (D) IM	Up to 45 minutes of anesthesia
Ketamine + Acepromazine	125 mg/kg (K) + 5 mg/kg (A) IP	Up to 120 minutes of anesthesia
Ketamine + Medetomidine	40 mg/kg (K) IP, IM + 0.5 mg/kg (M) SC	Up to 40 minutes of anesthesia
Fentanyl/Fluanisone (Hypnorm®) + Diazepam	1.0 ml/kg (F/F) + 2.5 mg/kg (D) IM, IP	Up to 60 minutes of anesthesia
Pentobarbital	37 mg/kg IP	Up to 90 minutes of anesthesia Caution! Potentially significant cardiovascular and respiratory depression, variable response
A-Chloralose (1%) + Urethane (40%) in a 7:1 mixture	8.0 ml/kg IP	Approximately 2 hours of anesthesia
Analgesia in Guinea Pigs		
Carprofen (Rimadyl®)	4 mg/kg SC	Up to 24 hours of analgesia
Ketoprofen	1 mg/kg SC, IM	Up to 24 hours of analgesia
Morphine	2-5 mg/kg, SC, IM	Up to 4 hours of analgesia
Meperidine	10-20 mg/kg IM, SC	Up to 3 hours of analgesia
Buprenorphine (Buprenex®)	0.05 mg/kg SC	Up to 12 hours of analgesia
Sedation in Guinea Pigs		
Acepromazine	0.5-1.0 mg/kg IM, 2.5 – 5 mg/kg IP	Light to moderate sedation
Diazepam	2.5 – 5.0 mg/kg IP, IM	Moderate to heavy sedation
Ketamine	22 - 44 mg/kg IM	Light to heavy sedation
Midazolam	1.0 – 5.0 mg/kg IM, IP	Heavy sedation

Note: Guinea pigs often have a large amount of pasty feed in their mouths that can cause airway obstruction when anesthetized. This residue can be removed by gently rinsing the mouth with water before induction of anesthesia. IM injections of ketamine may result in self-mutilation and muscle necrosis. Anticholinergic medication (e.g., atropine @ 0.05 mg/kg SC or glycopyrrolate @ 0.01-0.02 mg/kg SC) may be used to reduce bronchial secretions and salivation. Normal values: body temperature 37.2-39.5ºC (99-103.1ºF); heart rate 230-380/min; respiration rate 40-100/min.

Table VI. Commonly Used Anesthetics and Analgesics for Rabbits

University of South Florida provides the following table as a reference only, for use by IACUC-certified faculty and staff only.

Anesthesia in Rabbits	**Dose & Route**	**COMMENTS**
Isoflurane (Forane®) Halothane (Fluothane®) Enflurane (Ethrane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer, adequate ventilation or scavenging essential
Pentobarbital	30 – 40 mg/kg IV	Caution! Potentially significant cardiovascular and respiratory depression, variable response
Ketamine + Xylazine	35 – 50 mg/kg (K) + 5 – 10 mg/kg (X) IM	Minor procedures; up to 45 minutes of anesthesia; can supplement with ketamine @ 1/3 dose
Ketamine + Medetomidine	25 mg/kg (K) + 0.5 mg/kg (M) IM	
α-Chloralose	80 – 100 mg/kg IV	
Urethane	1000 mg/kg IV or IP	Caution! Prolonged anesthesia; terminal procedures only; carcinogenic and mutagenic
Equithesin	1 – 3 ml/kg	Fresh solutions only
Analgesia in Rabbits		
Morphine	2 – 5 mg/kg SC	Up to 3 hours of analgesia
Meperidine	10 mg/kg SC	Up to 3 hours of analgesia
Butorphanol (Torbutrol® 0.5mg/ml)	0.1 – 0.5 mg/kg SC, IM or IV	Up to 4 hours of analgesia
Buprenorpnine (Buprenex®)	0.01-0.05 mg/kg SC	Between 6 – 12 hours of analgesia
Carprofen	4.0 mg/kg SC	Up to 24 hours of analgesia
Ketoprofen	1.0 mg/kg SC or IM	Up to 24 hours of analgesia
Sedation in Rabbits		
Butorphanol + Acepromazine	1 mg/kg (B) + 1 mg/kg (A) IM	
Chlorpromazine	25 – 100 mg/kg IM	
Acepromazine	0.75 – 1.0 mg/kg IM	
Diazepam	5 – 10 mg/kg IM	
Ketamine	30 mg/kg IM	
Xylazine	3 – 5 mg/kg IM or SC	

Note: Anesthetic depth: Adequate anesthesia for surgery can be very difficult to obtain in rabbits, especially when barbiturates are used. Rabbits are prone to develop respiratory depression and edema when anesthetized. Atropinase: Although atropine is frequently administered to anesthetized animals to reduce oral and respiratory secretions and to support heart rate, many rabbits (up to 50%) have circulating atropinase and thus may demonstrate a reduced duration of effectiveness of this drug. Normal values: body temperature 38.5-39.0^{o}C (101.3-102.2^{o}F); heart rate 130-300/min; respiration rate 30-60/min.

Table VII. Commonly Used Anesthetics and Analgesics for Dogs

University of South Florida provides the following table as a reference only, for use by IACUC-certified faculty and staff only.

Anesthesia in Dogs	**Dose & Route**	**Comments**
Isoflurane (Forane®) Halothane (Fluothane®) Enflurane (Ethrane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer, adequate ventilation or scavenging essential
Pentobarbital	20 – 30 mg/kg IV	Caution! Divide dose and administer ½ as bolus and ½ to effect; between 30 – 45 minutes of anesthesia
Thiopental	8 – 12 mg/kg IV	Short acting, up to 15 minutes of anesthesia
Chloralose	80 – 110 mg/kg IV	Between 6 – 10 hours of anesthesia, premedicate with morphine @ 5 mg/kg, terminal procedures
Ketamine + Diazepam	10 mg/kg (K) + 0.5 mg/kg (D) IV (anesthesia for minor procedures) 5.5 mg/kg (K) + 0.3 mg/kg (D) IV (induction of anesthesia)	Premedicate with an anticholinergic Anesthesia can be maintained with inhalant anesthetic (e.g., isoflurane)
Ketamine + Midazolam	10 mg/kg (K) + 0.5 mg/kg (M) IV	Minor procedures; premedicate with anticholinergic
Telazole® (Tiletamine + Zolazepam)	6 – 8 mg/kg IM	Up to 1 hour of anesthesia
Telazole® + Xylazine + Butorphanol	6 – 8 mg/kg (T) + 0.5 mg/kg (X) + 0.2 mg/kg (B) IM	
Analgesia in Dogs		
Meperidine	2 – 10 mg/kg SC or IM	Up to 3 hours of analgesia
Morphine	0.25 – 5.0 mg/kg IM or SC	Between 4 – 6 hours of analgesia
Butorphanol (Torbutrol® 0.5 mg/ml)	0.2 – 0.4 mg/kg IM or SC	Between 2 – 5 hours of analgesia
Buprenorpnine (Buprenex®)	0.01 – 0.02 mg/kg SC	Between 8 – 12 hours of analgesia
Carprofen	2.2 mg/kg PO, or 5 mg/kg SC	Up to 12 hours of analgesia
Ketoprofen	2 mg/kg SC or IM	Up to 24 hours of analgesia
Fentanyl patch	<5 kg body weight = ½ of 25 µg/hr patch; 5 – 10 kg bdy wt = 25 µg/hr patch; 10 – 20 kg bdy wt = 50 µg/hr patch; 20 – 30 kg bdy wt = 75 µg/hr patch; > 30 kg bdy wt = 100 µg/hr patch	Each dose provides up to 72 hours of analgesia; place 12 hours prior to anticipated pain; do not apply heat to patch (e.g., from heating pads).
Sedation in Dogs		
Butorphanol + Acepromazine	0.2 – 0.4 mg/kg (B) + 0.02 – 0.05 mg/kg (A) SC, IM, IV	
Buprenorphine + Acepromazine	0.007 mg/kg (B) + 0.03 – 0.05 mg/kg (A) SC, IM	
Xylazine	0.5 – 1.0 mg/kg IM	
Chlorpromazine	1 – 6 mg/kg IM, SC	
Acepromazine	0.05 – 0.1 mg/kg IM, SC	Maximum administer ≤3 mg total

Note: Anticholinergic medication (e.g., atropine @ 0.02-0.04 mg/kg SC, IM, or glycopyrrolate @ 0.02 mg/kg IM, SC) may be helpful in anesthetized dogs to support the heart rate and reduce bronchial secretions, consult a USF veterinarian.
Normal values: body temperature 37.5-39^{o}C (99.5-102.2^{o}F); heart rate 70-120/min, respiratory rate 15-25/min.

Table VIII. Commonly Used Anesthetics and Analgesics for Cats

University of South Florida provides the following table as a reference only, for use by IACUC-certified faculty and staff only.

Anesthesia in Cats	**Dose & Route**	**Comments**
Isoflurane (Forane®) Halothane (Fluothane®) Enflurane (Ethrane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer, adequate ventilation or scavenging essential
Pentobarbital	20 – 30 mg/kg IV	Caution! Divide dose and administer ½ as bolus and ½ to effect; between 30 – 45 minutes of anesthesia
Ketamine + Diazepam	10 mg/kg (K) + 0.5 mg/kg (D) IV (anesthesia for minor procedures) 5.5 mg/kg (K) + 0.3 mg/kg (D) IV (induction of anesthesia)	Premedicate with an anticholinergic Anesthesia can be maintained with inhalant anesthetic (e.g., isoflurane)
Ketamine + Medetomidine	7.0 mg/kg (K) + 0.08 mg/kg (M) IM	Minor procedures; up to 45 minutes anesthesia
Analgesia in Cats		
Morphine	0.1 mg/kg IM or SC	Up to 4 hours analgesia; caution, mania and excitation with overdose
Meperidine	2 – 10 mg/kg IM or SC	
Buprenorpnine (Buprenex®)	0.005 – 0.01 mg/kg SC or IM	Up to 12 hours analgesia
Oxymorphone	0.05 – 0.15 mg/kg IM, SC or IV	Between 3 – 5 hours analgesia; Minimal respiratory depression
Carprofen	4.0 mg/kg SC or IV	Up to 24 hours analgesia
Ketoprofen	1.0 mg/kg SC, IM or IV	Up to 24 hours analgesia
Fentanyl patch	<2.5 kg body weight = ½ of 25 µg/hr patch; >2.5 kg bdy wt = 25 µg/hr patch	Each up to 5 days analgesia; place 8 hours prior to anticipated pain; do not apply heat to patch (e.g., from heating pads)
Sedation in Cats		
Butorphanol + Acepromazine	0.1 – 0.4 mg/kg (B) SC, IM or IV + 0.02 – 0.05 mg/kg (A) SC, IM or IV	
Ketamine	10 – 20 mg/kg (K) IM	
Acepromazine	0.05 – 0.1 mg/kg IM or SC	
Chlorpromazine	1.0 – 2.0 mg/kg IM	
Midazolam	0.2 – 0.4 mg/kg IV or IM	
Diazepam	0.2 – 0.4 mg/kg IV or IM	
Xylazine	0.4 – 0.9 mg/kg SC or IM	

Note: Acetaminophen (Tylenol) may be toxic in cats and should be used with extreme caution in this species. Cats are also sensitive to the toxic effects of aspirin, and fatalities have been reported. Although aspirin can be used in cats, other agents should be considered. Normal values: body temperature 38.0-39.5^{o}C (100.4-103.1^{o}F); heart rate 110-140/min; respiration rate, 20-30/min. Anticholinergic medication (e.g., atropine @ 0.02-0.04 mg/kg SC, IM, or glycopyrrolate @ 0.02 mg/kg IM, SC) may be helpful in anesthetized cats to support the heart rate and reduce bronchial secretions, consult a USF veterinarian.

Table IX. Commonly Used Anesthetics and Analgesics for Pigs

University of South Florida provides the following table as a reference only, for use by IACUC-certified faculty and staff only.

Anesthesia in Pigs	**Dose & Route**	**Comments**
Isoflurane (Forane®) Halothane (Fluothane®) Enflurane (Ethrane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer, adequate ventilation or scavenging essential
Ketamine + Xylazine	20 mg/kg (K) + 2 mg/kg (X) IM	Up to 20 minutes of anesthesia; for minor procedures
Ketamine + Acepromazine	33 mg/kg (K) + 1.1 mg/kg (A) IM	
Pentobarbital	5 – 15 mg/kg IV	Administer to effect
Ketamine + Telazole®	2.2 mg/kg (K) + 4.4 mg/kg (T) IM	Up to 30 minutes of anesthesia
Telazole® + Xylazine	2.0 - 8.8 mg/kg (T) + 2.2 mg/kg (X) IM	Up to 20 minutes of anesthesia; may produce cardiopulmonary depression
Ketamine + Telazole® + Xylazine	2.2 mg/kg (K) + 4.4 mg/kg (T) + 2.2mg/kg (X) IM	Up to 30 minutes of anesthesia; for minor procedures
Ketamine + Medetomidine	10 mg/kg (K) + 0.08 mg/kg (M) IM	Immobilization; light anesthesia
Analgesia in Pigs		
Aspirin	10 mg/kg PO	Up to 6 hours of analgesia; use enteric-coated tablet
Meperidine	4 – 10 mg/kg IM	Up to 4 hours of analgesia
Phenylbutazone	10 – 20 mg/kg PO	Up to 12 hours of analgesia; use to alleviate musculoskeletal pain
Buprenorpnine (Buprenex®)	0.005 - 0.01 mg/kg IM	Up to 12 hours of analgesia
Ketoprofen	1.0 – 3.0 mg/kg SC	Up to 24 hours of analgesia
Carprofen	0.5 - 4.0 mg/kg SC	Up to 24 hours of analgesia
Sedation in Pigs		
Acepromazine	0.11 – 1.1 mg/kg SC or IM	
Chlorpromazine	0.5 – 4.0 mg/kg IM or SC	
Diazepam	0.5 – 10 mg/kg IM	Usually combined w/other agents
Azaperone (Stresnil®)	2 – 8 mg/kg IM	

Note: Malignant hyperthermia (MH) is commonly reported in swine. The first cardinal clinical sign of MH is an elevation in end-tidal CO_2. MH is characterized by the sudden onset of muscle rigidity, tachypnea, tachycardia and hyperthermia (rectal temperatures up to 108^{o}F), followed by dyspnea, cardiac arrhythmias, apnea and death. Anesthesia (particularly with halothane, isoflurane, or ethrane), restraint, stress and excitement have all been reported to trigger this condition. Anesthetized swine should be monitored closely for the development of hyperthermia. Emergency measures include cessation of the anesthetic, cooling the body with ice water, and the IV administration of sodium bicarbonate and the muscle relaxant dantrolene (2-10 mg/kg). Normal values: temperature 38.0-40.0^{o}C (100.4-104.0^{o}F); heart rate 60-120/min; respiration rate 10-12/min. Anticholinergic: Glycopyrrolate (0.004-0.01 mg/kg IM) or atropine (0.05 mg/kg IM).

Table X. Commonly Used Anesthetics and Analgesics for Sheep and Goats

University of South Florida provides the following table as a reference only, for use by IACUC-certified faculty and staff only.

Anesthesia in Sheep & Goats	**Dose & Route**	**Comments**
Isoflurane (Forane®) Halothane (Fluothane®) Enflurane (Ethrane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer, adequate ventilation or scavenging essential
Diazepam + Ketamine	0.1 mg/kg (D) + 4.5 mg/kg (K) IV	Up to 20 minutes of anesthesia; for minor procedures
Xylazine + Ketamine (Goat) (Sheep) (Goat) (Sheep)	0.05 mg/kg (X) + 4-5 mg/kg (K) IV 0.2 mg/kg (X) + 4-5 mg/kg (K) IV 0.1 mg/kg (X) + 10-15 mg/kg (K) IM 0.2 mg/kg (X) + 10-15 mg/kg (K) IM	Up to 20 minutes of anesthesia; for minor procedures Up to 45 minutes of anesthesia
Pentobarbital	20-30 mg/kg IV	Administer to effect
Telazole®	2-4 mg/kg IV	Up to 30 minutes of anesthesia
Xylazine + Telazole®	0.1 mg/kg (X) + 4 mg/kg (T) IM 0.05 mg/kg (X) + 1 mg/kg (T) IV	Up to 60 minutes of anesthesia
Ketamine + Medetomidine	0.5-1 mg/kg (K) + 20-25 µg/kg (M) IM	Up to 60 minutes of anesthesia
Analgesia in Sheep & Goats		
Aspirin	50-100 mg/kg PO	Up to 12 hours of analgesia
Flunixin	1-2 mg/kg IV, IM	Up to 24 hours of analgesia; only administer post-operatively to conscious animals
Meperidine	2 mg/kg IM, IV	Up to 4 hours of analgesia
Butorphanol + Diazepam	0.05-0.1mg/kg (B) + 0.05-0.2 mg/kg (D) IV	Up to 4 hours of analgesia
Buprenorphine (Buprenex®)	0.005-0.01 mg/kg IM	Up to 4 hours of analgesia
Sedation in Sheep & Goats		
Acepromazine	0.05-0.1 mg/kg IM, SC	Moderate sedation
Diazepam	0.2-0.5 mg/kg IV, IM	Light sedation
Ketamine	20 mg/kg IM	Moderate to heavy sedation
Medetomidine	25 µg/kg IM	Light to heavy sedation
Xylazine	0.2 mg/kg IV, IM (Sheep) 0.05 mg/kg IV, IM (Goat)	Light to moderate sedation

Note: Medetomidine and Xylazine can produce hypoxia. Goats and sheep may be fasted for 24-36 hours to reduce the possibility of regurgitation and ruminal tympany (bloat). Water may be withheld 6-8 hours. Always intubate with a cuffed endotracheal tube to prevent aspiration if regurgitation occurs. Intraoperatively a stomach tube should always be placed in the rumen to prevent ruminal tympany, especially when positioned in lateral or dorsal recumbency. Normal values: temperature 38.0-40^{o}C (100.4-104.0^{o}F); heart rate 55-120/min (Sheep), 70-130 (Goat); respiration rate 10-30/min. Anticholinergic drugs are not routinely used during ruminant surgery, but are beneficial in treating bradycardia: glycopyrrolate (0.022 mg/kg IM, SC) or atropine (0.05 mg/kg IM, SC).

Table XI. Commonly Used Anesthetics and Analgesics for *Macaca* spp.

University of South Florida provides the following table as a reference only, for use by IACUC-certified faculty and staff only.

Anesthesia in *Macaca* spp	**Dose & Route**	**Comments**
Isoflurane (Forane®) Halothane (Fluothane®) Enflurane (Ethrane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer, adequate scavenging essential
Ketamine + Diazepam	15 mg/kg (K) + 1.0 mg/kg (D) IM	30-40 minutes of anesthesia
Ketamine + Xylazine	10 mg/kg (K) + 0.25-2.0 mg/kg (X) IM	30-140 minutes of anesthesia; duration is a function of the xylazine dose
Ketamine + Medetomidine	2-6 mg/kg (K) + 30-60 µg/kg (M) IM	Up to 60 minutes of anesthesia
Pentobarbital	20-30 mg/kg IV	30-60 minutes of anesthesia: reduce dose by $^1/_3$ to $^1/_2$ after administration of ketamine
Thiopental	15-20 mg/kg IV 5-7 mg/kg IV (induction)	5-10 minutes of anesthesia After administration of ketamine
Telazole®	4-6 mg/kg IM	45-60 minutes of anesthesia
Analgesia in *Macaca* spp		
Acetaminophen	10 mg/kg PO	Up to 6 hours of analgesia
Aspirin	20mg/kg PO 125 mg/kg rectal suppository	6 to 8 hours < 24 hours
Ketoprofen	5 mg/kg IM	Up to 8 hours of analgesia
Carprofen	2-4 mg/kg PO, SC	Up to 24 hours of analgesia
Ketorolac	15-30 mg/kg IM	
Flunixin	2-4 mg/kg, SC	Up to 24 hours of analgesia; only administer postoperatively to conscious animals
Meloxicam	0.1-0.3 mg/kg PO	Up to 24 hours of analgesia
Naproxen	10 mg/kg PO	Up to 12 hours of analgesia
Oxymorphone	0.15 mg/kg SC, IM, IV	Up to 6 hours of analgesia
Meperidine	2-4 mg/kg IM	Up to 4 hours of analgesia
Morphine	1-2 mg/kg SC, IM	Up to 4 hours of analgesia
Buprenorphine (Buprenex®)	0.005-0.01 mg/kg IM	Up to 8 hours of analgesia
Sedation in *Macaca* spp		
Acepromazine	0.2 mg/kg IM	Moderate sedation
Diazepam	1.0 mg/kg IM	Light to moderate sedation
Ketamine	5-20 mg/kg IM	Moderate sedation, immobilization
Xylazine	0.25-0.5 mg/kg IM	Light to moderate sedation

Note: Anticholinergics: Medetomidine and Xylazine can produce bradycardia and hypotension, in particular at the high end of the xylazine dose. These side effects can be prevented by pre-medicating with atropine (0.02-0.05 mg/kg IM) or glycopyrrolate (0.005-0.01 IM). Anticholinergics also reduce bronchial and salivary secretions. Food: Nonhuman primates should be fasted for at least 12 hours prior to elective surgery. Normal Values: temperature 37-39° C (98.6-103.1° F); heart rate 120-180/min; respiration rate 32-50/min.