The University of Newcastle
Animal Care and Ethics Committee
Methodology Document

<table>
<thead>
<tr>
<th>Document Number:</th>
<th>ACEC: 13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Document Name:</td>
<td>Anaesthesia and Analgesia</td>
</tr>
<tr>
<td>Date of ACEC Approval:</td>
<td>23 May 2014</td>
</tr>
<tr>
<td>Amendment History:</td>
<td>V2.0</td>
</tr>
<tr>
<td>Date of Next Review:</td>
<td>May 2017</td>
</tr>
<tr>
<td>Document Contact:</td>
<td>Manager, Animal Welfare and Training</td>
</tr>
</tbody>
</table>

1. Context/Overview

The NSW Animal Research Act and Regulation, and the "Australian Code for the Care and Use of Animals for Scientific Purposes", require that the use of anaesthetic and analgesic agents be appropriate to the species, the individual animal, and the scientific aims, and must be consistent with current veterinary or medical practice. Furthermore anaesthesia must be used for procedures that are likely to cause pain of a kind and degree for which anaesthesia would normally be used in current veterinary or medical practice. This document describes a range of anaesthetic techniques and analgesic agents recommended for many species of laboratory animals. It is intended to provide broad guidelines only, rather than exhaustive information on the range of agents and regimes available.

As new anaesthetic agents are continually being developed, researchers should consult with the Animal Welfare and Training Unit veterinarians regarding regimes that are not discussed in this document.

2. Definitions

In the context of this document:

**anaesthetic means** loss of sensation as the result of drug-induced depression of nervous tissue, either locally or centrally;

**analgesia means** reduction in sensitivity to painful stimuli without loss of consciousness;

**balanced anaesthesia means** the use of multiple drugs with complementary actions to induce and maintain anaesthesia; each drug used usually provides one component of anaesthesia, and can often be used at reduced doses to minimise adverse side effects;

**balanced analgesia means** the use of a combination of drugs with different modes of action to produce sequential blocks in the nociceptive pathways, and achieve beneficial additive or synergistic analgesic effects;

**bradycardia means** slow heart rate;
dissociative anaesthesia means the state of anaesthesia produced by drugs (e.g. ketamine) that disassociate the thalamo-cortical and limbic systems, resulting in a cataleptic state, usually with muscle rigidity;

general anaesthesia means loss of consciousness, loss of pain sensation, suppression of reflex activity and muscle relaxation;

light anaesthesia means the state of immobility and unconsciousness, with retention of reflex responses to even mildly painful procedures;

local anaesthesia/analgesia means loss of sensation in a prescribed body area (usually infers blockade of a specific nerve or infiltration of a small area with local anaesthetic, eg. intercostal nerve block);

narcosis means drug induced state of deep sleep, from which the patient may or may not be rousable;

neuroleptanalgesia means a state of quiescence, altered awareness and analgesia, produced by the administration of a combination of a neuroleptic (tranquilliser/sedative) agent and a narcotic (opioid) analgesic (eg. acetylpromazine + morphine);

regional anaesthesia/analgesia means loss of sensation in a specific body area (usually infers blockade of a large nerve or group of nerves with local anaesthetic, eg. epidural anaesthesia and affect a larger, though still limited, body area than local anaesthesia);

sedation means a state of CNS depression and drowsiness; including reduced awareness of surroundings and reduced apprehension and fear;

surgical anaesthesia means the stage/plane of general anaesthesia that is just deep enough to provide unconsciousness, muscle relaxation, and analgesia sufficient to allow painless surgery;

tranquillisation means a state of reduced anxiety and relaxation, without drowsiness.

3. Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td>central nervous system</td>
</tr>
<tr>
<td>CRI</td>
<td>constant rate infusion</td>
</tr>
<tr>
<td>IM</td>
<td>intramuscular</td>
</tr>
<tr>
<td>IP</td>
<td>intraperitoneal</td>
</tr>
<tr>
<td>IV</td>
<td>intravenous</td>
</tr>
<tr>
<td>NSAID</td>
<td>non-steroidal anti-inflammatory drug</td>
</tr>
<tr>
<td>PO</td>
<td>per os (by mouth)</td>
</tr>
<tr>
<td>SC</td>
<td>subcutaneous</td>
</tr>
<tr>
<td>WFI</td>
<td>water for injection</td>
</tr>
</tbody>
</table>
4. Disclaimer

These guidelines are accurate at the time of writing; however new, safer and more humane techniques will continue to be developed and the writers do not intend for the following guidelines to be used as a sole reference. Please use this paper as a guide, and supplement your reading with up to date material as required.

5. Guidelines

Contents

1. Context/Overview...................................................................................................................... 1
2. Definitions..................................................................................................................................... 1
3. Abbreviations .............................................................................................................................. 2
4. Disclaimer..................................................................................................................................... 3
5. Guidelines..................................................................................................................................... 3

PART 1. GENERAL INFORMATION................................................................................................. 5

PART 2. SPECIFIC CONSIDERATIONS ........................................................................................ 5

- Hypothermia ................................................................................................................................ 5
- Variations in response.................................................................................................................... 6
- Interactions with research protocol............................................................................................. 6
- Use of "stock solutions"................................................................................................................ 6
- Dilution of drugs............................................................................................................................ 6
- Reversible anaesthesia.................................................................................................................. 7
- Neonatal anaesthesia..................................................................................................................... 7

PART 3. ANAESTHETIC MANAGEMENT TECHNIQUES ................................................................ 7

- Pre-Anaesthesia ............................................................................................................................ 7
- Pre-anaesthetic fasting .................................................................................................................. 8
- Premedication ............................................................................................................................... 8
- Induction, Maintenance and Monitoring of Anaesthesia ............................................................... 8
- Stages of Anaesthesia .................................................................................................................... 9
- Anaesthetic overdose ................................................................................................................... 12
- Post anaesthesia ........................................................................................................................... 12
- Routes of Administration ............................................................................................................. 13
- Local anaesthesia ......................................................................................................................... 16

PART 4: COMMONLY USED CLASSES OF ANAESTHETIC AND ANALGESIC DRUGS ............... 17

- Alpha-2 adrenergic agonists – medetomidine, dexmedetomidine ................................................. 17
- Barbiturates- pentobarbitone, phenobarbitone, thiopentone ....................................................... 17
- Dissociative agents – ketamine, tiletamine ................................................................................... 17
- Gaseous anaesthetics – isofluorane, sevofluorane ..................................................................... 18
PART 5. ANALGESIA AND PAIN MANAGEMENT ......................................................... 20

General .................................................................................................................. 20
Strategies to maximise the success of treatment for pain ...................................... 21
Monitoring to assess the effects of treatment for pain ......................................... 21
Specific Analgesic techniques .............................................................................. 22

6. Species Specific—RECOMMENDED REGIMES ................................................. 22

CEPHALOPODS .................................................................................................... 22
FISH ....................................................................................................................... 23
AMPHIBIANS ...................................................................................................... 25
REPTILES ............................................................................................................. 27
BIRDS .................................................................................................................. 29
GUINEA PIGS ..................................................................................................... 31
MARSUPIALS ..................................................................................................... 33
MICE .................................................................................................................... 35
RABBITS ............................................................................................................ 37
RATS .................................................................................................................... 39
OTHER SPECIES .............................................................................................. 41

7. Essential Supporting Documents ...................................................................... 41

8. References ....................................................................................................... 41

9. APPENDICES .................................................................................................... 45

Appendix 1: Sample Anaesthetic Record ............................................................. 45
Appendix 2: Suggested dose rates for Non-Steroidal Anti-Inflammatory Drugs in laboratory animals ................................................................. 46
Appendix 3: Suggested dose rates for opioid analgesics in laboratory animals ....... 47
Appendix 4: Suggested dose rates for injectable anaesthesia in laboratory animals 48
Appendix 5: Table of Generic and Proprietary Names ........................................ 49
PART 1. GENERAL INFORMATION

**Analgesic** agents decrease or prevent the perception of pain.

**Anaesthesia** involves a temporary (reversible) depression of nervous tissue resulting in loss of sensation. General anaesthesia also involves loss of consciousness, muscle relaxation and immobilisation. Different anaesthetics have varying effects in these areas. The anaesthetic agent chosen must be safe and humane for the animal, safe for humans, and cause minimal interference to the experiment. It is important to note that while animals cannot feel sensations while under anaesthetic, nerve fibres can be “primed” to feel pain which is felt after the anaesthetic wears off. It is important to use pain relief in addition to anaesthesia for painful procedures, which will both reduce the amount of general anaesthetic used and assist with pain management after the procedure.

Many anaesthetic and analgesic agents are not registered for use in small laboratory animals. This means that extensive evaluation is necessary, not only of the physiological effects and efficacy of the agent as an anaesthetic or analgesic, but also of the histological effects on various tissues especially those at the injection site, and the effects on research parameters caused by these agents. Usually considerable literature is available that has been generated during the development and testing of anaesthetic and analgesic agents, often in the species being used in the research protocol. This information can be used to guide drug choices.

When selecting an anaesthetic regime, the following factors must be considered:

- scientific parameters and goals
- species to be used
- plane or depth of anaesthesia/analgesia required
- whether the procedure is recovery or non-recovery
- level of pain relief required
- duration of anaesthesia
- physiological interactions that may influence experimental results
- humaneness of the technique (eg. ease of induction, smoothness of recovery)
- side-effects of the drugs on the animal (eg. diarrhoea, vomiting)
- method(s) of administration and dose rates
- experience of investigators with technique
- anaesthetic monitoring techniques
- monitoring during the recovery period
- safety of investigators
- availability of equipment

PART 2. SPECIFIC CONSIDERATIONS

**Hypothermia**

Researchers should be aware of the risks of hypothermia in all anaesthetised animals. Hypothermia leads to altered drug metabolism and delayed anaesthetic recovery, increased rates of wound infection, increased peri-operative blood loss, arrhythmias and even death. High risk situations include neonatal or geriatric animals, combined general and regional anaesthesia and prolonged surgery time. **Hypothermia is a preventable complication.** Regular temperature monitoring and recording will lead to prompt identification and management. Specialised surgical
heat pads are available, some with integrated rectal thermometers. As an alternative, improvised hot water bottles which consist of warm water in a bottle or glove can be useful if the water temperature is carefully monitored. In addition commercial hand warmers and "space blankets" (improvised from alfoil) and bubble wrap can be helpful. Bandaging extremities (feet and tail) in surgery of extended duration is also recommended.

**Variations in response**
There are significant variations in response to anaesthetic and analgesic agents according to the species, strain and gender of the animal. There may also be considerable individual variation between animals of the same strain and gender. It is impossible to extrapolate from one species to another. The regimes described in this document may not always result in the described level of anaesthesia or analgesia due to these variations in response. When using an anaesthetic or analgesic regime for the first time in a different strain, or when changing to a regime not previously used, close monitoring of the animal to ensure that the necessary depth of anaesthesia or analgesic effect is achieved is required.

**Interactions with research protocol**
When selecting an anaesthetic or analgesic agent or regimen, it is important to consider potential interactions with the research protocol. To minimise these interactions, the major pharmacological and physiological effects of the various agents should be reviewed. It is important to appreciate that a superficial consideration of a compound's effects may be insufficient to assess its overall effects on the research protocol.

**Use of "stock solutions"**
Dilution of drugs may be necessary prior to their use in small laboratory animals. Such dilutions may also involve mixtures of common anaesthetic or drug combinations. However, the long-term storage and subsequent use of any "stock solution" following its dilution for use in a batch of animals does not accord with best veterinary or medical practice and is not recommended. Concerns regarding this practice include the lack of data with respect to:

- The stability of the components of the drugs when they are mixed and stored
- The length of time that a stock solution can be safely stored.
- The effect of dilution on the bacteriostatic action of the preservative in the parent solutions.
- Specific recommendations on the manner in which stock solutions should be stored.

**Dilution of drugs**
All dilutions of anaesthetic and analgesic drugs used in laboratory animals must be prepared freshly prior to use. Care must be taken that only compatible drugs are mixed in the same solution.

For most drugs, dilution with sterile "water for injection" (WFI) rather than saline is recommended in order to prevent precipitation. However, investigators should check the directions accompanying the drug.
Reversible anaesthesia
Some anaesthetic regimes are associated with prolonged recovery periods. During the recovery period, the animals remain susceptible to hypothermia and have some degree of respiratory and cardiovascular depression. These effects can be largely overcome by use of reversible anaesthetic regimens. Antagonists for opioids such as naloxone have been available for many years, and the alternative of using partial agonists (eg buprenorphine) or mixed agonist/antagonists (eg. butorphanol) to reverse anaesthesia while maintaining analgesia has also been well established. The α-2 adrenoreceptor antagonist, atipamezole, provides rapid and complete reversal of the α-2 adrenergic agonist medetomidine.

Neonatal anaesthesia
Anaesthesia of neonatal animals is challenging because they have a reduced capacity to detoxify a wide range of drugs and hence their response to anaesthetics can differ considerably from adult animals. Prolonged recovery may lead to depletion of hepatic glycogen stores and result in hypoglycaemia. Other problems include increased susceptibility to hypothermia, increased possibility of poor pulmonary and circulatory function, and rejection of the young by the mother following the procedure (particularly in rodents). For these reasons, it is preferable to use inhalation anaesthesia (eg. isoflurane) so that recovery is rapid and normal feeding is resumed as soon as possible. Neonatal animals usually require a higher concentration of anaesthetic (eg. neonatal rats require 2-3% isofluorane for maintenance compared to approximately 2% for adult rats (depending on the calibration of the machine)).

Hypothermia as an anaesthetic technique in neonatal rodents
Hypothermia has been recommended for anaesthesia of neonatal rats and mice up to 10-14 days of age. It seems likely that during hypothermia, the degree of suppression of the peripheral and central nervous system is sufficient to prevent the animal experiencing pain. Disadvantages include increased risk of ventricular fibrillation, tissue hypoxia and metabolic acidosis after rewarming.

Rapid chilling can be achieved by placement of the pups into a container placed on crushed ice or in ice water. Placement of pups directly onto a cold source may result in tissue necrosis and is not recommended. The resultant torpor may last up to 10 minutes. Recovery from anaesthesia can be rapid. However, aggressive re-warming techniques (eg. heating pads or lamps) should be avoided to avoid tissue damage. An incubator at 33°C for 20-30 minutes is appropriate.

PART 3. ANAESTHETIC MANAGEMENT TECHNIQUES

Pre-Anaesthesia
- Acclimatise the animal to handling over 5-7 days to reduce the effects of stress and the possibility of injury to animal and personnel during induction.
- Check that the animal is healthy. A shiny well groomed coat, bright eyes, and a normal level of activity and social interaction are all good indications of good health.
- Record body weight. This is necessary to accurately calculate drug dosages and it will assist in post-operative monitoring. Weighing small animals and birds is facilitated by having sensitive scales tared to a small clean lidded container in which to place the patient for restraint.
• Where possible measure body temperature. This is a useful reference point for assessing hypothermia during and after anaesthesia, and elevations in body temperature suggestive of infection post-surgical procedures.

**Pre-anaesthetic fasting**

Withhold food (12-16 hours) and water (3-4 hours) for those species that may vomit during induction of anaesthesia (cat, dog, ferret, non-human primate). Pre-anaesthetic fasting of small rodents and rabbits is generally unnecessary since vomiting during induction does not occur in these species. In addition, fasting of small animals may result in a depletion of glycogen reserves, and the development of hypoglycaemia. Pigs rarely vomit on induction although withholding food for 12 hours is common practice.

Rabbits and rodents are coprophagic. If an empty stomach is required for the research protocol, measures to prevent ingestion of faeces are necessary. Guinea pigs store food in their cheek pouches and may aspirate this material during induction. A short period of fasting (eg 4 hours) can minimise this risk.

Large or medium-sized birds (eg. ducks, chickens, pigeons) may be starved for 6-12 hours to reduce the risk of regurgitation of the contents of the crop. Smaller birds should not be fasted for longer than 2 hours, to avoid the risk of inducing hypoglycaemia.

Opinion varies as to whether ruminants should be starved before induction of general anaesthesia. Fasting and water deprivation may have little effect on the volume of digesta present in the rumen, and whether or not regurgitation of rumenal contents occurs. However, fasting may reduce the incidence of rumenal tympany (“bloat”) by decreasing the volume of fermentable ingesta. This appears to be a greater problem in animals that are grazing. Even with these precautions, some ruminants will develop rumenal tympany while others will regurgitate.

**Premedication**

Premedication is given to effect prior to administration of the general anaesthetic agent. Analgesics should be given pre-operatively to inhibit noxious input to the central nervous system, thus providing a degree of prevention as opposed to treatment of pain which provides more effective analgesia. These agents can be combined with a sedative (eg. acetylpromazine - buprenorphine).

Tranquilisers (eg. diazepam) may reduce the anxiety of the animal and assist in its restraint. Sedatives (eg acetylpromazine) act like tranquillisers and also cause drowsiness and muscle relaxation.

Anticholinergic agents (atropine or glycopyrrolate) reduce the side effects of many anaesthetic agents eg. the stimulation of respiratory secretions and the parasympathetic stimulation of the cardio-pulmonary system which can cause bradycardia. **Do not** use anticholinergic agents to treat bradycardia, either simultaneously with medetomidine or following medetomidine, as the combination could lead to adverse cardiovascular effects.

**NB: Following the use of a sedative, tranquilliser or analgesic, the dose of some anaesthetic agents may need to be reduced.**

**Induction, Maintenance and Monitoring of Anaesthesia**

Decide on the anaesthetic technique based on species, experimental protocol, and
whether the procedure is survival or non-survival. Anaesthetics should be administered with appropriate equipment, in a room away from other animals.

Following induction, place the animal in a position with its head and neck extended to help ensure that its airway remains clear and unobstructed.

Intubation of the trachea will ensure an adequate airway. This can be achieved in most species. The use of lignocaine spray on the larynx prior to intubation has been used to prevent laryngospasm that occurs in some species (eg. cats, diving birds).

Monitor effects of the anaesthetic by direct observation and also by specific equipment including:

- stethoscope or oesophageal stethoscope,
- Rectal or infra red thermometer
- Electrocardiograph.
- Pulse oximeter

More sophisticated equipment includes:

- Capnometer (end-tidal CO2)
- Blood pressure monitor (via Doppler or intra-arterial techniques)
- Blood gas analyser

*Respiratory obstructions may be caused by secretions, foreign objects, tongue, or abnormal neck positions.*

Body fluid maintenance is achieved by intravenous or subcutaneous infusion of suitable fluids (eg. Hartmans, normal saline) and is especially important with lengthy anaesthetics or invasive surgery.

The use of anaesthetic monitoring checklist is recommended. A sample checklist is provided in Appendix 1.

**Stages of Anaesthesia**

The time taken for an animal to pass through each stage of anaesthesia varies with the anaesthetic agent used and the response of the individual animal.

The signs of the stages of anaesthesia are based on:

- Observation of the patient
- Changes in blood pressure and pulse
- Eye patterns and reflexes
- Respiratory pattern
- Chest and abdominal muscles
- Capillary refill time and mucous membrane colour.

The sequential effects of an increasing arterial concentration of an anaesthetic agent can be summarised as follows:
• Analgesia and amnesia
• Loss of consciousness and motor co-ordination
• Reduction of protective reflexes
• Blockage of afferent stimuli
• Muscular relaxation
• Respiratory and cardiovascular depression
• Depression of cardiovascular and respiratory reflexes
• Apnoea - respiratory arrest
• Cardiac arrest

**The stages of anaesthesia involve:**

**Stage 1. Voluntary excitement.**
Stage of analgesia without loss of consciousness; some disorientation. Characterised by voluntary motor excitement, struggling and ataxia. This stage lasts from beginning of anaesthesia to loss of consciousness.

• heart rate (HR) increases
• respiration rapid and deep
• excessive salivation
• urine and faeces voided
• pupils normal or dilated.

**Stage 2. Involuntary excitement**
Stage of narcosis. Characterised by a period of involuntary excitement or delirium with the animal beginning to lose consciousness and voluntary control. Late in this stage, analgesia is present and, in humans, awareness and recall are absent.

• cortical depression and loss of consciousness
• release of higher centres control (exaggerated reflex struggling)
• pupils dilate
• brisk nystagmus may be present
• swallowing, retching, vomiting may occur
• irregular respiration with breath-holding.
• pharyngeal and laryngeal reflexes persist

**Stage 3. Surgical Anaesthesia.**
Characterised by loss of consciousness, pain sensation and powers of coordinated movement. Arbitrarily divided into 4 planes which reflect the progressive dose-dependent depression of the CNS from the cortex to the midbrain to the spinal cord.

**Plane 1:** Analgesia and muscle relaxation are only sufficient for minor non-invasive procedures.
- regular respiration - denotes onset of Stage 3
- pupils constricted
- nystagmus and change in position of eye
- lid and palpebral reflexes present
- salivation persists
- muscle tone persists
- strong pulse persists

**Plane 2:** Difficult to generalise with different agents. Analgesia and muscle relaxation are sufficient for most surgical procedures.
- eyeball may be rolled downwards and medially (alfaxalone and isofluorane) or centrally located and motionless (ketamine, medetomidine and other agents);
- decrease in depth and increase in rate of respiration. Surgical stimulation will create a respiratory response
- maintenance of heart rate and blood pressure (varies with species and agent)
- oral and pharyngeal reflexes may still be present in the cat
- diminished lacrimation and salivation
- diminished muscle tone

**Plane 3:** As this plane is achieved, all reflexes are abolished and paralysis of intercostal muscles begins. Respiratory effort changes as intercostal muscle paralysis develops; respiration becomes mainly abdominal.
- eyeball centrally fixed
- lacrimation, salivation, oropharyngeal reflexes abolished
- vagal reflexes due to traction on abdominal or thoracic viscera retained
- muscle relaxation marked
- weakened peripheral pulse

**Plane 4:** A dangerous level of anaesthesia characterised by complete paralysis of intercostal muscles, pupillary dilatation, and severe cardio-pulmonary depression.
- complete paralysis of intercostal and abdominal muscles
- absent lid and corneal reflexes
- dilated pupils and absent photomotor reflexes
- decreased heart rate; severely diminished cardiovascular compensatory reflexes
- Peripheral pulse may be absent

**Stage 4. Bulbar paralysis**
All reflex activity is lost. Characterised by jerky irregular respiration and respiratory arrest. Cardiac arrest follows closely after respiratory arrest. At this point, immediate vigorous corrective therapy is required to successfully resuscitate the patient.

**Anaesthetic overdose**
Indications of an anaesthetic overdose include:

- Respiration becomes slow and irregular, diaphragmatic or ceases,
- Mucous membrane and skin colour may be pale or cyanotic (bluish)
- Pulse is weak to imperceptible
- Blood pressure is very low
- Cardiac dysrhythmias may occur
- Capillary refill time progressively slows to 3 seconds or longer.

**Post anaesthesia**
Animal must be observed during recovery from anaesthesia to ensure:

- a patent airway.
- that the animal's body temperature is maintained.
- that it does not injure itself.
- that any post-operative pain is adequately controlled.

If an endotracheal tube is in place, it must not be removed until the swallowing reflex has returned. Non-ruminant species should be placed on their sides with head and neck extended. Ruminants should be propped up on their sternums to minimise the risk of over-distension of the rumen with gas (rumenal tympany or bloat) and of inhalation of regurgitated rumen contents.

The animal’s homoeothermic responses will remain depressed until it has recovered from anaesthesia. Thus, the ambient temperature of the recovery area should be warm (30-35°C for small rodents, 25-30°C for cats and dogs). Supplemental heat may be provided (eg. warming lamp, heat pad, incubator). However, care should be taken not to overheat the animal. Monitor both the body temperature of the animal and the temperature of its immediate environment.

Small rodents should be housed alone during recovery to prevent attack from cage mates. If surgery has been performed, cage bedding should be such as to prevent wound contamination.

If animals have undergone an invasive procedure, careful monitoring during the post-operative period is essential to assess whether analgesia has been effective, and whether additional analgesia is required. The dose or frequency of administration should be modified according to the needs of the individual animal. Fluids assist in the recovery of the animal. Normal saline (0.9% NaCl) can be given intravenously
(5mL/kg/hour) subcutaneously or intraperitoneally at a dose of up to 3-4% of the animal's body weight.

**Routes of Administration**

1. **Inhalation.**

Induction of anaesthesia can be achieved using a facemask. Induction chambers are generally not recommended as there is less control of over depth of anaesthesia, a greater potential for exposure of the operator to anaesthetic gases and anaesthetic gases such as isoflurane can irritate the eyes.

During the initial phase of mask induction, the animal should be allowed to become accustomed to breathing air through the facemask. 100% oxygen is introduced. Then the vaporiser concentration is gradually increased up to approximately 4% until the animal is anaesthetised. Once this is achieved, anaesthesia is maintained using 1 - 2.5% (isofluorane) concentration of the gas. Intubation is recommended. With animals <10kg an open circuit is used such as an Ayres T-piece or a Bain coaxial circuit, or one of the specialised rodent delivery circuits (‘mouse block’, rodent zero dead space circuit”). These provide a low resistance, low dead space circuit.

Induction chambers are usually made of a plastic or glass box of various sizes. Up to 5% of the gaseous anaesthetic agent, with high flow rates of oxygen (5+ litres per minute), is used until the animal loses its righting reflex. The chamber is then either filled with 100% oxygen, while the anaesthetic gas is evacuated from the chamber, or the lid of the chamber is opened under a fume hood to prevent exposure of the operator to anaesthetic gas. The animal is then taken out of the chamber, and placed on a facemask or intubated. Anaesthetic administration is continued at the maintenance level.

Use of an anaesthetic "jar", where the animal is placed into a chamber containing a pad of gauze or cotton wool soaked in liquid anaesthetic, is not recommended. With this technique, the concentration of anaesthetic achieved within the container is unpredictable and is invariably dangerously high if potent, easily vaporised anaesthetics such as isoflurane are used. In addition, direct contact with liquid anaesthetic is extremely unpleasant for the animal as it is irritant to mucous membranes. It is also difficult to prevent contamination of the environment with anaesthetic vapour and thus presents a potential occupational health and safety hazard.

Regardless of the method used, scavenging of excess anaesthetic gas must be performed, in a manner to prevent exposure of personnel to waste gases.

**Advantages**

- Relatively simple to administer.
- Accurate control over depth of anaesthesia.
- Rapid induction.
- Rapid recovery.

**Disadvantages:**

- Specialised equipment is usually needed.
• Constant monitoring of the animal is necessary.

**NB. Good ventilation and scavenging equipment is required at all times as some agents may be dangerous to personnel.**

2. *Intravenous.*

Induction of anaesthesia is usually rapid. With large animals, the jugular and cephalic veins are the most accessible vessels. In rodents, the tail vein is used, while in guinea pigs and rabbits, the marginal ear veins are used. In birds the tarsal vein is more useful than the brachial vein as it is more fixed in position and less likely to bleed and result in a haematoma following venepuncture. Following intravenous induction, anaesthesia may be maintained using gaseous agents, or continuous intravenous infusion.

**Advantages:**

• Rapid action of the anaesthetising agent.

• Drug can be administered to effect to provide the desired depth of anaesthesia. Thus, the dose of the administered drug can be tailored to the individual animal.

**Disadvantages:**

• Requires some expertise

• Good restraint of the animal is essential.

3. *Intraperitoneal.*

The onset of action is slower compared to intravenous administration, and the animal will pass through a phase in which it becomes progressively ataxic and may exhibit some excitation and hyperactivity, then lose its ability to right itself, and eventually lose consciousness. Anaesthesia then becomes progressively deeper until the pedal withdrawal reflex is lost. For rats, mice, guinea pigs and rabbits, use a 25-27g needle inserted 3mm lateral to the umbilicus on the right hand side of the animal. Larger gauge needles are useful for larger species (eg 22-23g for dogs, cats). Always draw back on the plunger prior to injection to ensure that the needle has not penetrated an abdominal organ.

**Advantages:**

• Relatively simple to administer.

**Disadvantages:**

• A “set dose” of the drug(s) is administered to the animal. Because it is impossible to adjust the dose according to the individual animal’s response, inadvertent over-dosing and under-dosing can occur

• Administration. Residual drug effects can persist for prolonged periods, and so full recovery can be very prolonged.

4. *Subcutaneous.*
The onset of action is slower compared to intravenous and intraperitoneal administration, and the animal will pass through a phase in which it becomes progressively ataxic, may exhibit some excitation and hyperactivity, then lose its ability to right itself, and eventually lose consciousness. Anaesthesia then becomes progressively deeper until the pedal withdrawal reflex is lost. Dorsolateral areas of neck and shoulder are the most useful sites.

**Advantages:**

- simple to administer

**Disadvantages:**

- A “set dose” of the drug(s) is administered to the animal. Because it is impossible to adjust the dose according to the individual animal’s response, inadvertent over-dosing and under-dosing can occur.

- Relatively large doses of anaesthetic must be given to produce the required effect. Absorption is slow relative to intravenous administration. Residual drug effects can persist for prolonged periods, and so full recovery can be very prolonged.

- Injection of an irritant compound can cause unnecessary pain or discomfort to the animal.

- Some drugs cannot be administered subcutaneously as they cause tissue damage and skin sloughing (eg. ketamine).

5. **Intradermal**

This is the site for many local anaesthetic injections. A very fine gauge needle (27-30g) is aimed at a very oblique angle so that the tip remains within the skin tissue. It is clear that the correct tissue space has been encountered when the operator can feel strong resistance to injection. If the needle is advanced too far the subcutaneous space will be encountered and injection of substance will be easy. A “bleb” of anaesthetic is sufficient to induce loss of pain sensation. Care should be taken to suck back with the syringe prior to injection to ensure that injectate is not going intravenously.

6. **Intramuscular.**

These injections are painful and should be avoided whenever possible. Larger volumes must be administered in multiple sites. Ensure that the needle is not in a blood vessel by withdrawal of the plunger before injecting.

**Advantages:**

- Simple to administer

**Disadvantages:**

- A “set dose” of the drug(s) is administered to the animal. Because it is impossible to adjust the dose according to the individual animal’s response, inadvertent over-dosing and under-dosing can occur.

- Relatively large doses of anaesthetic must be given to produce the required effect. Absorption is slow relative to intravenous
administration. Residual drug effects can persist for prolonged periods, and so full recovery can be very prolonged.

- Injection of an irritant compound can cause unnecessary pain or discomfort to the animal.
- In small animals, the injectate volume is large compared to the volume of muscle mass used for IM administration. This can result in unnecessary pain or discomfort in the animal. This route should be avoided in small rodents.

Other routes of administration include oral, epidural, intrathecal, and intra-articular.

**Local anaesthesia**

Local anaesthesia induces insensitivity to pain in a specific area of the body.

Use of local anaesthetic agents:

- Splash blocks – local anaesthetic is dripped on or in to the subcutaneous space at the closure of a skin wound as an adjunct to other pain management techniques
- Infiltration of a local anaesthetic
- Nerve blocks, where the agent is injected at a point distant from the area of interest to block nerve conduction to and from the site.
- Epidural anaesthetics are an example of the use of local anaesthesia to block sensation in a larger area of the body (regional anaesthesia).
- Specific ocular local anaesthetics are available (Alcaine®, Ophthaine®). These agents are very effective but there is a risk of corneal damage with repeated use.
- Dermal anaesthetics – Emla cream, a topical application of lignocaine and prilocaine, when applied to the skin 20 minutes before a procedure, provides circumscribed loss of sensation in the area of application. It is useful for cannula insertion, and very minor procedures.
- Bupivicaine is a long acting local anaesthetic, which can confer loss of local sensation for up to 8 hours after administration.

Local anaesthesia is used commonly in rodents as an adjunct to pain relief. In larger animals it can be used as a sole anaesthetic provided that the animal is immobilised in some way that does not cause distress. Local anaesthetics can be used together with a sedative to keep the animal calm and still during a procedure. It is important to remember that local anaesthetic agents have systemic effects and can alter heart rate and rhythm and other physiological parameters. Care should be taken so that agents are not administered intravenously, and that the total volume of agent used is minimal for the purpose.

Addition of an opioid such as morphine or buprenorphine to lignocaine and bupivicaine has been shown to effectively double the anaesthetic duration of action. Addition of sterile sodium bicarbonate to the local anaesthetic solution can reduce sting due to the normally low pH.

Local anaesthetics do not provide restraint, nor do they provide relief from anxiety. The addition of a sedative to the regime can correct this.
PART 4: COMMONLY USED CLASSES OF ANAESTHETIC AND ANALGESIC DRUGS

**Alpha-2 adrenergic agonists – medetomidine, dexmedetomidine**

Alpha-2 adrenergic agonists are a class of sympathomimetic agents popular in animal research because they offer deep sedation and good pain relief, they are easy to administer (by intraperitoneal or intramuscular injection) and they are reversible. These drugs work by inhibition of norepinephrine release in the brain stem. At low doses both sedative and analgesic effects of α-2 agonists are dose dependent. As dose is increased there is a ceiling on the degree of analgesia and further dosing only acts to lengthen the duration of sedation and increase the risk of adverse events. For this reason the dose of α-2 agents should be minimised by using synergistic agents (usually opioids or dissociatives) as part of a balanced anaesthetic regime.

Side effects are frequent with α-2 agonists. Commonly there is an initial hypertension (due to peripheral vasoconstriction) which results in a baroreceptor-mediated reflex bradycardia. As the peripheral effects diminish, central α-2 actions predominate, causing decreased blood pressure and decreased cardiac output. **Giving anticholinergics (eg atropine) to reduce bradycardia is contraindicated.** Severe bradycardia should be treated with an alpha-2 adrenergic agonists reversal agent such as atipamezole. Other side effects include short term cardiac arrhythmias, decreased respiratory rate, cyanosis of peripheral mucous membranes due to peripheral vasoconstriction, vomiting, increased urine output, transient hyperglycaemia (due to inhibition of insulin secretion and resulting in marked diuresis) and increased myometrial tone and intrauterine pressure. **Medetomidine and dexmedetomidine have replaced xylazine in veterinary practice due to their greater α-2: α-1 affinity (approximately 1620:1 for medetomidine compared with 160:1 for xylazine). This increased selectivity results in more predictable and effective sedation and analgesia and fewer side effects as, generally but not exclusively, α-2 receptors are associated with sedation and anaesthesia while α-1 receptors are associated with adverse cardiovascular effects.** Note: The diuretic effect of the alpha 2 agonists is more marked in medetomidine than xylazine.

**Barbiturates- pentobarbitone, phenobarbitone, thiopentone**

Barbiturates such as pentobarbitone, thiopentone and phenobarbitone were once commonly used as anaesthetics in veterinary and research protocols. The use of barbiturates in animal research is now largely confined to euthanasia with pentobarbitone. Phenobarbitone has a role in veterinary medicine as an anti-seizure medication.

**Dissociative agents – ketamine, tiletamine**

Dissociative anaesthesia is a unique form of anaesthesia characterised by analgesia and amnesia with minimal effect on respiratory function. Ketamine is the most common dissociative anaesthetic used in human and veterinary practice. Under the influence of ketamine alone, the animal can swallow and open eyes but cannot process information. Dissociatives are a class of hallucinogen, and recovery from anaesthesia can be accompanied by delirium, excitement, disorientation and confusion. These effects are minimised by combining the dissociative with other agents such as an α-2 agonist or diazepam. Another example of a dissociative
anaesthetic is tiletamine, which is marketed as Zoletil, tiletamine mixed in a fixed-ratio combination with the benzodiazepine, zolazepam.

**Note: Ketamine is an S8 drug (Drug of dependence). An Authority for the Department of Health is required to obtain and use it. And there are specific record keeping requirements associated with it.**

**Gaseous anaesthetics – isofluorane, sevofluorane**

Gaseous anaesthetics are highly titratable agents commonly used in research and human and veterinary practice. An anaesthetic apparatus is required for administration of these anaesthetics. Gaseous anaesthetics can pose a risk to the operator, and special caution should be used if any researchers are pregnant due to a reportedly increased risk of spontaneous abortion. A scavenging system, which removes waste gases from the laboratory either to the outside of the building or to purpose built activated charcoal canisters, is essential.

**Local anaesthetic agents – lignocaine, bupivacaine, proparacaine, prilocaine**

Lignocaine is a low cost local anaesthetic with quick onset (5-10 minutes) and short duration of action (1-2 hours)

**Bupivacaine** is a more expensive agent that has slower onset (20-30 minutes) and longer duration of action (6-8 hours)

**Proparacaine** is an ocular local anaesthetic agent preparation

**Prilocaine** is an alternative local anaesthetic agent, often used in dentistry, and available as a topical cream. In combination with lignocaine, it is incorporated into Emla patches which provide topical local anaesthesia

**Opiates and synthetic opioids**

Opiates comprise a group of alkaloids that have an analgesic effect mediated by opiate receptors in the central nervous system. Opiate drugs (eg morphine and codeine) are distinguished from opioid drugs because they are naturally occurring alkaloids derived from the sap of the opium poppy. Opioids (eg butorphanol, buprenorphine, methadone, pethidine and fentanyl) are synthetic drugs that resemble morphine in pharmacological effect.

Opiates and opioids are well absorbed by oral, rectal and parenteral routes. Fentanyl can also be administered by the transdermal route. Opiates and opioids are also distinguished by whether they are pure agonists (eg morphine, methadone, pethidine and fentanyl) or partial agonists (eg butorphanol and buprenorphine) at the centrally located (\(\mu, \kappa, \delta, \sigma, \) and \(\epsilon\)) receptor sites (agonists bind and activate a receptor, whereas antagonists bind without causing activation). It is important not to administer agonist and mixed agonist drugs concurrently as pain relief will be compromised. Pure antagonist drugs (eg naloxone) are used to reverse the effect of the administered opioid.

The selection of a particular opioid and the initial dose should be made on

- The expected intensity of the pain (pure agonists provide more intense analgesia than partial agonists)

- The duration of action required (buprenorphine has the longest duration of action (6-8 hours) vs morphine and methadone (4 hours) vs pethidine and butorphanol (1 hour) and fentanyl (20 minutes)
- The desired speed of onset (methadone and fentanyl act rapidly after IV administration while morphine and pethidine given IV are likely to cause histamine release)

- **Note:** The opioids and opiates are classified as S8 drugs (Drugs of dependence). An Authority for the Department of Health is required to obtain and use it. And there are specific record keeping requirements associated with it.

**Neuroleptics - azaperone**

Azaperone is used to sedate pigs prior to minor procedures, including transport.

Neuroleptanalgesia is a form of analgesia accompanied by general quiescence and psychic indifference to environmental stimuli, without loss of consciousness, and produced by the combined administration of a major tranquilizer (neuroleptic) and a narcotic (e.g., fentanyl/flunisone and fentanyl/droperidol). Neuroleptanalgesia combines profound analgesia with sedation.

**Phenothiazines – acetylpromazine**

Acetpromazine is commonly used as a sedative and pre-anaesthetic agent in veterinary medicine. It has no analgesic action. It can be used in combination with dissociatives and opioids to lower the dose of each drug used.

**Steroid Anaesthetics - alfaxalone**

Alfaxalone is registered for use only in cats and dogs, but has gained wide acceptance as a safe physiological anaesthetic agent in a variety of vertebrate species from fish to companion animals. Alfaxalone is a water soluble steroid anaesthetic. It has a wide safety margin, a short duration of action, is rapidly eliminated from the body, causes minimal disruption to cardiopulmonary function, gives a smooth induction, causes no tissue reaction or pain on injection, and confers good muscle relaxation and does not have cumulative action, so it can be used repeatedly to “top up” anaesthesia. It is usually administered intravenously but may be administered intramuscularly and intraperitoneally. IM and IP routes result in a more variable anaesthetic effect. In amphibians it may be used transdermally and fish may be anaesthetised via gill washes.

Alfaxalone can be safely combined with α-2 agonists, opioids and acetylpromazine. **Alfaxalone has no analgesic properties.**

**Benzodiazepam Sedatives diazepam, midazolam, zolazepam**

Benzodiazepines are anxiolytic anticonvulsant muscle relaxant drugs which also cause sedation

**Reversing agents for benzodiazepines**

If severe respiratory depression develops, the reversal agent flumazenil can be given at a dose of 0.01 mg/kg, slow IV, in both cats and dogs. Flumazenil has a short half-life, so it may need to be repeated.

**Hypnotics – propofol, urethane, tribromoethanol**

Hypnotic anaesthetics are a class of psychoactive drugs.
**Propofol** is an alkylphenol derivative suspended in a hyperlipid emulsion. It is a rapidly acting injectable agent ideal for short procedures. Repeated boluses of propofol are not advisable. Due to the lipid emulsion which promotes bacterial growth, opened propofol should be used within 6-12 hours.

**Urethane** is a long-acting (8-10h) anaesthetic with minimal cardiopulmonary depression. The drug is used for long procedures in rodents. Despite the fact that it is carcinogenic and is only allowed to be used with special justification and only for non-recovery procedures, it is the anaesthetic of choice for many rodent respiratory physiologists due to its minimal effect on respiratory frequency.

**Tribromoethanol** (Avertin) is a short acting anaesthetic used in rodents and amphibians. It is no longer commercially available, and must be made up from a powder and stored in the dark at 4°C. **Repeated use of this drug is associated with an increase in morbidity and mortality.** The drug is irritant and can result in adhesions in the abdominal cavity after IP injections, it may also cause intestinal ileus (cessation of intestinal motility). Use of this drugs requires particular justification.

**PART 5. ANALGESIA AND PAIN MANAGEMENT**

**General**

Pain can result in significant and undesirable physiological, biochemical and behavioural changes in the animal. Providing effective pain relief can have a dramatic effect on the speed with which animals return to normal following surgical procedures. Analgesia also decreases the unwanted experimental variables associated with pain and stress.

Anaesthesia does not equate with analgesia. General anaesthesia produces loss of consciousness and hence prevents perception of pain while the animal is unconscious. However, noxious stimuli will still be transmitted to and processed by the CNS. Central hypersensitivity can develop in the spinal cord and brain. Thus, while pain perception is absent while the animal is unconscious, post-operative pain perception can be heightened. Some anaesthetic agents (eg. alfaxalone) do have analgesic effects must always be used concurrently with an analgesic agent if the animal is to undergo a painful procedure under anaesthesia.

Analgesic agents can be broadly divided into two groups - the opioids or narcotic analgesics, and the non-steroidal anti-inflammatory drugs (NSAIDs). Note that in almost all cases (with the exception of the orally administered synthetic opioid tramadol) the opioids are Schedule 8 drugs, and require a specific Authority from the Department of Health, secure lock and key storage and careful record of usage. In addition to these two groups of drugs:

- Local anaesthetics can also be used to provide post-operative pain relief by blocking all pain sensation from the affected area.

- In some species, α-2 agonists may provide significant pain relief (eg. ruminants).

Analgesic agents can be administered via the parenteral routes (intravenous, subcutaneous, intramuscular, intraperitoneal), oral administration (eg tramadol), epidural and intrathecal routes, or via transdermal patches (fentanyl).
The oral opioid tramadol (a synthetic codeine preparation) is reported to lower the seizure threshold.

Non-pharmacological methods for controlling post-operative or post-procedure pain include acclimatisation of the animal prior to performance of the procedure. This will act to decrease anxiety and enhance the effect of concurrently administered analgesic agents. Other non-pharmacological methods include maintaining warmth and comfort during the post-operative period, nutritional support, and access to conspecific animals in social species.

**Strategies to maximise the success of treatment for pain**

1. **Pre-emptive analgesia**

In general, post-operative pain can be controlled more readily if analgesia is provided pre-operatively or intra-operatively. Initiating treatment before acute insult is believed to inhibit peripheral and central sensitisation. For this reason, pain relief measures should be undertaken prior to surgical procedures wherever possible.

2. **Multimodal or balanced analgesia**

Perception of pain arises from a combination of peripheral and central hypersensitivity involving a multitude of pathways, mechanisms and transmitter systems. Thus it is unlikely that a single class of analgesic will completely alleviate pain, irrespective of the dose used. A combination of drugs with different modes of action can be used to produce sequential blocks in the noxious pathways, and achieve beneficial additive or synergistic analgesic effects. With this approach, lower doses of any one analgesic agent can usually be used, thereby reducing potential undesirable side effects while improving the control of pain.

For example, opioids can be combined with NSAIDs, where the opioid acts to dampen peripheral and central afferent noxious transmission and the NSAID acts peripherally to decrease the amount of local inflammation and hence the noxious information entering the CNS. Adding a local anaesthetic to this regime can provide additional analgesia by blocking transmission in individual nerves.

NMDA receptor antagonists (eg. ketamine in sub-anaesthetic doses) can be used to reduce central sensitisation. Sedatives and tranquillisers can also be used to decrease anxiety and stress that have been shown to heighten responses to pain.

**Monitoring to assess the effects of treatment for pain**

Because of the individual variation in response to analgesic agents, animals must be monitored carefully during the post-operative period to assess whether or not analgesia has been effective, and whether or not additional analgesia is required. The dose or frequency of administration should be modified according to the needs of the animal.

As a general guide:

- relatively minor procedures (eg. vascular catheterisation) - a single dose of analgesic is administered, either an opioid (eg. buprenorphine) or an NSAID (eg. carprofen).

- more invasive surgical procedures (eg. laparotomy) - analgesic administration may continue for days, until the animal appears comfortable. A common regime is a combination of opioid with an NSAID for 24-36 hours, followed by an NSAID alone for a further 24-36 hours.
The Animal Care and Ethics Committee has developed guidelines on the recognition and assessment of pain in animals. These guidelines, and other resource documents on this subject, may be accessed via the animal ethics website: http://www.newcastle.edu.au/research-and-innovation/resources/animal-ethics/managing-approved-projects#painanddistress

**Specific Analgesic techniques**

1. **Buprenorphine jelly**
   Oral administration of buprenorphine is possible using jelly in rats, mice, guinea pigs, and rabbits:

   Acclimatise the animals to consumption of jelly over several days or weeks. Dissolve 85g of jelly crystals in 250mL of boiling water. Place aliquots of 4mL of jelly liquid in ice-block moulds for refrigeration. It may be necessary to try a few flavours to see which is most palatable.

   When analgesia is required, 3 buprenorphine sublingual tablets (Temgesic®, Reckitts and Coleman, 0.2 mg/tablet) are crushed into the base of each ice-block mould and moistened with 0.5 mL warm water, prior to the addition of 3.5 mL of warm jelly (total 4 mL). The jelly disks are set at 4-8°C. For acute pain, the number of disks given to each animal is calculated on a dose rate of 2 mg/kg.

   Do not use injectable form of buprenorphine for oral preparation as it is too bitter.

2. **Transdermal opioid patches**

   In animals recovering from major surgery, transdermal opioid patches should be considered. Fentanyl (Durogesic) patches are commercially available, and though not registered for use in rodents, provide significant long acting pain relief. The smallest patch available provides 12ug fentanyl per hour, and although it constitutes an “off label” usage, the patches may be cut to size, providing the operator is very careful not to expose themselves to the transdermal preparation. Doses vary with thickness of skin and size of animal but as a guide 0.25 x 12ug/hr durogesic patch /kg is a starting point. If possible patches should be applied 2-4 hours before surgery.

   Note: Janssen-Cilag Pty Ltd specifically advise in the product insert not to cut the fentanyl patches. This is due to the danger of exposing the operator to the drug contain in the patch due to the handling of the patch while cutting. The use of gloves while handing and / or cutting patches significantly reduces this risk.

6. **Species Specific– RECOMMENDED REGIMES**

**CEPHALOPODS**

**General Considerations**

Cephalopods can be difficult to handle without sedation. They are easily stressed, and readily react with a defensive response termed “inking”. They should be transported and anaesthetised in seawater from their own environmental to maintain appropriate mineral and electrolyte balance. The operator should wear non powdered pre-moistened gloves to handle the animals in order to avoid disturbing
their external mucus layer. Skin contact with detergents, solvents and/or abrasive materials (eg dry paper towels) directly to the skin should be avoided.

**ANAESTHESIA**

Cephalopods are usually anaesthetised by immersion. The two most common anaesthetic agents used with cephalopods are magnesium chloride (preferred) and ethanol.

- **Ethanol** is prepared in a 1.5-3% solution (15-30mL/L) diluted in seawater and causes a rapid induction (1 minute). The animal should be fully submerged.

- **Magnesium chloride** is prepared at a concentration of 6.8g/L in seawater. Induction time is 6-12 minutes and there are few side effects. The safety margin is high and the animals experience a smooth induction, after which gills should be intermittently perfused with anaesthetic seawater.

Both anaesthetic regimes require additional pain relief. It is suggested that an analgesic such as butorphanol or meloxicam be used at a dose rate extrapolated from lower vertebrate literature, in any potentially painful procedure. This will make the best effort at optimising patient care even though we do not currently have pharmacokinetic or efficacy data for analgesic agents in cephalopods.

Depth of anaesthesia is difficult to assess. Absence of withdrawal reflexes and absence of response to pressure on the globe can be used. Normal respiratory rate for a 100-800g Octopus vulgaris is 30 breaths/minute. Pulse oximeters cannot be used due to the presence of haemocyanin instead of haemoglobin.

Recovering cephalopods are placed in anaesthetic free seawater. As the animal wakes up, its extended flaccid tentacles will retract in response to light pinching. Gradually it will recover its righting ability and tone in its extremities.

Resuscitation involves squeezing and relaxation of the body to assist anaesthetic – free water circulation over the gills.

**FISH**

**General Considerations**

Fish may be anaesthetised by immersion, injection or application of the anaesthetic agent to the gills. The suggested dose rates provided vary greatly because most dose rates have been validated only in a small number of species. Use the lowest dose rate initially and increase incrementally until an effective dose if achieved.

Surgical anaesthesia is identified by a lack of activity, a loss of equilibrium, shallow gill ventilation movements, no reflex reactivity (eg no movement to a tail pinch), a reduced heart rate and decreased muscle tone.

Non powdered pre-moistened gloves should be worn when handling animals in order to avoid disturbing their external mucus layer. Skin contact with detergents, solvents and/or abrasive materials (eg dry paper towels) directly to the skin should be avoided. It is advisable to fast fish for 24-48 hours prior to anaesthesia to reduce faecal contamination and regurgitation. Use water taken from the original holding tank for transport, anaesthetic induction and recovery. Maintain adequate oxygenation of holding tanks throughout the anaesthetic (supply oxygen via an air
pump or similar device). Maintain water temperature at the species normal optimum throughout the procedure.

ANAESTHESIA

Surgical anaesthesia in fish should be accompanied by artificial ventilation of the gills with either fresh or anaesthetic containing water. A number of fish anaesthetic “machines” have been described, most designed around the fountain concept, where a submersible pump is used to generate a steady water flow. The fish is placed on a surgical platform so that tubes can deliver anaesthetic containing water through the patient’s mouth and over its gills. Anaesthetised fish can be maintained for several hours with these systems. A more labour intensive alternative is to have an assistant syringe anaesthetic intermittently over the gills. In either case the water provided should be well aerated and maintained at the temperature of the normal environment of the fish.

Anaesthetic agents commonly used are alfaxalone, Tricaine methanesulfonate (MS-222), eugenol (clove oil), ketamine, ketamine/medetomidine and lignocaine. These agents require additional pain relief if painful procedures are to be carried out. Butorphanol 0.1 – 0.4mg/kg IM or SC and meloxicam 0.2mg/kg IM have been used successfully to provide pain relief in fish. IM injections are typically administered under a scale on either side of the dorsal fin (mid-point). To inject subcutaneously or intramuscularly, ensure that the fish is sufficiently sedated and partially submerged in water.

Combining anaesthetic agents in fish may provide a more complete anaesthesia that a single agent, and complementary effects between some agents allow lower doses to be used, resulting in fewer adverse effects e.g. MS-222 combined with Quinaldine in rainbow trout and northern pike resulted in lower mortality rates and fewer adverse side effects.

Anaesthetic monitoring involves observation of the rate of movement of the operculum (the rigid flap that covers the gills), observation of the gill colour and (to assess surgical anaesthesia) loss of response to a firm pinch at the base of the tail. At the end of the procedure to speed recovery, create a flow of oxygenated water over the gills by moving the fish back and forth in the water, or opening and closing the mouth several times.

- **Alfaxalone** has a wide margin of safety and has been used to successfully anaesthetise fish at a concentration of 5mg/L. Induction time is 2-6 minutes and duration of anaesthetic up to 30 minutes if anaesthetic is trickled through gills by an assistant or a fountain. Alfaxalone causes no undesirable side effects and recovery is smooth.

- **Tricaine methanesulfonate (MS222)** has a wide margin of safety. A neutral buffered stock solution is made as follows: 10g/L MS-222 buffered to pH 7.0-7.1 by adding 10g/L NaHCO3. This can be stored in a cool dark spot for up to 30 days. Fish are immersed in the solution. Water should be aerated to prevent hypoxaemia. Induction takes 5-20 minutes. Analgesia and muscle relaxation is excellent. Recovery takes 25-70 minutes. Undesirable side effects include ileus, abdominal adhesions and increased mortality. It is usually recommended only for terminal (non-recovery) studies.
- **Benzocaine** must first be dissolved in an organic solvent such as ethanol. Can be used via immersion (50-500mg/l) or sprayed onto the gills as 1 g/l. Do not use topical anaesthetic products marketed for mammals.

- **Eugenol** diluted 1/10 with 95% ethanol to improve solubility and then diluted ½ - ¼ to yield a 25-50 mg/L solution, will readily anaesthetise bony fish; however, recovery can be prolonged. Safety margins with the use of eugenol are low.

- **Ketamine** is administered intramuscularly at a dose of 66-88mg/kg and will result in immobilisation for short procedures. Complete recovery can take over an hour.

- **Ketamine/medetomidine**: 1-2mg/kg ketamine PLUS 0.05-0.1mg/kg medetomidine administered intramuscularly provides immobilisation with some pain relief and may be reversed with atipamazole 0.2mg/kg intramuscularly.

- **Quinaldine**: Has been used as a bath at a dose rate of 50-100mg/l for induction followed by 15-60mg/l for maintenance. The solution is acidic and should be buffered with sodium bicarbonate.

- **Lignocaine** may be used as a local anaesthetic in fish. Care should be taken with small fish. Do not exceed 1-2mg/kg total dose.

**ANALGESIA**

The following agents have been shown to have efficacy against painful stimuli in some species of fish:

- **Butorphanol**: 0.1- 0.4 mg/ kg IM, SC
- **Meloxicam**: 0.2 mg/kg IM.
- **Lignocaine**: 0.1-2mg/kg IM
- **Morphine**: 5 mg/kg IM and IP

**AMPHIBIANS**

**General Considerations**

Non powdered pre-moistened gloves should be worn to handle aquatic amphibians in order to avoid disturbing their external mucus layer. Skin contact with detergents, solvents and/or abrasive materials (eg dry paper towels) should be avoided. It is advisable to fast amphibians for 24-48 hours prior to anaesthesia to reduce faecal contamination and regurgitation. If the species of interest is an aquatic amphibian keep it moist during anaesthesia and recovery. Use water taken from the original holding tank for transport, anaesthetic induction and recovery. When inducing a terrestrial amphibian in an immersion bath, keep its head and nares above the water line to prevent accidental drowning. Maintain adequate oxygenation of holding tanks throughout the anaesthetic (supply oxygen via an air pump or similar device). Maintain water temperature at the species normal optimum throughout the procedure. Amphibians can remain out of water for long periods of time if they are kept moist and should be wrapped in damp cloth for transportation.
**Note:** Pulmonary respiration may cease under a surgical plane of anaesthesia, however, cutaneous respiration is sufficient to prevent hypoxia.

### ANAESTHESIA

Amphibians may be anaesthetised by immersion, or by gaseous or injectable agents. Anaesthetic monitoring is done mainly by observation, looking for gular movement, voluntary muscle movement, righting reflex and monitoring of heart rate (watch ventral midline, caudal to the shoulders, or apply an ECG monitor or ultrasonic doppler). Normal heart rates for amphibians are temperature dependent and are not yet well established, but trends are useful. A pulse oximeter can be used in amphibians to measure heart rate but oxygen saturation is not yet validated in amphibians, but again trends are useful. Surgical anaesthesia is reached when there is a loss of withdrawal reflex immediately before all gular pumping is lost.

If supplemental anaesthesia is needed, anaesthetic solution can be dripped on to the animal’s skin. At the end of anaesthesia, amphibians should be washed in warm chlorine free water. Aquatic species should be placed in a well oxygenated temperature controlled moist environment for recovery. Terrestrial species should also be kept in a moist temperature controlled environment. Do NOT raise the amphibian’s body temperature above that of the species’ normal optimum in an attempt to speed recovery. Increased body temperature will increase metabolism and oxygen requirements, and cutaneous respiration may not be sufficient to maintain adequate oxygenation in this situation. Close observation is necessary until the animals are moving around normally.

Intramuscular (into the thigh muscles), subcutaneous and intraperitoneal injections can be given to frogs but alcohol swabs should not be used as alcohol is absorbed through the skin and may cause skin irritation. Injection into the dorsal lymph hearts is simple as they are located pulsating on either side of the urostyle (the long unsegmented bone which is a number of fused vertebrae and forms the posterior part of the vertebral column).

A number of anaesthetic agents have been found to be effective in some species of amphibians, however effectiveness and safety on one species does not guarantee similar effectiveness and safety in another species.

The most popular general anaesthetic agents used with amphibians are alfaxalone, tricaine methanesulfonate (MS222), benzocaine, eugenol (clove oil) and isofluorane.

- **Alfaxalone** has a wide safety margin and may be administered to effect by dropping the solution on to the moist skin of the amphibian. “Topping up” is possible with the same method as alfaxalone does not have a cumulative action. It may also be used via intramuscular or intravenous injection at an initial dose rate of 5-10 mg/kg. The effectiveness of transcutaneous administration varies significantly with the species.

- **Tricaine methanesulfonate (MS222)** has a wide margin of safety. A neutral buffered stock solution is made as follows: 0.5-2g/L MS-222 buffered to pH 7.0-7.1 by adding 10g/L NaHCO3. This can be stored in a cool dark spot for up to 30 days. Amphibians are immersed in the solution. Water should be aerated to prevent hypoxaemia. Induction takes 5-20 minutes and can be maintained by
wrapping frog in cotton wool moistened with this solution, or dripping the solution onto the skin of the animal. Do not leave the animal in the bath after induction as overdose can occur. Analgesia and muscle relaxation is excellent. Recovery takes 25-70 minutes.

50-200mg/kg MS222 can be injected into dorsal lymph hearts, with subsequent substantial reduction in both induction and recovery times.

- **Benzocaine** must be dissolved in ethanol and then made into a bath at a concentration of **200-300mg/L for frogs** and **50mg/L for tadpoles**.

- **Clove oil** (eugenol) used via immersion at **300-450 mg/L** with induce anaesthesia in many amphibians but has been associated with gastric prolapse (which resolved spontaneously) in leopard frogs.

- **Isofluorane** can be directly applied to the skin at the rate of 0.07 - 0.015 mL/g bodyweight. Alternatively the isoflurane can be mixed with water (0.35 mL isoflurane to 125 mL water). Another method which results in a more rapid induction and recovery time is to apply isoflurane/KY jelly and water mix to the skin of the dorsum, using a thick solution of 3mL liquid isoflurane, 3.5mL K-Y jelly and 1.5mL water. (0.025-0.035mL/g). The percutaneous absorption of isoflurane is species dependent, the thicker skin of toads requiring higher dose rates.

Isofluorane can also be vapourised isoflurane in a water bath – 5% isoflurane vaporised in oxygen is bubbled into the water bath in which the animal is placed to effect.

*Note - an effective method of scavenging waste anaesthetic gas must be devised to use these systems eg induction of the isoflurane anaesthesia in a fume hood.*

All methods provide adequate sedation and/or anaesthesia. Animals should be removed from the isoflurane mixture immediately after induction to prevent deep and prolonged anaesthesia.

**ANALGESIA**

Amphibians are known to respond to pain with the release of endogenous opioids. Cold has been shown to reduce pain thresholds. A number of analgesics are recommended as follows (note: opioids may disrupt breeding cycles in amphibians):

- **Fentanyl** 0.5 mg/kg SC. Analgesia > 4 hours

- **Buprenorphine** 38 mg/kg SC. Analgesia > 4 hours

- **Dexmedetomidine** 40 - 120mg/kg SC. Analgesia > 4 hours

- **Morphine** 40 mg/kg SC. Analgesia > 4 hours

- **Meloxicam** 0.4 mg/kg PO, SC, Intra coelomic (every 24 hours)

**REPTILES**

**General Considerations**
Reptilian response to common sedatives is less predictable than in mammals. The metabolic rate of amphibians is 1/10 to 1/3 lower and varies widely with species, temperature, age, diet and gender. After feeding, basal metabolic rate increases 30-40X and this lasts for 7 days. Reptiles are ectotherms, and each species has a “preferred optimal temperature zone (POTZ)”. Patient should be fasted from between 4 hours and 24 hours prior to anaesthesia, as reptiles may suffer from impaired digestion. Every effort should be made to stabilise the patient medically, to ensure adequate hydration, and to warm the patient to its POTZ prior to anaesthetising. Non-crocodilians lack a diaphragm. Most snakes only have a right lung. Generally reptiles are episodic breathers with CO₂, O₂ and pH all affecting ventilation.

Following induction, intubation is relatively easy, with the glottis easily visualised on the ventral midline of the oral cavity. Uncuffed tubes are used in chelonians and crocodiles, due to their complete tracheal rings. Reptiles do not usually ventilate spontaneously under anaesthetic, and intermittent positive pressure ventilation (by hand or with a ventilator) should be used to provide adequate oxygen and inhalant anaesthetic. 4-6 breaths per minute is normal. Monitoring should involve observation of heart rate (by oesophageal stethoscope, or Doppler probe), respiratory rate, muscle tone (jaws and limbs) and oxygen saturation (trends are valuable). On recovery, maintain ventilation but swap to room air. Respiratory drive is dictated by low O₂, not high CO₂ as in mammals.

Access to veins in reptiles usually involves cutting down, with the exception of coccygeal veins in snakes, turtles and lizards, in the ventral midline of the tail. Intramuscular injections are best given in the epaxial muscles in the cranial half of the body of snakes, and the musculiest part of the upper foreleg (either the triceps/deltoid of the biceps) in lizards and chelonians. Fluids should be given at a rate of 5-10mL/kg during anaesthesia, either intraosseous or IV. Intraosseous injections are usually only given to lizards, and usually either the proximal tibia or distal femur are used. Alternatively a subcutaneous bolus may be given.

ANAESTHESIA

A number of agents have been used to induce anaesthesia in reptiles. For short non-painful procedures such as radiography, the vagal-vagal response (also known as the “oculovagal reflex” or the oculocardiac reflex”) can be used. Pressure over the eyes of most large lizards and crocodilians for about a minute will cause a decrease in heart rate and blood pressure and the reptile may become inactive. It should be noted that animals may be roused from this condition by a loud noise, or physical stimulation. It should also be noted that pressure over the eyes can manifest as cardiac arrhythmias, which may include bradycardia, nodal rhythms ectopic beats, ventricular beats or asystole.

- **Alfaxalone** may be used intravenously or intramuscularly, 5-10mg/kg, and “topped up” to effect if the procedure is long. It produces good muscle relaxation, and while the cardiorespiratory effects have not been fully evaluated in reptiles, there appears to be minimal dose-dependent respiratory depression.

- **Ketamine/ Medetomidine** combination may be given intramuscularly in most species and results in good muscle relaxation and good pain relief. Ketamine is given at a dose rate of 10mg/kg and medetomidine may be given in the same syringe at a dose of 0.1-0.3mg/kg. Reverse the medetomidine with atipamezole.

- **Zoletil (tiletamine and zolzepam)** may be given intramuscularly at a dose of 2-4mg/kg IM, but it is associated with prolonged recoveries.
- **Isofluorane** is an excellent choice of anaesthetic, but due to the three chambered reptilian heart, which admixes oxygenated and non-oxygenated blood, there is often a mismatch of blood concentration and anaesthetic depth. It is wise to induce the animal with an injectable agent and maintain on isofluorane.

- **Local anaesthesia:**
  - **Bupivacaine** may be used by local infiltration as a local anaesthetic, at a dose rate of 1-2mg/kg or to effect. This gives 4-12 hours of local anaesthesia to treated area.

**ANALGESIA**

- **Buprenorphine** 0.01- 0.03mg/kg IV or IM every 12 hours
- **Carprofen** may be used at a dose of 1-4mg/kg PO, SC, IM, or IV every 24 hours, followed by a half dose every 1-3 days.
- **Meloxicam** 0.1-0.5mg/kg PO or SC every 24 -48 hours
- **Morphine** 0.1 – 0.2 mg/kg PO or SC every 24 hours
- **Tramadol** 5-10 mg/kg PO every 24 hours

Recent studies have shown **butorphanol** to provide inadequate pain relief in reptiles. **Buprenorphine and carprofen can be used concurrently at the above doses where additional pain relief is required.**

**BIRDS**

**General Considerations**

Prior to anaesthesia avian patients should be fasted (4-6 hours) and in a stable condition. A filled crop should be emptied. Larger birds can be fasted overnight. Waterfowl, and possibly other birds, have a 'dive response' that can prevent normal respiration when the beak is closed. When anaesthetising waterfowl, a large face mask that permits opening of the patient's beak should be used. In some larger birds it is also possible to place an anaesthetic mask directly over the opening of the trachea (the glottis).

Fluid therapy (Hartmans or 0.9% saline) is advised for dehydrated birds or extended surgery. The proximal tibiotarsus is frequently used for intraosseous catheterisation and fluid administration. With the patient restrained (preferably under anaesthesia), the chosen leg is extended at the hip and flexed at the stifle. The bird's leg is stabilised and the orientation of the tibiotarsus and its location within the surrounding leg muscles is determined. A 22-25 g standard needle is inserted into the stifle just lateral or medial to the patellar tendon. While aligned with the diaphysis, the needle is gently rotated and advanced (from proximal to distal) through the flattened cranial portion of the proximal tibiotarsus into the marrow. The needle should be advanced...
approximately one third to one half the length of the tibiotarsus. Fluids should be warmed before administration and can be given at a rate of 10mL/kg/hour.

Monitoring blood pressure is extremely useful as a sensitive indicator of the bird’s health and anaesthetic depth. A Doppler unit should be used, with the probe placed over one of the visible vessels (eg cutaneous ulnar/wing vein and ulnar artery which crosses the medial elbow region). The cuff is placed on the humerus. Mean systolic pressure is approximately 150mmHg.

Avian patients are positioned as needed for the given procedure, but are generally in dorsal or lateral recumbency. Unless absolutely necessary for the given procedure, birds should not be placed in a dorsoventral position while under anaesthesia as the bird’s body weight can inhibit normal thoracic movement and respiration. The bird’s head should be elevated to prevent leakage of crop and other intestinal contents and potential aspiration. Supplemental heat (ideally, an overhead heat lamp) should be provided to maintain the bird’s warmth.

It is advisable to use clear surgical drapes where possible so that the patient can be easily visualised and monitored. Monitoring includes recording of heart rate, respiration rate, pedal reflex, palpebral reflex and corneal reflex. The palpebral reflex is present only in lightly anesthetised birds.

Respiratory rate and character are the most reliable indicators of depth of anaesthesia in birds. A surgically anaesthetised bird will have no palpebral or pedal reflex, a sluggish corneal reflex, good muscular relaxation and a slow deep, regular respiration.

In recovery, birds often go through a period of delirium, with vigorous wing flapping. Patients should be wrapped lightly in a towel and placed in a warm dark quiet place, with all monitoring equipment removed. If necessary the mouth should be cleaned of any regurgitation.

**ANAESTHESIA**

Local anaesthetic agents are not recommended for birds as very high doses are required and these may result in toxic effects.

- **Isofluorane** is currently the anaesthetic of choice for birds. It offers rapid induction and recovery, easy control of anaesthetic depth, improved oxygenation due to concurrent use of oxygen, and recovery that is not dependent on metabolic or excretory pathways. It should be kept in mind that Isofluorane causes hypoventilation in birds and is more likely to cause respiratory depression than in mammals. Birds are induced with 3-5% isofluorane via a mask using a non-rebreathing (Bain) circuit, intubated with a non-cuffed size 2-3 intratracheal tube and maintained on 2-3% isofluorane. Decreases or changes in heart rate are often mirrored and preceded by changes in respiration. Underlying diseases (heart, lung and air sac disorders), as opposed to human induced overheating and pain, are more frequently associated with dyspnea in birds. Dyspnoea (abnormal rate or character of breathing) may occur due to an obstruction (such as a mucus plug) in the trachea or endotracheal tube, poor cardiovascular perfusion (heart disease and anaemia), fluid or blood filled lungs (pulmonary oedema, inflammation and haemorrhage) and decreased or diseased air sac space resulting from improper restraint/positioning, ascites, bleeding, organomegaly, other abdominal masses and air sacculitis. Correction of dyspnea is aimed at identifying and addressing the underlying cause.
- **Alfaxalone** may be administered at a rate of 5mg/kg into the pectoral muscle after sedation with intramuscular injection with diazepam 0.2mg/kg /butorphanol 0.1mg/kg IM. Anaesthesia should last approximately 30 minutes.

- **Propofol** 1-5 mg/kg IV provides a short duration anaesthesia and can be used as an induction agent prior to isoflurane anaesthesia. Provides no analgesia so an adjunct analgesic must be used for painful procedures.

### ANALGESIA

Analgesics are poorly studied in birds, and as a wild species they do not tend to exhibit overt signs of pain. Some signs of pain could include guarding a limb, picking feathers over a limited area, acting aggressively, having focal muscle contractions, shivering, anorexia, or intensively fearful or phobic responses to basic handling or approaches (fear of a person touching a painful area or falling on a sore keel). It is the subtle, and not overt, signs of pain that more likely predominate in painful avian patients. Wide variation in responses to analgesics can occur between major groups of birds. Keeping in mind that all the side effects of analgesics have not been studied in birds, suggestions include:

- **Meloxicam** 0.1 - 0.5 mg/kg PO every 24 hours (recommended)
- **Butorphanol** 1-4 mg/kg IM or PO every 6 hr.
- **Buprenorphine** 0.01-0.05 mg/kg SC, IP, IV every 6 hr
- **Tramadol** 5mg/kg PO/IV every 12 hr.
- **Carprofen** 1-2 mg/kg PO/IV/IM . Highest effects for 1-2 hours post administration.

### GUINEA PIGS

#### General Considerations

Since guinea pigs cannot vomit, fasting prior to the procedure is not necessary. However, guinea pigs nearly always have “cud” in their mouths that can obstruct their airway or become aspirated, so it is necessary to clear the oral cavity and cheeks of food with a cotton tip on induction. They have long narrow airways which cause resistance and large amounts of dead space. Calculating accurate dosages of anaesthetics on a bodyweight basis is difficult since the gastrointestinal tract may contribute to up to 20% of total body weight. Pre-emptive analgesia with an opioid is recommended, and sedation prior to anaesthesia will reduce stress. Inhalational anaesthesia is preferred as it provides better control of anaesthetic depth and provides for the administration of oxygen. However in the absence of specialised equipment a variety of injectable agents are available. Endotracheal intubation is difficult but not impossible due to the inability to open a guinea pig's mouth very wide or to visualise the larynx. An otoscope is used to guide a urinary catheter towards the larynx. A small spray of local anaesthetic is directed at the larynx, the otoscope is removed and after 2-3 minutes the urinary catheter is passed through and into the trachea. A small uncuffed endotracheal tube is then threaded over the urinary catheter and into the trachea.
Monitoring under general anaesthetic is critical. A nominated anaesthetist should monitor palpebral reflex, pedal reflex, and general muscle tone as well as body temperature, respiratory rate, heart rate, tissue colour, capillary refill time and if possible blood pressure and saturated oxygen concentration.

Post-operative care involves placing the animal on its side, head extended in a clean, dry, warm (30°C) box in a dark quiet room in a position where recovery can be monitored. Ensure that animals do not become hypothermic. Post-anaesthetic complications such as respiratory infections, digestive disturbances and generalised depression and inappetence are frequently seen.

**Physiologic Parameters**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Temperature</td>
<td>37.2-39.5°C</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>240-310 bpm</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>40-100 bpm</td>
</tr>
<tr>
<td>Tidal Volume</td>
<td>2.3-5.3 ml/kg</td>
</tr>
</tbody>
</table>

**ANAESTHESIA**

Guinea pigs may be pre-medicated with atropine (0.1-0.2mg/kg SC, IM) 30 minutes prior to anaesthetic to decrease bronchial and salivary secretions and treat bradycardia. Ensure that the use of atropine is compatible with the anaesthetic drugs used.

- **Ketamine / Medetomidine (Ketamine 40 mg/kg, medetomidine 0.5 mg/kg IP)** will provide 20-30 minutes of surgical anaesthesia. DO NOT use atropine with medetomidine. Medetomidine can be reversed with **atipamezole 1.0 mg/kg IM**, which reverses hypotension and respiratory depression, but also removes relaxation and some of the analgesia. Note; The dose of ketamine can be reduced by using an opioid premedication.

- **Ketamine/ Diazepam (Ketamine 30 mg/kg, diazepam 2 mg/kg IP)** provides 20-30 minutes of light anaesthesia.

- **Propofol 3-5 mg/kg IV** provides 5 minutes of surgical anaesthesia.

- **Urethane (1500mg/kg IP, IV)** gives long duration anaesthesia and is used for **NON RECOVERY PROCEDURES ONLY**. The solution should be freshly made up on the day of use, and may be carcinogenic to the handler.

- **Isoflurane** is mixed with oxygen with a calibrated vapouriser and administered at a concentration of 4-5% via a face mask or in an anaesthetic chamber for induction. Anaesthesia is maintained using 1.5-3% isoflurane via face mask or endotracheal tube.

- **Local anaesthetics** Lignocaine and bupivacaine may be combined in a single syringe to rapid onset, long duration local anaesthesia (and analgesia).
  
  - **Lignocaine** dilute to 0.5%. Do not exceed 2mg/kg total dose SC or intracincisional.
- **Bupivacaine** Dilute to 0.25%. Do not exceed 1-2 mg/kg total dose SC or intracisional.

- **Lignocaine/ bupivacaine** Combine in one syringe. Do not exceed 1 mg/kg lignocaine and 1 mg/kg bupivacaine total dose.

**ANALGESIA**

Analgesia is best given prior to the commencement of any painful procedure such as surgery. There are two major classes of analgesic (opioids and non-steroidal anti-inflammatory drugs) which may be used in conjunction to provide optimal pain relief e.g. Morphine or buprenorphine combine with carprofen or meloxicam are suitable choices.

- **Buprenorphine** 0.05-0.1 mg/kg SC 8-12 hourly
- **Morphine** 2-5 mg/kg SC, IM 4 hourly
- **Butorphanol** 0.025-0.4 mg/kg SC, IM 8 hourly
- **Carprofen** 1-4 mg/kg PO, SC 12 hourly
- **Meloxicam** 0.5 mg/kg PO, SC once daily.
- **Tramadol** 5-10 mg/kg PO 12- 24 hourly
- **Fentanyl** If longer acting pain relief is required fentanyl patches should be considered (0.25 x 12ug/hr durogescic patch /kg). Buprenorphine may also be administered orally in a jelly (see Part 5).

**MARSUPIALS**

**General Considerations**

This section primarily relates to wallabies. For information regarding other species please contact the University veterinarian.

Where possible, pre-anaesthetic fasting for 12-24 hours should be practised for foregut-fermentative ruminant-type marsupials (kangaroos and wallabies)

Stress is a major cause of mortality in marsupials. This can be limited by careful and efficient handling. The shape of holding yards is important: there should be a narrow funnelled corner in wallaby yards to enable cornering of animals for stress free capture. Wallabies should be held in hessian bags to create a dark warm quiet environment. Prior to any anaesthesia, the animals should be premedicated with an anxiolytic or a sedative.

Intubation of wallabies is difficult but not impossible due to their long narrow mouth cavity. An otoscope is used to guide a urinary catheter to the larynx and passed through into the trachea. A small endotracheal tube is then threaded over the urinary catheter and into the trachea. Alternatively for shorter procedures animals can be maintained with a close fitting face mask.

Monitoring follows regular guidelines: monitor respiratory and cardiac rate, degree of muscle tone, mucous membrane colour, body temperature, and pinch, righting and
palpebral reflexes. Pulse oximetry and doppler blood pressure monitoring if available are also useful.

**Physiologic Parameters (Tammar Wallaby)**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Temperature</td>
<td>36.4°C</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>65-100 bpm</td>
</tr>
</tbody>
</table>

**ANAESTHESIA**

The dose of injectable agents can be adjusted according to whether the desired result is simple sedation and immobilisation or full surgical anaesthesia. Dissociative agents have been widely used in marsupials, often by dart gun. The literature reports a wide variation of dosages for ketamine that have been used; due to poor visceral analgesia and muscular rigidity ketamine is best combined with medetomidine and an opioid. Tiletamine-zolazepam is also widely used.

- **Preanaesthetic agents:**
  - **Diazepam** 1-2 mg/kg IM provides good sedation for procedures such as blood collection, and is also a good premedication prior to gaseous anaesthesia.
  - **Atropine** 0.1 mg/kg IM produces cardiovascular protective effects and reduces salivation.

- **Isoflurane** Wallabies are restrained in hessian bags with their heads poking out far enough to allow a close fitting mask induction using 4% isofluorane until the desired plane of anaesthesia is reached. Maintain via mask or endotracheal tube or isofluorane. Increased sensitivity to noise stimuli is normal.

- **Ketamine/ Medetomidine:** Ketamine (4-7mg/kg IM) + medetomidine (100-200μg/kg IM). Medetomidine can be reversed with atipamezole (50-400 μg/kg IM).

- **Ketamine/ Diazepam:** Ketamine (3 mg/kg IM) + diazepam (1-2 mg/kg IM)

- **Afaxalone:** 1.5-3 mg/kg IV, 5-8 mg/kg IM

- **Tiletamine +zolazepam** 20-30 mg/kg IM. Used for examination alone. This combination can be used as an induction agent (2.5 mg/kg IV) for intubation and gaseous anaesthetic with isofluorane and O2.

- **Propofol** 6-8 mg/kg slowly IV. Transitory apnoea may occur.

- **Local anaesthetics** Lignocaine and bupivacaine may be combined in a single syringe to rapid onset, long duration local anaesthesia (and analgesia).
  - **Lignocaine** dilute to 0.5%. Do not exceed 2mg/kg total dose SC or intracincisional.
  - **Bupivacaine** Dilute to 0.25%. Do not exceed 1-2 mg/kg total dose SC or intracincisional.
- **Lignocaine/ bupivacaine** Combine in one syringe, Do not exceed 1 mg/kg lignocaine and 1 mg/kg bupivacaine total dose.

**ANALGESIA**

- **Buprenorphine:** 0.01 mg/kg SC every12 hr
- **Meloxicam:** 0.1 – 0.2 mg/kg SC, IM, PO every 24 hr
- **Carprofen** 2-4 mg/kg IV, SC, PO every 24 hr
- **Fentanyl patches:** If longer acting pain relief is required fentanyl patches should be considered (0.25 x 12ug/hr durogesic patch /kg).

**MICE**

**General Considerations**

Prior to anaesthesia mice should be examined to confirm that they are in good health. Disease markedly increases the risk of mortality during anaesthesia. Mice do not need to be fasted as they cannot vomit and fasting may result in a depletion of glycogen reserves, and the development of hypoglycaemia. Animals should be weighed accurately just prior to sedation.

Pre-emptive analgesia with an opioid or non-steroidal anti-inflammatory or combination of the two is recommended when painful procedures are carried out under anaesthesia.

Due to their small size mice rapidly become hypothermic when anaesthetised. Warming pads must be used during anaesthesia. Inhalation anaesthesia delivery sets are available that warm the anaesthetic gas as it is delivered to the animal.

Monitoring under general anaesthetic is critical. A nominated anaesthetist should monitor palpebral reflex, pedal reflex, tail pinch reflex, and general muscle tone as well as body temperature, respiratory rate, heart rate, tissue colour, capillary refill time and if possible blood pressure and saturated oxygen concentration.

Post-operative care involves placing the animal on its side, head extended in a clean, dry, warm (30°C) box in a dark quiet room in a position where recovery can be monitored. Ensure that mice do not become hypothermic.

**Physiologic Parameters**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Temperature</td>
<td>36.5- 38.0°C</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>325- 750 bpm</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>95-165 bpm</td>
</tr>
<tr>
<td>Tidal Volume</td>
<td>0.09-0.23 ml</td>
</tr>
</tbody>
</table>
ANAESTHESIA

There are many anaesthetic regimes that are useful in the mouse. Selection of the appropriate regime should be based on experience, ease of use, safety and appropriateness for the research being undertaken.

- **Isofluorane.** Inhalation anaesthesia is recommended as a safe, effective, adjustable and easily reversible method of anaesthetising mice. Induction is possible using an anaesthetic chamber or facemask with 4% isofluorane in oxygen. A vaporiser is necessary for this. Mice may be maintained using a facemask at with 1-2.5% isofluorane in oxygen. Endotracheal intubation is possible but difficult.

- **Propofol** 26 mg/kg IV provides surgical anaesthesia for 5-10 minute.

- **Propofol/ medetomidine/ fentanyl:** Propofol (75mg/kg IP) + medetomidine (1.0 mg/kg IP) + fentanyl (0.2mg/kg IP) produces surgical anaesthesia for 15 minutes and restraint for 30 minutes. Anaesthesia can be partially reversed with atipamezole (1 mg/kg SC).

- **Ketamine/ medetomidine:** Ketamine 50-75mg/kg IP combined with Medetomidine 1 mg/kg IP provides up to 30 minutes of anaesthesia. Use the higher dose of ketamine in female mice. Addition of an opioid may be needed for painful procedures (see regime above) and effects can be variable in some strains. Medetomidine can be reversed with atipamezole 1 mg/kg SC. *Note: Use with caution in male mice of strains prone to urinary tract obstruction as this combination has been associated with urethral obstruction in some male mice.*

- **Alfaxalone** 5mg/kg IV, 15 mg/kg IM or 20mg/kg IP provides 5 minutes of anaesthesia.

- **Local anaesthetics** Lignocaine and bupivacaine may be combined in a single syringe to rapid onset, long duration local anaesthesia (and analgesia).
  
  o **Lignocaine** dilute to 0.5%. Do not exceed 2mg/kg total dose SC or intracisional.
  
  o **Bupivacaine** Dilute to 0.25%. Do not exceed 1-2 mg/kg total dose SC or intracisional.
  
  o **Lignocaine/ bupivacaine** Combine in one syringe, Do not exceed 1 mg/kg lignocaine and 1 mg/kg bupivacaine total dose.

ANALGESIA

- **Buprenorphine** 0.05-0.1 mg/kg SC every 8-12 hr Buprenorphine may also be administered orally in a jelly (see Part 5).

- **Morphine** 2-5 mg/kg SC every 2-4 hr

- **Butorphanol** 1-5 mg/kg SC, IM every 4 hr

- **Meloxicam** 1-5mg/kg PO, SC every 24 hr

- **Carprofen** 2 mg/kg SC, PO every 12 hr

- **Tramadol** 5-40mg/kg SC, IP

- **Fentanyl:** If longer acting pain relief is required fentanyl patches should be considered (0.25 x 12ug/hr durogesic patch /kg).
RABBITS

General Considerations

Before any procedure is undertaken in rabbits, they should be checked for health, especially for any signs of respiratory disease or discharge. Rabbits do not need to be fasted as they cannot vomit, but they should be moved, preferably in their own cages, into the laboratory for 2-4 hours and observed prior to any procedure. Rabbits may accumulate food in the oral cavity and withdrawing food one hour prior to anaesthesia will minimise the chance of food in the mouth being inhaled during anaesthetic induction. Animals should be weighed accurately just prior to sedation.

Intubation of rabbits is challenging due to their long oral cavity. A blind intubation technique can be used where the rabbit’s head is extended so that the oral cavity forms a straight line with the trachea, an uncuffed endotracheal tube is advanced while listening down the endotracheal tube for breath sounds, on inspiration the tube is advanced into the trachea. The larynx can also be visualised using an otoscope. A urinary catheter is guided to the larynx and a small spray of local anaesthetic is directed at the larynx. The otoscope is then removed and after 2-3 minutes the urinary catheter is passed through and into the trachea. A small uncuffed endotracheal tube is then threaded over the urinary catheter and into the trachea.

Post-operative care involves placing the rabbit on its side, head extended, in a clean, dry, warm (30°C) box in a dark quiet room in a position where recovery can be monitored. Ensure that animals do not become hypothermic. Post-anaesthetic complications such as respiratory infections, digestive disturbances and generalised depression and inappetence are frequently seen.

Pre-emptive sedation/analgesia with an opioid, non-steroidal anti-inflammatory or combination of the two is recommended.

Monitoring under general anaesthetic is critical. A nominated anaesthetist should monitor palpebral reflex, pedal reflex, tail pinch reflex, and general muscle tone as well as body temperature, respiratory rate, heart rate, tissue colour, capillary refill time and if possible blood pressure and saturated oxygen concentration (see Appendix 1 for sample monitoring checklist).

Post-operative care involves placing the rabbit on its side, head extended, in a clean, dry, warm (30°C) box in a dark quiet room in a position where recovery can be monitored. Ensure that animals do not become hypothermic. Post-anaesthetic complications such as respiratory infections, digestive disturbances and generalised depression and inappetence may be seen.

Physiologic Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Temperature</td>
<td>38.5-39.5°C</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>205-235 bpm</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>30-60 bpm</td>
</tr>
<tr>
<td>Tidal Volume</td>
<td>4-6 ml/kg</td>
</tr>
<tr>
<td>Oxygen consumption</td>
<td>0.48 ml/hr/g BW</td>
</tr>
</tbody>
</table>
ANAESTHESIA

Induction of anaesthesia using gaseous anaesthetic agent is hazardous because of the prevalence of breath holding in rabbits. Sedation does not block this response. It is preferable to induce anaesthesia with an injectable agent and maintain the rabbit on an inhalation anaesthetic. If induction with an inhalation agent is required, the animal should be observed closely for episodes of breath holding. Rabbits should be premeditated prior to general anaesthesia to ensure a smooth induction and recovery and provide preemptive pain relief.

- **Isoflurane** Maintenance by endotracheal intubation. Maintenance of gaseous anaesthesia by mask is not recommended in rabbits because of the prevalence of breath holding in this species.
- **Alfaxalone** 1 mg/kg IV to effect provides short term anaesthesia.
- **Propofol** 5-10 mg/kg IV provides short term anaesthesia. A continuous rate infusion of propofol can be given to maintain anaesthesia 0.5-1.5 mg/kg/min.
- **Ketamine/ Medetomidine**: Ketamine (25 mg/kg IM) and medetomidine (0.5 mg/kg IM), provides about 30 mins of surgical anaesthesia after opioid sedation. Anaesthesia can be partially reversed using **atipamezole** (1 mg/kg SC or IV).
- **Fentanyl/ medetomidine**: Fentanyl (8µg/kg) and medetomidine (330 µg/kg) administered in combination by intravenous injection produce good surgical anaesthesia after opioid sedation, but some animals may make spontaneous movements in response to non-painful stimuli. An advantage of this combination is that it can be completely reversed using **atipamezole** (1 mg/kg IV) and **naloxone** (1 mg/kg IV).
- **Local anaesthetics** Lignocaine and bupivacaine may be combined in a single syringe to rapid onset, long duration local anaesthesia (and analgesia).
  - **Lignocaine** dilute to 0.5%. Do not exceed 2mg/kg total dose SC or intracinsional.
  - **Bupivacaine** Dilute to 0.25%. Do not exceed 1-2 mg/kg total dose SC or intracinsional.
  - **Lignocaine/ bupivacaine** Combine in one syringe, Do not exceed 1 mg/kg lignocaine and 1 mg/kg bupivacaine total dose.

ANALGESIA

- **Morphine** 2-5 mg/kg SC or IM 2-4 hourly
- **Buprenorphine** 0.01-0.05 mg/kg SC, IM, IV 6-12 hourly Buprenorphine may also be administered orally in a jelly (see Part 5).
- **Butorphanol** 0.1-0.5 mg/kg SC, IM, IV every 4 hours
- **Carprofen** 4 mg/kg SC 24 hourly or 1.5 mg/kg PO 12 hourly
- **Meloxicam** 0.2 mg/kg SC, IM every 24 hr
- **Tramadol** 4.4mg/kg IV (PO – not recommended in this species as adequate plasma concentrations (based on human levels) are hard to achieve)
- **Fentanyl:** If longer acting pain relief is required fentanyl patches should be considered (0.25 x 12ug/hr durogesic patch /kg).

**RATS**

**General Considerations**

Before any procedure is undertaken in rats, they should be checked for health, especially for any signs of respiratory disease or discharge. Rats do not need to be fasted as they cannot vomit, but they should be moved, preferably in their own cages, into the laboratory for 2-4 hours and observed prior to any procedure. Animals should be weighed accurately just prior to sedation. Pre-emptive analgesia with an opiate or non-steroidal anti-inflammatory or combination of the two is recommended.

Intubation of rats is challenging due to their long oral cavity. The rat's head is extended so that the oral cavity forms a straight line with the trachea. An otoscope is used to guide a urinary catheter to the larynx. A small spray of local anaesthetic is directed at the larynx, then the otoscope is removed and after 2-3 minutes the urinary catheter is passed through and into the trachea. A small uncuffed endotracheal tube is then threaded over the urinary catheter and into the trachea.

Monitoring under general anaesthetic is critical. A nominated anaesthetist should monitor palpebral reflex, pedal reflex, tail pinch reflex, and general muscle tone as well as body temperature, respiratory rate, heart rate, tissue colour, capillary refill time and if possible blood pressure and saturated oxygen concentration. Rats must be kept warm during anaesthesia using a warming pad.

Post-operative care involves placing the rat on its side, head extended, in a clean, dry, warm (30°C) box in a dark quiet room in a position where recovery can be monitored. Ensure that animals do not become hypothermic. Post-anaesthetic complications such as respiratory infections, digestive disturbances and generalised depression and inappetence may be seen.

**Physiologic Parameters**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Temperature</td>
<td>35.9-37.5°C</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>250- 450 bpm</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>70- 115 bpm</td>
</tr>
<tr>
<td>Tidal Volume</td>
<td>0.6-2.0 ml</td>
</tr>
</tbody>
</table>

**ANAESTHESIA**

- **Isoflurane:** Induction is carried out with 4% isofluorane using an anaesthetic chamber or facemask. The animal is maintained on 1-2.5% isofluorane using a facemask or intubation with a catheter. Rats may be intubated, however this can enhance anaesthetic risks because of increased resistance from very small diameter endotracheal tube. Active ventilation (positive pressure ventilation) may be needed to ensure adequate administration of both gaseous anaesthetic and oxygen when intubated.
- **Alfaxalone**: 5mg/kg IV, 10mg/kg IM or 20 mg/kg IP) produces good short term (5 minutes) surgical anaesthesia. IM and IP route are not as reliable as IV.

- **Propofol**: 10 mg/kg IV provides 5 minutes of surgical anaesthesia. A constant rate infusion can be used to provide longer anaesthesia.

- **Fentanyl/ medetomidine**: Fentanyl (300 µg/kg IP) and medetomidine (300 µg/kg IP) can be mixed and administered as a single injection. The combination provides about 60 minutes of surgical anaesthesia. This anaesthetic combination can be fully reversed by administration of **atipamezole** (1 mg/kg SC or IP) to reverse the medetomidine, and either **naloxone** (0.1 mg/kg IV, 1.0 mg/kg IP or SC), **butorphanol** (0.1 mg/kg iv, 2 mg/kg IP or SC) or another mixed agonist/antagonist opioid analgesic to reverse the fentanyl.

- **Propofol/ Medetomidine/ Fentanyl**: Propofol (100mg/kg IP) combined with Medetomidine (0.1 mg/kg IP) and Fentanyl (0.1 mg/kg IP) provides surgical anaesthesia for 25 minutes and can be reversed using **atipamezole** (0.5 mg/kg IP or SC).

- **Ketamine/ Medetomidine**: Ketamine (75 mg/kg IP) and medetomidine (0.5 mg/kg IP) will provide good surgical anaesthesia for about 30 minutes. Opioid premedication may be required for painful procedures, however the use of buprenorphine should be avoided with this anaesthetic combination as unexpected deaths have been observed. (The combination may be partially reversed using **atipamezole** (1 mg/kg SC or IP).

- **Local anaesthetics**: Lignocaine and bupivacaine may be combined in a single syringe to rapid onset, long duration local anaesthesia (and analgesia).
  - **Lignocaine**: dilute to 0.5%. Do not exceed 2mg/kg total dose SC or intracincisional.
  - **Bupivacaine**: Dilute to 0.25%. Do not exceed 1-2 mg/kg total dose SC or intracincisional.
  - **Lignocaine/ bupivacaine**: Combine in one syringe, Do not exceed 1 mg/kg lignocaine and 1 mg/kg bupivacaine total dose.

**ANALGESIA**

- **Carprofen**: 5 mg/kg SC, PO every 12 hr
- **Meloxicam**: 1-2 mg/kg SC, PO every 12 hr
- **Tramadol**: 5-20 mg/kg PO or SC q 12-24 hr
- **Butorphanol**: 2 mg/kg SC every 4 hr
- **Buprenorphine**: 0.02-0.05 mg/kg SC, IV, IP every 6-12 hr, 2-10mg/kg PO q 8-12hr. Buprenorphine may also be administered orally in a jelly (see Part 5). **DO NOT** give buprenorphine as a pre anaesthetic agent to rats anaesthetised with ketamine medetomidine as deaths have occurred. It can be used post operatively.
- **Fentanyl:** Fentanyl patches provide strong long lasting pain relief and should be considered (0.25 x 12ug/hr durogesic patch /kg) where intense pain relief is required.

**OTHER SPECIES**

For other species or for information about other anaesthetics and analgesics please contact the Animal Welfare and Training Unit.

7. Essential Supporting Documents

- Australian code for the care and use of animals for scientific purposes.

8. References

- Burnside et al. A comparison of medetomidine and its active enantiomer dexametomidine when administered with ketamine in mice. BMC Veterinary Research 2013, 9:48


9. APPENDICES

Appendix 1: Sample Anaesthetic Record

<table>
<thead>
<tr>
<th>Premedication:</th>
<th>Induction:</th>
<th>Maintenance:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time:</td>
<td>Time:</td>
<td>Signature:</td>
</tr>
<tr>
<td>Drug(s)/dose:</td>
<td>Drug(s)/dose:</td>
<td></td>
</tr>
<tr>
<td>Route of administration:</td>
<td>Route of administration:</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time (10 minute intervals)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pedal reflex (Y/N)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palpebral reflex (Y/N)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ear pinch reflex (Y/N)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart Rate (bpm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory Rate (bpm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mucous membrane colour</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capillary Refill time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxygen saturation (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arterial Blood Pressure (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body temperature (°C)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isofluorane (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Appendix 2: Suggested dose rates for Non-Steroidal Anti-Inflammatory Drugs in laboratory animals.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Rat</th>
<th>Mouse</th>
<th>Guinea Pig</th>
<th>Rabbit</th>
<th>Bird</th>
<th>Wallaby</th>
<th>Amphibian</th>
<th>Fish</th>
<th>Reptile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carprofen</td>
<td>5 mg/kg SC q24h</td>
<td>2 mg/kg SC, PO q12h</td>
<td>1-4 mg/kg PO, SC q12h</td>
<td>1.5 mg/kg PO q12h</td>
<td>1-2 mg/kg q8-24h</td>
<td>2-4 mg/kg IV, SC, PO q24h</td>
<td></td>
<td></td>
<td>1-4 mg/kg PO, SC, IM, IV q24h</td>
</tr>
<tr>
<td></td>
<td>1.5 mg/kg PO q12h</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meloxicam</td>
<td>1-2 mg/kg SC, PO q24h</td>
<td>1-5 mg/kg PO, SC q24h</td>
<td>0.5 mg/kg PO, SC q24h</td>
<td>0.2 mg/kg SC, IM q24h</td>
<td>0.1-0.5 mg/kg PO 24 hourly</td>
<td>0.1-0.2 mg/kg SC, PO, IM q24h</td>
<td>0.4 mg/kg PO, SC q24h</td>
<td>0.2 mg/kg IM</td>
<td>0.1-0.5 mg/kg PO, SC q24-48h</td>
</tr>
</tbody>
</table>
Appendix 3: Suggested dose rates for opioid analgesics in laboratory animals

<table>
<thead>
<tr>
<th>Drug</th>
<th>Rat</th>
<th>Mouse</th>
<th>Guinea Pig</th>
<th>Rabbit</th>
<th>Bird</th>
<th>Wallaby</th>
<th>Amphibian</th>
<th>Fish</th>
<th>Reptile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>0.02-0.05 mg/kg SC, IV, IP q6-12h 0.1-0.3mg/kg PO q8-12h</td>
<td>0.05-0.1 mg/kg SC q8-12h</td>
<td>0.05 – 0.1 mg/kg SC q8-12h</td>
<td>0.01-0.05 mg/kg SC, IP or IV q6-12h</td>
<td>0.01-0.05 mg/kg IM</td>
<td>0.01 mg/kg SC 12 hourly</td>
<td>38 mg/kg SC</td>
<td></td>
<td>0.01-0.03 mg/kg IV, IM q12h</td>
</tr>
<tr>
<td>Butorphanol</td>
<td>1.0-2.0 mg/kg SC q2-4h</td>
<td>1.0-5.0 mg/kg SC q4h</td>
<td>0.025-0.4mg/kg SC, IM, q8h</td>
<td>0.1-0.5 mg/kg SC, IM, IV q4-6h</td>
<td>1-4 mg/kg IM 6 hourly</td>
<td></td>
<td>0.1-0.4 mg/kg IM, SC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine</td>
<td>2-5 mg/kg SC, IM q4h</td>
<td>2-5 mg/kg SC, IM q4h</td>
<td>2-5 mg/kg SC, IM q4h</td>
<td>2-5 mg/kg SC, IM q4h</td>
<td>40mg/kg SC</td>
<td></td>
<td>5 mg/kg IM, IP</td>
<td>0.1-0.2 mg/kg PO, SC q24h</td>
<td></td>
</tr>
<tr>
<td>Tramadol</td>
<td>5-20 mg/kg PO, SC q12h</td>
<td>5-40 mg/kg SC, IP</td>
<td>5-10 mg/kg PO q12h</td>
<td>4.4 mg/kg IV</td>
<td>5 mg/kg PO, IV q12h</td>
<td></td>
<td></td>
<td>5-10 mg/kg PO q24h</td>
<td></td>
</tr>
<tr>
<td>Fentanyl</td>
<td>0.25 x 12ug/hr durogesic patch/kg</td>
<td>0.25 x 12ug/hr durogesic patch/kg</td>
<td>0.25 x 12ug/hr durogesic patch/kg</td>
<td>0.25 x 12ug/hr durogesic patch/kg</td>
<td>0.25 x 12ug/hr durogesic patch/kg</td>
<td>0.25 x 12ug/hr durogesic patch/kg</td>
<td>0.5 mg/kg SC q4-6h</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix 4: Suggested dose rates for injectable anaesthesia in laboratory animals

*Note:* there may be strain specific and species specific differences in responses to the regimes indicated below. Always use the lowest dose initially and evaluate anaesthetic depth in all cases before proceeding. Consult the University Veterinarian before using a new anaesthetic regime to ensure it is suitable for purpose.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Rat</th>
<th>Mouse</th>
<th>Guinea Pig</th>
<th>Rabbit</th>
<th>Bird</th>
<th>Wallaby</th>
<th>Reptile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alfaxalone</td>
<td>5mg/kg IV</td>
<td>20 mg/kg IP</td>
<td>5 mg/kg IV</td>
<td>20mg/kg IP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketamine + medetomidine</td>
<td>75 mg/kg IP + 0.5 mg/kg IP</td>
<td>50-75 mg/kg IP + 1 mg/kg IP</td>
<td>40 mg/kg IP + 0.5 mg/kg IP</td>
<td>25 mg/kg IM + 0.5 mg/kg IM</td>
<td>4-7 mg/kg IM + 0.1-0.2 mg/kg IM</td>
<td>10 mg/kg IM + 0.1-0.3 mg/kg IM</td>
<td>0.05-0.4 mg/kg IM</td>
</tr>
<tr>
<td>Reverse medetomidine with atipamezole</td>
<td>1 mg/kg SC or IP</td>
<td>1 mg/kg SC or IP (add fentanyl 0.2 mg/kg for painful procedures)</td>
<td>1 mg/kg SC</td>
<td>1 mg/kg SC or IV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketamine + Diazepam</td>
<td>75 mg/kg IP +5 mg/kg IP</td>
<td>100 mg/kg IP + 5 mg/kg IP</td>
<td>30 mg/kg IP or IM + 2 mg/kg IP or IM</td>
<td>25 mg/kg IM + 5 mg/kg IM</td>
<td>3 mg/kg + 1-2 mg/kg</td>
<td>20-40mg/kg IM +1.0-1.5mg/kg IM</td>
<td></td>
</tr>
<tr>
<td>Fentanyl + medetomidine</td>
<td>300 ug/kg IP + 300 ug/kg IP</td>
<td></td>
<td></td>
<td>8 ug/kg + 330 ug/kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reverse medetomidine with atipamezole</td>
<td>1 mg/kg SC, IP</td>
<td></td>
<td></td>
<td>1 mg/kg SC, IV (1 mg/kg IV)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reverse Fentanyl with Butorphanol (or naloxone)</td>
<td>2mg/kg SC, IP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propofol + medetomidine + Fentanyl</td>
<td>100mg/kg IP+ 0.1mg/kg IP+ 0.1 mg/kg IP</td>
<td>75mg/kg IP + 1 mg/kg IP+ 0.2 mg/kg IP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reverse medetomidine with atipamezole</td>
<td>0.5mg/kg IP</td>
<td>1 mg/kg IP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propofol</td>
<td>10 mg/kg IV</td>
<td>26 mg/kg IV</td>
<td>3-5 mg/kg IV</td>
<td>5-10 mg/kg IV</td>
<td>1-5 mg/kg IV</td>
<td>6-8 mg/kg IV</td>
<td></td>
</tr>
<tr>
<td>Tiletamine/zolazepam (Zoletil®)</td>
<td>40 mg/kg IP</td>
<td>80 mg/kg IP (restraint only)</td>
<td>40 - 60 mg/kg IM (sedation)</td>
<td></td>
<td>20-30 mg/kg IM 2.5 mg/kg IV (for induction)</td>
<td>2-4 mg/kg IM (prolonged recovery)</td>
<td></td>
</tr>
<tr>
<td>Tiletamine/zolazepam + medetomidine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urethane (non-recovery)</td>
<td>1000-1500 mg/kg IP</td>
<td>1500 mg/kg IV or IP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

48
<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Proprietary (trade) names</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alfaxalone</td>
<td>Alfaxan</td>
</tr>
<tr>
<td>Atipamezole</td>
<td>Antisedan</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td>Bupivacaine, Marcaine</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Temgesic, Subutex</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Temgesic, Subutex</td>
</tr>
<tr>
<td>Butorphanol</td>
<td>Butomidor, Buphensive, Dolorex, Torbugesic</td>
</tr>
<tr>
<td>Carprofen</td>
<td>Carrieree, Rimady, Tergive</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Pamlin, Valium</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Durogesic Patches, Fentanyl</td>
</tr>
<tr>
<td>Ketamine</td>
<td>Ketamine, Ketamav, Ketamil</td>
</tr>
<tr>
<td>Lignocaine</td>
<td>Lignocaine, Lignocaine</td>
</tr>
<tr>
<td>Medetomidine</td>
<td>Domitor</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>Meloxicam, Metacam, Meloxivet, Loxicam, Reliven</td>
</tr>
<tr>
<td>Propofol</td>
<td>Repose, Aquafol, Pacifol</td>
</tr>
<tr>
<td>Tiletamine+zolazepam</td>
<td>Zoletil</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Tramadol, Tramal, Tramedo, Zydol</td>
</tr>
</tbody>
</table>