FLORIDA INTERNATIONAL UNIVERSITY

SOP #: 602.01

Title: **SOP -** Anesthesia of Laboratory Animals

Approvals:

Attending Veterinarian _____ **Date:** 10/11/12

Assistant Director LAR _____ **Date:** 10/11/12

1. Purpose

1.1 To carry out surgical procedures on animals, pain perception must be completely suppressed. This can be achieved either by general anesthesia, which produces loss of consciousness, or by local or regional anesthesia.

1.2 To ensure that a selected anesthetic regimen provides an appropriate degree of intra-operative analgesia

2. Responsibility

2.1 ACF Veterinary Staff, Principal investigators, laboratory technicians.

3. Definitions

3.1 General anesthesia: involves loss of consciousness, analgesia, suppression of reflex activity and muscle relaxation.

3.2 Dissociative Anesthesia - the state of anesthesia produced by drugs (e.g. Ketamine) that dissociate the thalamocortic and limbic systems, resulting in a cataleptoid state, usually with muscle rigidity.

4. Guidelines

4.1 The ideal anesthetic/analgesic regimen must balance several goals:

4.1.1 It should provide pre-emptive analgesia so that animal pain is already being treated as the general anesthetic is wearing off, to prevent sensitization ("ramp-up") of pain

sensory mechanisms, and to lower the overall amount of general anesthetic required for the procedure.

4.1.2 It should be precisely titrated to assure that animals receive adequate anesthesia to block pain sensation, to produce unconsciousness, and to produce immobility without experiencing hemodynamic instability or life-threatening anesthetic overdoses.

4.1.3 It should not interfere with the study that the animals are on.

4.1.4 It should not result in unhealthy post-operative side-effects.

4.1.5 It should not cause pain or distress on induction or recovery.

4.2 Surveys of anesthetic deaths in human surgical operations have identified that hypoxia and anesthetic overdose are the most common events in anesthetic mishaps. These are probably the most common causes of anesthetic deaths in veterinary patients. A greater proportion of cardiac arrests in human patients occurred during induction of anesthesia.

4.3 Pre-Anesthetic Evaluation

4.3.1 History

4.3.1.1 Previous anesthetic experience: History of hypothermia, prolonged recovery, unusual reaction, warrants a change in anesthetic drugs and special management.

4.3.1.2 History of previous illness: History of disease, for example renal or hepatic disease, should be considered when choosing anesthetic drugs.

4.3.1.3 Recent use or concurrent use of drugs: Many drugs influence the effects of anesthetic drugs (Cimetidine, when given for several days before anesthesia inhibits microsomal drug metabolism in liver and prolongs duration of action of diazepam and barbiturates)

4.3.2 Physical Examination

4.3.2.1 Age - Newborn, pediatric, juvenile, adult, and geriatric: when compared to the adult patient, these different age groups have altered responses to anesthesia.

4.3.2.2 Weight: important to calculate drug dosages

4.3.2.3 Temperament - Placid, excitable, aggressive, and depressed: these different levels of central nervous system stimulation will alter the amount of drug needed to produce sedation or anesthesia. Altered responses should be expected in some circumstances; diazepam may worsen the attitude of an excited patient, and Xylazine will be relatively ineffective in an excited patient.

4.3.2.4 Evaluation of systems - Temperature, pulse, and respiratory rate, auscultation of heart and lungs, to identify abnormalities. For example, the presence of bradycardia dictates cautious use of opioids (narcotic analgesics) or Xylazine, and auscultation may identify unexpected evidence of cardiac disease.

4.3.2.5 Laboratory Data (Hematology/Biochemistry/Urine analysis/Radiology)

4.3.2.6 Recommendations for baseline tests vary but it is usual practice to determine the CBC, BUN, liver enzymes, and urinalysis, on older dogs or those which require major surgery, or which are sick.

4.3.3 Classification of Anesthetic Risk (Assigned at the time of pre-anesthetic evaluation)

4.3.3.1 Class I. A patient having no systemic disease.

4.3.3.2 Class II. A patient that has a minor not significant, systemic defect and is undergoing an elective surgical or medical procedure.

4.3.3.3 Class III. A patient who is to be anesthetized who has in addition to its surgical condition, a systemic disease which is serious but not immediately fatal.

4.3.3.4 Class IV. A patient who is undergoing a major surgical procedure and has in addition a disease which might in itself be immediately fatal.

4.3.3.5 Class V. A patient who is moribund and in need of urgent surgery as a life-saving measure.

4.3.3.6 E. If anesthesia is part of an emergency procedure the risk number is followed by an E.

4.3.4 Plan Formulation

4.3.4.1 **Rodents and Rabbits: Food and water is not withheld due to their inability to vomit**

4.3.4.2 Administer antibiotics: Antibiotics are better administered before induction of anesthesia. Some antibiotics (K penicillin, gentamicin) may cause hypotension when administered intravenously during anesthesia. Other drugs (procaine penicillin) may cause anaphylactic or allergic reactions which may not be recognized early enough because symptoms are masked during anesthesia.

4.3.4.3 Pre-anesthetic medication: Administration of drugs before induction of anesthesia. Most commonly used drugs are anticholinergics, tranquilizers, benzodiazepines, sedatives, and opioids.

4.3.4.4 Reasons for pre-medication include:

4.3.4.4.1 To calm the animal to enable administration of anesthetic without struggle.

4.3.4.4.2 To decrease gastrointestinal motility and prevent vomiting on induction or in recovery.

4.3.4.4.3 To decrease secretions of salivary glands and mucous glands of the respiratory tract.

4.3.4.4.4 To block vagal reflex.

4.3.4.4.5 To decrease adverse effects of other anesthetic drugs.

4.3.4.4.6 To reduce subsequent doses of general anesthetic drugs and increase the safety margin.

4.3.4.4.7 To reduce pain and/or movement in the recovery.

4.3.4.4.8 Common drugs used: atropine or glycopyrrolate is commonly used for its antisialagogue and vagolytic activity; sedative drugs used: phenothiazine, opioids, benzodiazepines, and alpha-2 agents.

4.4 Rodent Anesthesia

4.4.1 Inhalant Anesthesia

4.4.1.1 Inhalation anesthesia is superior to most injectable forms of anesthesia in safety and efficacy. It is easy to adjust the anesthetic depth. Because the anesthetics are eliminated from the blood by exhalation, with less reliance on drug metabolism to remove the drug from the body, there is less chance for drug-induced toxicity.

4.4.1.2 Inhalation anesthetics are always administered to effect, because the dosage can vary greatly among individual animals and different animal species.

4.4.1.3 The disadvantages to inhalant anesthesia are the complexity and cost of the equipment needed to administer the anesthesia, and potential hazards to personnel. All inhalant drugs are volatile liquids.

4.4.1.4 Isoflurane is the method of choice for rodent anesthesia. It is safe and very easy to use and provides rapid recovery as well as excellent control over anesthetic depth. Induction and awakening are rapid. Gas waste must be scavenged properly.

4.4.1.5 Induction of Anesthesia

4.4.1.5.1 Place the animal in the induction chamber.

4.4.1.5.2 Adjust the flow meter to 0.8–1.5 L/min.

4.4.1.5.3 Adjust the isoflurane vaporizer to 2%–5% (depending by the desired speed of induction).

4.4.1.5.4 The system delivers a precisely blended mixture of oxygen and Isoflurane. Anesthetic waste gases are actively scavenged and pass through an activated charcoal air filter canister that releases safe, filtered air back into the room.

4.4.1.6 Maintenance of Anesthesia:

4.4.1.6.1 Use the nose cone connected to the Bain Circuit and the Active Scavenging System.

4.4.1.6.2 Adjusts the flow meter to 0.5–0.8 L/min.

4.4.1.6.3 Adjust the isoflurane vaporizer to 1.5%–2% (depending by the desired anesthesia depth).

4.4.1.6.4 Prevent heat loss until the animal recovers.

4.4.1.6.5 Note: There are strain and species differences in the response to isoflurane: some animals are more sensitive than others. Also, transient post-operative immune suppression has been noted in mice following use of isoflurane (Markovic and Murasko, 1993).

4.4.2 Injectable anesthesia

4.4.2.1 Injectable anesthetics are, in general, metabolized by the liver and excreted by the kidneys. Animals with liver or kidney disease should not be anesthetized with these agents. Inhalation anesthetics are safer for use in sick or debilitated animals, because there is minimal metabolism, the amount of anesthetic administered can be controlled and one can cease administration as the situation dictates.

4.4.2.2 As with inhalation anesthesia, injectable anesthetics are given to effect. Effects may vary among individuals. Drugs should be listed in the protocol with approximate dose ranges. Dosages listed are guidelines. These are starting points which must be titrated up or down for the individual animal, or for the particular application (procedures conducted, animal age and strain differences).

4.4.2.3 It is not acceptable to conduct surgical procedures unless the animal is fully anesthetized.

4.4.2.4 Analgesic doses and frequency of administration is more difficult to gauge. Caution is required for overnight pain management.

4.4.2.5 If a drug is scheduled by the Controlled Substances Act of 1970, licenses are required to purchase them, and written records must be kept of their use.

4.4.2.6 Methods used:

4.4.2.6.1 Dissociative anesthetics: Ketamine which is a widely used anesthetic in a variety of species. In low doses, Ketamine provides chemical restraint with some analgesia. In higher doses, it may provide short-term surgical anesthesia in some species. In most instances, Ketamine is used in combination with other injectable agents. Disadvantages of Ketamine include some irritancy due to low pH, and insufficient anesthesia in some species and strains (especially mice) for some procedures. Ketamine is a Class III controlled substance.

4.4.2.6.2 Ketamine-α2-agonists combinations (Ketamine-Xylazine) Ketamine may be combined with the α2-agonists (Xylazine) in the same syringe to produce a deep level of sedation. In some situations in some species and strains an adequate depth of anesthesia for surgery may be attained. In other cases, this sedation may require an inhalant agent to achieve surgical anesthesia. It is generally safer to titrate to effect with inhalant anesthetic from a precision vaporizer than with supplemental injections of Ketamine or Ketamine-Xylazine combinations.

4.4.3 Topical anesthesia

4.4.3.1 Proparicaine may be used as a local anesthetic during retro-orbital blood collection from mice. Instill one drop on the eye and wait for a couple of minutes before performing the procedure.

4.4.3.2 Local anesthetic/analgesic drugs (Lidocaine and Bupivicaine) may be useful both during surgery, and post-operatively. They block nerve conduction when applied locally at sufficient concentration. Lidocaine has a fast onset of action, and provides a couple of hours of analgesia. Bupivicaine has a slower onset of action (up to 30 minutes) but provides up to 12 hours of residual analgesia. Both are infiltrated subcutaneously at the surgical site.

5. References

5.1 The Guide for Care and Use of Laboratory Animals.

5.2 Flecknell, P., Laboratory Animal Anesthesia; Academic Press, New York; 1996.

5.3 Kohn, D.F., Benson, G.J., Wilson, S.K., White, W.J., Anesthesia and Analgesia in Laboratory Animals; Academic Press, New York

5.4 Markovic SN, Murasko DM. 1993. Anesthesia inhibits interferon-induced natural killer cell cytotoxicity via induction of CD8+ suppressor cells. Cell Immunol. 151:474-80.