ANIMAL CARE AND USE STANDARD

The Animal Care & Use Standards are designed to provide guidance regarding good practice to institutional animal users and carers, as well as Animal Ethics Committees (AECs), on the care and use of animals for scientific purposes such as research and teaching. The Standards are evidence-based, reflecting current or accepted good practice and allow for the flexibility that is required in research and teaching activities using animals.

ANALGESIA

This standard has been developed by the University of Melbourne Animal Care & Use Standards Committee, and endorsed by the University of Melbourne Animal Welfare & Ethics Committee.

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1. ASSOCIATED STANDARDS

This standard should be read in conjunction with the following University of Melbourne Animal Care & Use Standards:

- General anaesthesia of mice and rats
- Training in non-surgical procedures
- Administration of substances by oral gavage in mice and rats
- Monitoring of animals – post-issue to the investigator
- Surgery and aseptic technique of mice and rats

2. SUMMARY

2.1 Analgesia refers to the absence or loss of sensibility to pain without loss of consciousness. Analgesic agents are substances administered to an animal that provides relief from pain by reducing or inhibiting the ability to feel or perceive it.

2.2 The type and strength of analgesia will vary according to the type of procedure being undertaken. Methods of analgesic administration can include injectable, topical or oral delivery.

2.3 To reduce pain and distress to animals used in research, analgesia must be approached from several avenues. Analgesic and anaesthetic drugs should be combined with non-pharmacological methods to enhance their effectiveness. Providing a quiet environment, low-stress handling, good nutrition and ensuring surgeons are appropriately skilled can all contribute to better pain control.

2.4 This Standard aims to provide investigators with an understanding of the key principles of pain management in animals used in research that can be applied across all species.

2.5 In this initial version of the Analgesia Standard, dose rates of analgesics are provided for rats, mice, guinea pigs, rabbits, ferrets, cats, dogs, horses, cattle, pigs and sheep. Further species will be added with future revisions or if requested by the AEC.

2.6 This document is not intended to be a wholly comprehensive list of available options, but should provide a starting point to assist in the selection of appropriate analgesic agents. Investigators are advised to consult multiple references and the Animal Welfare Officer (AWO) to identify the most appropriate methods and drug doses for their given species and set of circumstances.

3. BENEFITS & RISKS

3.1 When given pre-emptively, analgesia reduces the intensity of painful stimulation, prevents central wind-up or sensitisation, improves comfort levels after surgery, decreases the amount of anaesthesia required to maintain a surgical plane and results in a smoother recovery. Animal welfare is thus improved by ensuring adequate analgesia is administered.

3.2 Where appropriate analgesia is not provided, animals in pain and discomfort are more likely to self-traumatize surgical wounds, show decreased appetite and become quiet and depressed in mentation. This poses an increased risk of post-operative infection and wound dehiscence, as well as dehydration, weight loss and general malaise. This is primarily a welfare concern and may also compromise research outcomes by creating altered physiological and hormonal states in the animal under investigation, leading to invalid results.

4. PROCEDURE/PROTOCOL

4.1 Pre-emptive analgesia should be provided whenever possible. Analgesic drugs are most effective when given prior to the onset of a painful stimulus, allowing for enhanced peri-operative pain management.

4.2 Multi-modal analgesia should be utilised whenever possible to provide optimal levels of pain relief. Analgesic drugs with different mechanisms of action provide a complimentary and increased level of pain control when given in combination, and often lower doses of an individual agent may be used. Lower doses of individual drugs may lessen the risk of undesirable side effects.

4.3 Types of Analgesic agents

4.3.1 Local anaesthetics (e.g. Lignocaine, Bupivacaine)

Provide analgesia by acting directly at nerves near the required site and inhibiting transmission of painful stimuli back to the brain. It may be injected into tissues and allowed to perfuse around nerves, or applied topically to skin and given time to permeate through. The time required for lignocaine based preparations to be effective at numbing skin will vary according to the drug preparation, species and their skin type.

Compared to lignocaine, bupivacaine has a significantly slower onset of action, a prolonged duration of action and cannot be safely given intravenously. There may be transient pain associated with injection of local anaesthetic agents; for this reason, they should preferably be used in anaesthetised animals. The use of these agents in the conscious animal should be considered in the context of the species and the procedure, with the method that causes the least distress or discomfort selected.

4.3.2 Non-Steroidal Anti-Inflammatory Drugs- NSAIDs (e.g. Meloxicam, carprofen)

This class of drugs act as non-selective inhibitors of cyclooxygenase (COX) enzyme, and are known to have analgesic and anti-inflammatory effects.

4.3.3 Paracetamol

Generally classed on its own, this is a COX-2 selective drug that can be safely combined with NSAIDs or opioids for multi-modal analgesia. Paracetamol has a narrow safety margin in many animals and is lethal if given to cats.

4.3.4 Opioids (e.g. buprenorphine, butorphanol)

Act at opioid receptors (primarily μ or κ) to provide analgesia, though common side effects may also include sedation, respiratory depression, euphoria or constipation. As each species group has varying types and ratios of these receptors, the effects of the agent may vary in different species. Investigators need to be aware of any species differences before selecting opiates for procedures and should consult with the AWO or a veterinarian where required. It should be noted that for some reptile groups, the use of certain opioids has been shown to be ineffective for analgesia.

4.4 Minimum Analgesia Requirements

- Subcutaneous tissue injury, implantations or procedures that leave the muscle wall intact
  - NSAIDs
  - Minimum of 24hrs post-operative analgesia

- Incisions through the muscle wall or entering the abdominal cavity, retro-peritoneal space or thoracic cavity
  - NSAIDs for 48hrs and opioids for first 24hrs
  - Minimum of 48hrs post-operative analgesia
- Orthopaedic procedures
  - NSAIDs and opioids
  - Minimum of 48hrs post-operative analgesia
- Craniotomy
  - Opioids
  - Minimum of 48hrs post-operative analgesia

4.4.1 Analgesia is mandatory where surgical procedures are carried out on rodents. Procedures involving anaesthesia and surgery, opening of body cavities or orthopaedics must receive a minimum of opiate level and NSAID analgesia, unless a demonstrable medical reason exists to omit the NSAID and is approved by the AWO and AEC.

4.4.2 Intravenous injections may require topical local anaesthetic prior to being given, however the pain associated with this procedure is of short duration compared to most surgical procedures.

4.4.3 Where a novel procedure is conducted that has the potential to be painful, analgesia must be provided as the default standard to maintain animal welfare. The AWO must be invited to observe and provide analgesic advice for procedures where uncertainty exists about the required level of analgesia.

4.5 Common Analgesic Agents

4.5.1 ***Appendix I*** contains a list of some commonly used analgesic drugs by species, and outlines dosing information from the NHMRC guidelines (where available) and current published literature. It is not intended to provide an exhaustive list, and the AWO or a registered veterinarian should be consulted for additional information where required.

4.5.2 Investigators should ensure they are aware of any potential side effects or withholding periods relevant to their species, and be aware that not all analgesic drugs are registered for use in all species. Use of a drug in a species for which it is not registered is considered “off-label” use.

4.5.3 Methods of delivery for analgesic drugs

4.5.3.1 Subcutaneous (SC)

An injection under the skin, typically over the scruff or flanks, is the most common and straightforward method of analgesic delivery. Ideally, solutions should be non-irritant to the animal to reduce pain or discomfort associated with the procedure.

4.5.3.2 Intramuscular (IM)

The substance is injected into the belly of a muscle or group of muscles. Some agents may cause muscle necrosis or pain if given repeatedly by this method, so sites should be rotated and the minimum volume size used to limit this.

4.5.3.3 Intravenous (IV)

The substance is injected into a vein. Where repeated administration is required, investigators are encouraged to assess if indwelling intravenous catheters (permanent or temporary) may be suitable. This will reduce the discomfort experienced by the animal, ensure consistent delivery of the substance into the vein and minimise trauma to the vessel and perivascular area.

4.5.3.4 Intraperitoneal (IP)

An injection is made into the lower abdominal cavity (known as the ‘peritoneal cavity’ or ‘peritoneum’). This is most commonly used in rodents as it can be done without the need for anaesthesia by trained technicians. Caution should be exercised to avoid inserting the needle too far into the abdomen and causing damage to the bowel and other organs.

4.5.3.5 Orally (PO)

A substance can be delivered directed into the mouth by oral gavage, syringe or drench, via a tablet, or in food or water, depending on the size and type of the animal. Care should be used to mask the presence of any unpleasant tasting substances in order to promote a positive experience for the animal.

4.5.3.6 Oral transmucosal (OTM)

The substance needs to come into contact with a mucosal surface, such as the inner cheeks, under the tongue or rectum. No needle is generally used to deliver the agent topically over a mucosal surface where it is absorbed into the body. This method is most commonly used when administering buprenorphine to cats, as OTM delivery yields the same or faster absorption as intravenous use, but with less requirement for restraint.

4.5.3.7 Local infiltration

This requires the anaesthetic substance (usually a local anaesthetic) to be drawn up into needle and syringe. The needle with attached, filled syringe is then inserted into the middle of the tissue region where numbing is required, and the drug is slowly injected into the tissue as the needle is withdrawn. This allows the anaesthetic agent to diffuse into the nearby tissue. The ideal time for injection of local anaesthetic agents for this purpose is after the animal is under general anaesthesia, but before any tissue damage (e.g. surgery) has occurred.

4.5.3.8 Nerve blocks

Using knowledge of the nervous system anatomy for the species under consideration, local anaesthetic agents are used to target specific nerves that provide sensation or innervation to a required area (e.g. Mandibular nerve blocks prior to tooth extraction, ring blocks for equine distal limb examination). The technique is as described in 4.5.3.7 to diffuse local anaesthetic into tissue, however the precise location and depth of needle insertion will depend on the target nerves.

4.6 Use of topical analgesic creams

The use of topical gels or creams containing lignocaine, prilocaine or combinations of these drugs should be considered where the pain associated with conducting a procedure is greater than the stress induced by restraint to apply the gel/cream in the first instance. Topical creams must be applied and given time to take effect before the painful stimulus occurs in order to prevent the start of the painful wind up. Analgesic creams must be applied to the designated area of skin following removal of hair, for sufficient time to cause numbing and loss of nerve sensation in the dermis and epidermis of the skin. The onset and duration of analgesia and the depth of activity is dependent on the duration of application and will vary with each species.

4.6.1 EMLA cream

The most widely available preparation is EMLA ® cream (2.5% lignocaine and 2.5% prilocaine) which has been extensively studied in humans, however limited published data is available for animal species. The most common undesirable side effect noted across most species is a blanching or mild erythema of the skin in contact with the cream.

4.6.1.1 Ingredients

Each 1 gram of cream contains 25 mg of lignocaine, 25 mg of prilocaine, polyoxyethylene fatty acid esters (as emulsifiers), carboxypolymethylene (as a thickening agent), sodium hydroxide to achieve a pH of 9.4, and purified water.

4.6.2 Use in humans

The cream is applied to skin as a 2 mm layer then covered with an adhesive bandage for 60 minutes for standard application in humans. At the end of this time the bandage is removed and the cream wiped away. The local anaesthetic agents have been shown to penetrate 2.9 mm deep in human skin after 60 minutes and achieve up to 180 minutes of analgesia due to the reservoir effects of the drug in the dermis and epidermis.

4.6.3 Use in animals

A handful of studies are available looking at the effects of EMLA cream on rabbit, rat and feline skin. Rabbit skin is thinner and more permeable than human skin, allowing the cream to be more rapidly absorbed and take effect in as little as 20 minutes. Unpublished observations by veterinary anaesthetists report a numbing effect in rabbits following application of 1-2 mm of EMLA cream, left uncovered for 30-60 minutes. At least one published study found using 1 ml of cream, applied in a 2 mm layer and covered with adhesive bandage and plastic wrap to be effective in dogs, though in practice the time for onset of action is from 20-30 minutes after application. In contrast, application of EMLA cream to already furless areas of skin on the tail of rats was found to have no appreciable benefit prior to venipuncture. It is important to note that in many laboratory species the stress of

restraint, hair removal, cream application and bandage placement/ removal may outweigh any potential benefit obtained by numbing. In these instances, the stress involved with the use of analgesic creams may pose a greater welfare risk than the brief venipuncture alone. Consultation with the AWO is advised when considering the use of a topical analgesic cream.

4.6.3.1 Method of application

Fur should be removed by clipping or shaving the area (depilatory creams are not suitable) prior to applying a 1-2 mm layer of EMLA cream and covering the area with a non-absorbent dressing (e.g. Cling wrap and /or Vetwrap). The amount used should be the smallest possible volume that achieves analgesia for the animal but avoids passing a toxic threshold. It can be difficult with topical drug application to determine how much active ingredient is being absorbed systemically, so a maximum dose should be calculated based on lignocaine concentration prior to use.

4.6.3.2 Duration of application

The duration and depth of analgesia in human skin is a useful starting point, however it should be noted that the structure, thickness and permeability of animal skin may be vastly different. This information may be applicable to other species depending on the thickness of the tissue and contact time, but as animal skin is often more permeable (e.g. Rabbits) the duration of onset may be much shorter. Unpublished observations from experienced investigators and veterinary staff should be considered in the absence of clear scientific data. A duration of 15–20 minutes appears sufficient in dogs and cats. Penetration depth of analgesia has been reported to be time dependent and from 2–6 mm in dogs.

5. MONITORING & INTERVENTION

5.1 Prevention and reduction of pain

5.1.1 Analgesic drugs are only one component of a multi-modal approach to pain control, which begins with prevention and efforts to reduce the intensity of the painful stimulus. Animal carers must be competently trained in correct handling techniques to ensure minimal stress to the animal. Restraint for procedures should not be performed for any longer than is required to achieve the desired task. As with all work involving animals, it is absolutely essential that their welfare be maintained throughout all aspects of a project.

5.1.2 Activities that decrease anxiety and stress will enhance the effect of concurrently administered analgesic agents. Non-pharmacological methods for controlling pain can include acclimatisation of the animal before the procedure, good husbandry, offering enrichment, nutritional support, and access to conspecifics for social animals.

5.1.3 In some instances, the use of anxiolytic agents as a premedication prior to anaesthesia may be warranted as part of a pain management protocol. Used appropriately, these medications have the ability to reduce pain and distress following a procedure. Investigators should discuss the use of anxiolytic agents in their particular species with the AWO as required.

5.2 Monitoring effectiveness of analgesia

5.2.1 Some individual variation in how an animal responds to analgesic agents may occur, so animals must be carefully monitored after a procedure to assess this. The dose or frequency of drug administration should be modified according to the effectiveness of pain control in each animal. The dosing options listed in section 4.5 should be considered a starting point to guide agent selection.

5.3 Recognizing pain in animals

5.3.1 Pain has the ability to cause physiologic changes. An animal may experience fluctuations in body temperature, respiration rate, heart rate and blood pressure. These things are often not practical to measure directly in laboratory animals (if possible at all) and so observations of behaviour, body position and feeding habits are relied upon for monitoring instead.

5.3.2 It is essential that researchers and animal carers familiarise themselves with the normal behaviour and physiology of the species under observation prior to any procedures in order to recognise any abnormalities resulting from pain or distress. The AWO, a veterinarian familiar with the species or an experienced investigator should be consulted if unsure what to look out for. This should occur prior to

submitting ethics applications, as species-specific knowledge will be required to prepare monitoring and intervention sheets for the project.

5.3.3 Trainers that are teaching monitoring relating to signs of pain should provide the content, format and/or competency assessment sheets to the AWO prior to commencement of training new people.

5.4 General signs associated with pain in animals may include:

- Decreased appetite
- Weight loss
- Alteration from usual demeanour (e.g. calm animals may become aggressive when handled, active animals become unusually lethargic)
- Abnormal vocalisation (e.g. urgent, repetitive sounds)
- Fluctuations in heart and breathing rates
- Reduced interaction with cage mates in social species
- Further species specific signs of pain may also be found within the NHMRC guidelines, available online at http://www.nhmrc.gov.au/

5.5 Intervention Criteria

5.5.1 Evidence of any of the above signs warrants further examination and assessment for pain and discomfort. Actions taken may include provision of additional analgesic drugs, supportive care such as warmth and rehydration or assisted feeding where appropriate.

5.5.2 Researchers are required to provide an Intervention Criteria Sheet specific to the project being undertaken. This sheet must include timely checks to monitor animals post-procedure, monitoring criteria, intervention points and an action plan should an animal reach these points. If in any doubt, technicians or researchers should contact the AWO for advice.

5.5.3 Sample Intervention Criteria Sheets are available on the website of the Office of Research Ethics and Integrity (http://orei.unimelb.edu.au/content/forms-templates-guidance-documents).

6. ADDITIONAL INFORMATION

Additional information can be found in the "Guidelines to promote the wellbeing of animals used for scientific purposes: The assessment and alleviation of pain and distress in research animals" (2008), freely available online at https://www.nhmrc.gov.au/guidelines/search.

7. ENFORCEABLE REQUIREMENTS

7.1 Administration of drugs by competent personnel or trainees under the direct supervision of competent investigators.

7.2 Weighing the animal prior to calculation of drug dosages.

7.3 Animals observed immediately after injections given to assess for adverse reactions.

7.4 Competency must be demonstrated on more than one occasion before people are permitted to administer medications unsupervised.

8. EXEMPTIONS

Where adherence to this Standard conflicts with proposed work, the University's AECs may grant exemptions to all or part of the Standard. To seek exemption, applications should clearly outline how the proposed work deviates from the Standard, and justify the need for this. Before seeking exemption, it is recommended that you consult with the University's AWO.

9. UNEXPECTED ADVERSE INCIDENTS

An unexpected adverse event is any event, which impacts negatively on the wellbeing of animals, and which was not anticipated, or has occurred at a frequency or severity in excess of what was anticipated in line with the AEC approval. This can be a single or cumulative event, and will normally involve unexpected mortality, morbidity or injury. Anyone identifying an unexpected adverse event must act to remove and/or minimise any immediate risk to animals. Immediately thereafter, the University's AWO and relevant Animal Facility Manager must be notified of the event. The AWO will advise researchers of the appropriate response.

10. GLOSSARY

Scientific Term	Lay Description
Analgesia	Lack of pain sensation
Analgesic	An agent (usually a drug) able to relieve or lessen the sensation of pain
Anaesthesia	Loss of consciousness, usually induced by administration of specific drugs/ agents
Anxiolytic agent	A drug/ medication that alleviates anxiety
Central wind-up	Central wind-up, also known as pain wind-up or central sensitization, refers to changes that occur in the brain in response to repeated nerve stimulation. Specifically, repeated exposure to a painful stimulus will change the pain threshold and result in a stronger pain response.
Dehiscence	Wound break down or a failure to heal, typically after surgery
Drench	Administration of a liquid drug (such as worming) by mouth, to an animal. Generally refers to cattle, sheep or horses.
Mentation	State-of-mind
Peri-operative	The period around the time of a surgical operation, including before, during and after the surgery.
Premedication	A single agent or combination of agents given prior to anaesthesia, designed to calm the animal and reduce stress before a procedure

11. REFERENCES & RESOURCES

The following source material contributed to the development of this Standard:

- Flecknell, P.A., Liles, J.H., & Williamson, H.A. (1990). The use of lignocaine-prilocaine local anaesthetic cream for pain-free venepuncture in laboratory animals. *Laboratory Animals*, 24(2): 142-146.
- NHMRC (2008). Guidelines to promote the wellbeing of animals used for scientific purposes.
- Voipio, H.M., Baneux, P., de Segura, I.G., Hau, J., & Wolfensohn, S. (2008). Guidelines for the veterinary care of laboratory animals: report of the FELASA/ECLAM/ESLAV Joint Working Group on Veterinary Care. *Laboratory animals*, 42(1): 1-11.
- Wahlgren C.F. and Quiding H. (2000). Depth of cutaneous analgesia after application of a eutectic mixture of the local anesthetics lidocaine and prilocaine (EMLA cream). *J Am Acad Dermatol,* 42: 584–588.
- Plumb D.C. (2015). Plumb's Veterinary Drug Handbook, 8th Edition. Wiley-Blackwell Publishers, USA.

The following resources may provide additional or supplementary information:

- An Introduction: Recognising Post-Operative Pain in Animals. Online Tutorial; http://www.ahwla.org.uk/site/tutorials/RP/RP01-Title.html
- NHMRC (2008). Guidelines to promote the wellbeing of animals used for scientific purposes.

APPENDIX I:

Suggested dose rates of some commonly used analgesic agents

- Abbreviations: SC= Subcutaneous; IM= Intramuscular; IV= Intravenous; IP= Intraperitoneal; PO= Orally; OTM= Oral transmucosal
- Frequency of dosing: q= every; h= hours; time fraction given in whole numbers.

i. Mouse

Class	Drug	Dose/ Route/ Frequency
Local	Bupivacaine	< 2 mg/kg local infiltration
Local	Lignocaine	< 4 mg/kg topical
NSAID	Meloxicam	1-2 mg/kg IM, PO, SC q24h
NSAID	Carprofen	5 mg/kg SC, q12-24h
	Paracetamol	1-2 mg/ml of drinking water (use flavoured products); 200 mg/kg PO q24h
Opioid	Buprenorphine	0.05-0.1 mg/kg IM, IV, SC q4-12h
Opioid	Butorphanol	1-2 mg/kg SC, IP q2-4h

ii. Rat

Class	Drug	Dose/ Route/ Frequency
Local	Bupivacaine	< 2 mg/kg local infiltration
Local	Lignocaine	< 4 mg/kg local infiltration, topical
NSAID	Meloxicam	1-2 mg/kg PO, SC q12-24h
NSAID	Carprofen	5 mg/kg IM, PO, SC q12-24h
	Paracetamol	1-2 mg/ml of drinking water (use flavoured products); 200 mg/kg PO q24h
Opioid	Buprenorphine	0.01-0.05 mg/kg IM, SC q8-12h
Opioid	Butorphanol	1-2 mg/kg SC q4h

iii. Rabbit

Class	Drug	Dose/ Route/ Frequency
Local	Bupivacaine	< 2 mg/kg local infiltration
Local	Lignocaine	0.4 mL 1.5% solution for epidural anaesthesia
NSAID	Meloxicam	0.2-1 mg/kg SC q24h; 1-2 mg/kg PO, SC q12h
NSAID	Carprofen	1.5 mg/kg PO q12h or 4 mg/kg SC q24h
Opioid	Buprenorphine	0.01–0.05 mg/kg SC, IM, IV q6-12h
Opioid	Butorphanol	0.1–0.5 mg/kg IV q4h

iv. Guinea Pig

Class	Drug	Dose/ Route/ Frequency
Local	Bupivacaine	1 mg/kg local infiltration
Local	Lignocaine	1 mg/kg local infiltration
NSAID	Meloxicam	0.2-0.5 mg/kg IM, PO, SC
NSAID	Carprofen	2.5 mg/kg SC q24h
Opioid	Buprenorphine	0.05 mg/kg SC q8-12h
Opioid	Butorphanol	1-2mg/kg SC q4h (short acting)

v. Ferret

Class	Drug	Dose/ Route/ Frequency
Local	Bupivacaine	< 2 mg/kg local infiltration
Local	Lignocaine	1-2 mg/kg local infiltration
NSAID	Meloxicam	0.2 mg/kg IM, SC q24h; 0.3 mg/kg PO q24h
NSAID	Carprofen	1-4 mg/kg SC q12-24h; 4 mg/kg PO q24h
Opioid	Buprenorphine	0.01-0.03 mg/kg IM, IV, SC q8-12h
Opioid	Butorphanol	0.01-0.03 g/kg IM, IV, SC q8-12h

vi. Dog

Class	Drug	Dose/ Route/ Frequency
Local	Bupivacaine	1-2 mg/kg local infiltration
Local	Lignocaine	1-2 mg/kg bolus slow IV, followed by a CRI of 1.5-6 mg/kg/hr. (Generally used with an opiate) , local infiltration, topical
NSAID	Meloxicam	0.2mg/kg PO, IV, SC day 1, then 0.1mg/kg PO q24h
NSAID	Carprofen	4.4mg/kg PO, SC q24h or 2.2mg/kg PO, SC q12h
	Paracetamol	15 mg/kg PO q6-8h
Opioid	Buprenorphine	0.01-0.02mg/kg IV, SC, IM q6-8h
Opioid	Methadone	0.1-0.5 mg/kg IV, SC, IM q4-6h

vii. Cat

Class	Drug	Dose/ Route/ Frequency
NSAID	Meloxicam	0.2 mg/kg SC, PO, then 0.1 mg/kg PO daily
NSAID	Carprofen	2–4 mg/kg SC or IV once 2 mg/kg PO for 4 days, then every other day
	Paracetamol	**Contraindicated- fatal liver toxicity**
Opioid	Buprenorphine	0.01-0.03 mg/kg IM, IV, OTM q6-8h
Opioid	Butorphanol	0.4–0.8 mg/kg SC, IM q2–4h

viii. Pig

Class	Drug	Dose/ Route/ Frequency
NSAID	Ketoprofen	3 mg/kg IM once only
NSAID	Carprofen	2-4 mg/kg IV, SC q24h
NSAID	Flunixin	1–2 mg/kg IV, SC q24h
Opioid	Buprenorphine	0.01 mg/kg IM, IV q6-12h
Opioid	Butorphanol	0.1–0.3 mg/kg IM q4h
Opioid	Fentanyl	Transdermal: 50–100 µg/hr applied 8–12hrs prior to surgery. Reapply every 72 hrs.

ix. Sheep

Class	Drug	Dose/ Route/ Frequency
NSAID	Meloxicam	0.5 mg/kg IV q12h; 2 mg/kg PO on first day, then 1 mg/kg PO q24h
NSAID	Carprofen	1.5–2.0 mg/kg IV, SC q24h
	Flunixin	2 mg/kg, IV, SC q24h
Opioid	Buprenorphine	0.005–0.010 mg/kg IM, IV q4h
Opioid	Butorphanol	0.5 mg/kg IM, SC q2-3h
Opioid	Fentanyl	Transdermal: 2 µg/kg/hr applied 24hrs prior to surgery. Remove after 72 hrs.

x. Cattle

Class	Drug	Dose/ Route/ Frequency
NSAID	Meloxicam	0.5 mg/kg SC, IV once off; 0.5-1mg/kg PO q24-48h
NSAID	Flunixin	1.1-2.2 mg/kg IV q6-12h
NSAID	Phenylbutazone	5-10 mg/kg PO q24-48h
Opioid	Butorphanol	0.1 mg/kg IV q3-4h; not to exceed 48 hours

xi. Horse

Class	Drug	Dose/ Route/ Frequency
NSAID	Flunixin	1.1 mg/kg IV, IM,PO q24h (up to 5 days)
NSAID	Phenylbutazone	4.4 mg/kg q12h (day 1) followed by 2.2 mg/kg PO q12h. 2.2-4.4 mg/kg IV q12h (maximum 5 days), then PO
Opioid	Butorphanol	0.1 mg/kg IV q3-4h; not to exceed 48 hours