Sedation/Tranquilization, Anesthesia and Analgesia in Laboratory Animals and Veterinarian-Recommended Formularies VVC Updated 4/26/24

Policy

All procedures likely to cause pain or distress in animals must be done under appropriate sedation/tranquilization, anesthesia and/or analgesia unless specifically exempted in an approved Animal Use Protocol. Recommended drugs for management of pain and distress may be found in the formulary below. Use of any other drug(s) not on this list must be clearly justified and approved in an Animal Use Protocol. Justification not only includes an explanation of why the requested drug is appropriate, but also why one of the recommended drugs will not serve the same purpose or will interfere with the experiment.

Overview

Sedation and/or tranquilization, general anesthesia, and analgesia may be required for a variety of animal uses from restraint and minor procedures such as blood collection or imaging to major invasive surgery. Animal anesthesia and analgesia are crucial components of the animal use protocol, and appropriate pain management is central to the provision of adequate veterinary care, not adjunctive. It is not only a professional and ethical obligation, but also a key contributor to successful research outcomes. Managing pain successfully requires a continuum of care based on a well-thought-out plan that includes anticipation, early intervention, and evaluation of response on an individual basis.

UCAR requires that pain is prevented whenever possible and treated aggressively whenever diagnosed, unless a strong scientific justification precludes it. The US Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training, and thus PHS Policy, require that "unless the contrary is established, **investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals**." Exceptions to this principle are permitted only in the minority of protocols approved by UCAR as Category E and require robust scientific justification.

Balanced anesthetic and multimodal, pre-emptive analgesic regimens are the current standards of care in veterinary medicine and are required under this policy. A multimodal approach combines drugs from a variety of classes to maximize the desired effects while minimizing potential undesirable side effects that occur with over-reliance on a single agent, e.g. balanced anesthesia and analgesia. It is not acceptable to conduct surgical procedures unless an animal is in a surgical plane of anesthesia. UCAR requires that pre-emptive analgesia be administered prior to the first incision for all surgical procedures unless otherwise scientifically justified in the protocol.

The Ideal Anesthetic/Analgesic Regimen

The ideal anesthetic/analgesic regimen must several criteria:

1. Minimize any pain or distress associated with handling or the induction of anesthesia
2. Be precisely titratable to assure that animals receive adequate anesthesia to produce unconsciousness and immobility and to block pain sensation without causing hemodynamic instability
3. Provide pre-emptive analgesia so that pain is already being treated as the general anesthetic is wearing off to prevent sensitization of pain sensory mechanisms, and to lower the overall amount of general anesthetic required for the procedure
4. Not interfere with the research goals
5. Not result in undesirable intra- or post-operative side effects
6. Be compatible with available equipment, other medications, and staff training

In planning any procedure that may cause pain or distress, a veterinarian must be consulted for advice regarding the proper use of sedatives/tranquilizers or anesthetics. Veterinary judgment is necessary to determine the appropriate level of sedation or anesthesia required based on the species and invasiveness of the procedure. Additionally, different procedures and surgeries may require different levels of analgesic therapy for which veterinary input is required.

Volatile inhaled anesthetics (such as isoflurane) delivered via a precision vaporizer allow titration of anesthetic delivery to the needs of the individual animal for the procedure. Adjusting the percentage of anesthetic gas to modify depth of anesthesia is generally safer than repeated administration of injectable drugs; thus, **inhaled anesthetics are usually the maintenance anesthetic of choice**. However, injectable agents are often required as pre-medications to sedate or restrain the animal for anesthetic induction before a maintenance anesthetic can be used. In some cases, inhaled anesthetics may be contraindicated or unnecessary, and an injectable regimen may be more appropriate based on the invasiveness and/or length of the procedure. Additionally, inhalant anesthetics lack analgesic effects, so injectable anesthetics and/or analgesics are often given in conjunction with gas anesthetics.

Pre-emptive analgesia is implemented by administration of analgesics prior to the first incision during surgical procedures. Use of pre-emptive analgesics significantly reduces the required concentration of anesthetic gases, resulting in minimization of cardiovascular and respiratory depression secondary to volatile anesthetics and a faster recovery from anesthesia. Additionally, pre-emptive analgesia prevents sensitization of pain receptors to reduce post-operative pain.

Adjunctive, non-pharmacologic analgesic therapy should be employed whenever practical. Such methods may include providing warmth, a comfortable area for the animal to rest, use of cold and heat as appropriate to modulate inflammation, and increased ease of access to food and water. Special considerations are required in some species, ages, or types of procedures. These considerations may include administration of additional drugs, fluid therapy, or handling of the animal, and supportive care should be planned ahead of the procedure.

All staff anesthetizing animals must have appropriate training. Veterinary consultation is available at all times, and investigators are required to seek veterinary input in planning of surgical or potentially painful procedures.

Drug Dosages and Frequencies of Administration

All animals experiencing a major survival surgery must be provided with systemic analgesics for no less than 3 days following the procedure, and analgesic therapy should only be discontinued at the direction of a veterinarian or based on an observation that the animal is not painful at the time the next analgesic dose is due. Furthermore, the level of invasiveness of the surgery may require a more aggressive analgesic regimen (e.g., local anesthetic for minimal invasiveness without expectation for prolonged pain, local anesthetic plus NSAID for mild to moderate pain, local anesthetic plus NSAID and opioid for moderate to severe pain) as determined by veterinary staff during the UCAR protocol review.

Special attention must be paid to analgesic doses and frequencies. UCAR requires that investigators take into account overnight, weekend, and holiday pain management in selecting the most appropriate analgesic regimen. **It is not acceptable to give drugs at greater intervals than those prescribed and known to adequately manage pain.**

Note that all doses included in this formulary are approximations and must be titrated to the animal's strain, age, sex, and individual responses. Significant departures from these doses should be discussed with a veterinarian. Doses will also vary depending on what other drugs are being administered concurrently.

DCM Anesthetic and Analgesic Formulary

This document contains recommendations for best practice use of sedatives/tranquilizers, anesthetics, and analgesics based on the current standard of care. While all of the drug combinations listed here are considered safe and effective, the selections shaded in gray represent the DCM best practice approach to anesthesia and analgesia in these species and should be followed whenever possible. The drugs contained within this formulary are not exhaustive of all possible anesthetics and analgesics that can be used in laboratory animals, and investigators should consult with a DCM veterinarian if an alternative agent is desired to achieve the scientific goal. Veterinary staff continuously review outcomes of surgical and anesthetic procedures as well as the literature for refinements, and update their recommendations and clinical practice periodically to reflect the evolving standard of care.

Abbreviations	
SID	Once daily (every 24 hours)
BID	Twice daily (every 12 hours)
TID	Three times daily (every 8 hours)
QID	Four times daily (every 6 hours)
IM	Intramuscular
IP	Intraperitoneal
IV	Intravenous
SQ	Subcutaneous
CRI	Constant rate infusion
PO	Per os (by mouth)

LOCAL ANESTHETICS

Local anesthetics can be used in all species at similar doses, with the exception of cats. Nerve blocks should be considered prior to surgery whenever possible. Alternatively, infiltration of the surgical site with a local anesthetic at closing can significantly reduce pain in the post-operative period. Bupivicaine is the local anesthetic of choice due to its relatively long duration of action (6-8hrs compared to 2-4 hours of analgesia from lidocaine).

In all species, a maximum of 2mg/kg bupivicaine or 6mg/kg lidocaine should be administered. Although these drugs have relatively short half-lives, a variety of studies have shown that they reduce post-operative pain long after the drug has been metabolized and eliminated, demonstrating the power of prevention of nociceptor wind-up in controlling pain.

For animals experiencing a craniotomy, a regional scalp block with 2mg/kg bupivicaine is recommended. The supraorbital nerves are blocked as they emerge from each orbit by palpating the supraorbital notch, inserting the needle along the upper orbital margin, perpendicular to the skin, just medial to the supraorbital foramen. The occipital nerve is then blocked as it exits the skull near the occipital protuberance. The occipital artery on the back of the skull is palpated, and bupivicaine is injected medially after careful aspiration to avoid intra-arterial injection. These three injections are sufficient to regionally block the scalp for the region of most head post and chamber placements.

MOUSE FORMULARY

DRUG NAME and DOSE	ROUTE & FREQUENCY	NOTES
Anesthetic Induction		
Sodium Pentobarbital (Nembutal) 30-90mg/kg	IP	Beware of dose related deep anesthetic plane, respiratory depression, narrow margin of safety, hypothermia and prolonged recovery. (ref # 1 & 11)
Ketamine 100mg/kg + Xylazine 10mg/kg	IP	General anesthesia for surgical procedures < 1 hour. Do not supplement.
Ketamine 100mg/kg + Diazepam OR Midazolam 5mg/kg	IP	General anesthesia for surgical procedures < 1 hour. Do not supplement
Ketamine 50-75mg/kg + Dexmedetomidine 0.5-1.0mg/kg	IP	General anesthesia for procedures < 1 hr. Do not supplement.
Ketamine 100mg/kg + Xylazine 20mg/kg + Acepromazine 3mg/kg	IP	Causes prolonged anesthesia, but can partially reverse xylazine with atipamezole or yohimbine. Do not redose
Isoflurane	1-4%	Generally first choice agent in rodents because it can be easily titrated to deliver dose required for anesthesia especially for procedures > 1 hr. Induce rodent in a chamber at 3-4%, then reduce to 1-2% for procedure
Analgesics		
Meloxicam 1-2mg/kg	PO, SQ q12-24h	NSAID
Carprofen (Rimadyl) 5 mg/kg	SQ q 24 hours	NSAID
Ketoprofen 5mg/kg	SQ q 24 hours	NSAID
Buprenorphine 0.1mg/kg	SQ, IP q 4 hours	Buprenex – given every 4 hours. Buprenex given pre-emptively followed by BUP SR 4 hours later. Opioid, useful in addition to an NSAID for multimodal analgesia for moderate to severe pain.
Buprenorphine SR 0.5 – 1.0 mg/kg	SQ q 72h	https://redcap.urmc.rochester.edu/redcap/surveys/?s=74DXF7JD3N
Ethiqa XR 3.25 mg/kg	SQ q 72 hours	https://www.urmc.rochester.edu/animal-resource/sr-buprenorphine.aspx
Acetaminophen Liquid 110-305 mg/kg. Both water and gel must be used in combination and will contain 1.1 mg/ml of Acetaminophen	Oral	Used only when NSAIDs and Opiates are contraindicated due to experimental design. Direction listed on pages 12-13.

RAT FORMULARY

DRUG NAME and DOSE	ROUTE & FREQUENCY	NOTES
Anesthetic Induction		
Sodium Pentobarbital (Nembutal) 30-60mg/kg	IP	Beware of dose related deep anesthetic plane, respiratory depression, narrow margin of safety,

		hypothermia and prolonged recovery. (ref # 1 & 11)
Ketamine 40-80mg/kg + Xylazine 5-10mg/kg	IP	General anesthesia for surgical procedures < 1 hour. Do not supplement.
Ketamine 75mg/kg + Diazepam OR Midazolam 5mg/kg	IP	Light anesthesia for brief procedures. Do not supplement.
Ketamine 50-75mg/kg + Dexmedetomidine 0.25mg/kg	IP	General anesthesia for surgical procedures < 1 hour. Do not supplement.
Isoflurane	1-4%	Generally first choice agent in rodents because it can be easily titrated to deliver dose required for anesthesia Induce rodent in a chamber at 3-4%, then reduce to 1-2% for procedure
Analgesics		
Meloxicam 1-2mg/kg	PO, SQ q12-24h	NSAID
Carprofen 5mg/kg	SQ, PO SID q 24 h	NSAID - Oral doses may need to be increased (9).
Ketoprofen 5mg/kg	IM, SQ, PO SID	NSAID - Oral doses may need to be increased
Buprenorphine 0.01-0.05 mg/kg	SQ q 4 h	Buprenex – given every 4 hours. Buprenex given pre-emptively followed by BUP SR 4 hours later. Opioid, useful in addition to an NSAID for multimodal analgesia for moderate to severe pain. (ref # 9, 14)
Buprenorphine SR 1 – 1.2 mg/kg	SQ q 72h	https://www.urmc.rochester.edu/animal-resource/sr-buprenorphine.aspx
Ethiqa XR 0.65 mg/kg	SQ q 72 hours	https://www.urmc.rochester.edu/animal-resource/sr-buprenorphine.aspx

ANESTHETICS FOR OTHER RODENTS

Drug & Dose Range	Species	Route	Comments
Isoflurane Induce 3-5%; Maintenance 2-3%	All		

50-70mg/kg ketamine + 2-3mg/kg xylazine 27mg/kg ketamine + 0.6mg/kg xylazine	Gerbil Blind mole rat	SC IM	Higher dose induces surgical plane of anesthesia
100mg/kg ketamine + 5mg/kg diazepam	Gerbil	SC, IP	For surgical procedures < 1 hour. Do not supplement. Use isoflurane for longer procedures.
Ketamine/Dexmedetomidine Ketamine 50-75 mg/kg + Dexmedetomidine 0.5-1.0 mg/kg	Gerbil	IP	Anesthesia for less than 1 hr. Do not redose. Use isoflurane for procedures > 1 hr.

ANALGESICS FOR OTHER RODENTS

Drug	Species	Route & Frequency	Comments
NSAIDS			

Meloxicam 2mg/kg loading dose, followed by 1mg/kg	Mole Rat	PO, SC; SID	
	OPIOIDS		
Buprenorphine	Rodents	SC, PO; QID-BID	https://www.urmc.rochester.edu/animal-resource/sr-buprenorphine.aspx
Morphine	Naked Mole Rat		AVOID – causes hyperalgesia and severe aggression

BIRD FORMULARY

DRUG NAME and DOSE	ROUTE & FREQUENCY	NOTES
Anesthesia		
Isoflurane		Bird can be placed in a chamber or induced via mask. Intubation in birds is relatively easy.
Ketamine 1.5-6 mg/kg + Dexmedetomidine 40-160mcg/kg	SQ	Can be used to maintain anesthesia delivered continuously SQ diluted in LRS Reverse dexmedetomidine with atipamezole 0.5mg/kg SQ
Ketamine 10-50mg/kg + Diazepam 0.5-2mg/kg	IM	
Analgesics		
Carprofen 1mg/kg	SQ SID-BID	NSAID
Meloxicam 0.1mg/kg 0.5mg/kg BID	IM SID PO	NSAID
Buprenorphine 0.01-0.05mg/kg	IM TID-BID	Opioid agonist-antagonist
Butorphanol 0.5-2mg/kg	IM QID	Opioid agonist-antagonist

RABBIT FORMULARY

DRUG NAME and DOSE	ROUTE & FREQUENCY	NOTES
Sedation		
Acepromazine 0.75mg/kg	IM	Produces a peripheral vasodilation useful for venipuncture
Dexmedetomidine 0.05mg/kg	SQ	Produces moderate sedation, useful for minimally invasive procedures less than 30 minutes
Induction		
Ketamine 10-20mg/kg + Dexmedetomidine 0.1mg/kg	SQ	IM administration of ketamine may cause myonecrosis, vasculitis, and axonal degeneration with resultant self-trauma Dermal ulcers may occur even with SQ administration, so 1ml saline can be injected at the same site following administration
Ketamine 44mg/kg + Xylazine 5mg/kg	SQ	
Maintenance		
Isoflurane	1-2% (MAC = 2%)	Laryngeal masks may be utilized in place of endotracheal tubes as rabbits are difficult to intubate
Analgesics		
Meloxicam 0.3-0.5mg/kg	SQ or PO SID	NSAID – useful for mild to moderate pain
Buprenorphine 0.02-0.05mg/kg	SQ or IV BID-QID	Opioid
Buprenorphine SR 0.12mg/kg	SQ q 72hr	Sustained release formulation that eliminates frequent dosing requirement

NONHUMAN PRIMATE FORMULARY

DRUG NAME and DOSE	ROUTE & FREQUENCY	NOTES
Sedation/Tranquilization		
Ketamine 5-15mg/kg	IM	To be used only for chemical restraint, any invasive procedures require additional drugs

Ketamine 10mg/kg + Diazepam 0.5mg/kg ± Atropine 0.04mg/kg OR Glycopyrrolate 0.004mg/kg	IM	Usually requires another agent for intubation. To be used only for chemical restraint prior to surgery or minimally invasive procedures. Glycopyrrolate is more effective at reducing bronchial secretions Anticholinergics may not be routinely necessary, but when desired, glycopyrrolate is preferable over atropine for control of bronchial secretions.
Ketamine 1-3mg/kg + Medetomidine 0.15mg/kg	IM	Medetomidine is alpha-2 agonists that are associated with bradycardia that should not be treated with atropine • Reversible with atipamezole at 0.22mg/kg IM Dexmedetomidine can be used as an alternative to medetomidine at 0.02-0.05mg/kg IM
Ketamine 8-10mg/kg + Midazolam 0.25mg/kg	IM	Diazepam causes pain on intramuscular injection and is not tissue soluble, so midazolam is preferred over diazepam for IM injections. Since midazolam is tissue soluble, it produces more reliable sedation that may allow intubation at this dose.
Induction		
Propofol 2-4mg/kg	IV	Recommended as an alternative to masking with isoflurane to allow intubation following one of the above pre-medications
Maintenance		
Isoflurane	1-3% (MAC = 1.3%)	Dose-dependent hypotension due to a reduction systemic vascular resistance especially pronounced when >2%
Analgesics		
Meloxicam 0.2mg/kg followed by 0.1mg/kg	IM or SQ SID	A COX-2 specific NSAID with fewer side effects than other less specific NSAIDs. The oral formulation does not last 24hrs in macaques, so the parenteral formulation should be used
Meloxicam SR 0.6mg/kg	SQ q72h	Sustained release formulation of meloxicam
Buprenorphine 0.01-0.04 mg/kg	IM or SC TID-BID	An opioid useful as an adjunctive agent to NSAIDs; required for major invasive surgeries If the lowest dose (0.01mg/kg) is chosen, it must be given every 6-8hrs. Higher doses (0.03mg/kg) may be administered every 12hrs.
Buprenorphine SR 0.12-0.2mg/kg	SQ q 72hrs	Sustained release formulation of buprenorphine that lasts for 72hrs
Oxymorphone 0.15mg/kg	IV q1-2h	Opioid - useful adjunctive analgesic intra-operatively; also useful for ocular stabilization during OCT imaging following sedation/anesthesia with one of above protocols
Fentanyl 7-10mcg/kg/hr	IV CRI	Opioid – useful intra-operatively for balanced anesthesia in procedures associated with moderate to

		severe pain

SWINE FORMULARY

DRUG NAME and DOSE	ROUTE & FREQUENCY	NOTES
Pre-Medication / Induction		
Ketamine 33mg/kg + Acepromazine 1.1mg/kg + Atropine 0.05mg/kg	SQ	A butterfly catheter attached to a syringe can be used to avoid stress associated with restraining pigs. Behind the ears is the most easily accessible site for SQ injections in swine. This combination will not be adequate for intubation
Ketamine 10mg/kg + Medetomidine 0.2mg/kg	SQ	Sufficient for intubation. Medetomidine reversible with same volume of atipamezole (Antisedan) IM
Propofol 2-4mg/kg	IV	Used to induce general anesthesia for intubation; administer slowly to effect
Maintenance		
Isoflurane	1-2%	
Amiodarone 10mg/kg + 0.5mg/kg/hr	IV	Amiodarone is an anti-arrhythmic drug useful to prevent arrhythmias common in anesthetized swine especially during cardiac manipulation
Lidocaine 2-4mg/kg , then 0.3mg/kg/hr CRI	IV	Indicated for ventricular arrhythmias
Analgesics		
Carprofen 3-4mg/kg	PO BID SQ or IM SID	An NSAID, can be administered IM prior to procedure, then continued orally afterwards.
Meloxicam 0.4mg/kg	PO or SQ SID	Can increase bleeding time in swine
Buprenorphine 0.02-0.05 mg/kg	IV, IM or SC BID-TID	Useful for breakthrough pain
Buprenorphine SR 0.18mg/kg	SQ q72hrs	Sustained release formulation eliminates need for frequent dosing

RUMINANT FORMULARY

DRUG NAME and DOSE	ROUTE & FREQUENCY	NOTES
Sedation		
Midazolam 0.3mg/kg + Fentanyl 0.0025mg/kg	IV	Sedation resulting in sternal recumbency for 20-30 minutes (adequate for quick minimally invasive procedures)
Pre-Medication		
Midazolam 0.5mg/kg + Fentanyl 0.005mg/kg	IV	Excellent sedation resulting in lateral recumbency for 30-45 minutes
Ketamine 7.5mg/kg + Midazolam 0.4mg/kg + Glycopyrrolate 0.004mg/kg	IV	Useful for IV sedation to produce lateral recumbency for animal transport and catheter placement
Induction		
Propofol 2-4mg/kg	IV	Administer slowly to effect for intubation Causes apnea with rapid administration

Maintenance		
Isoflurane	1-2%	
Fentanyl 5-20mcg/kg/hr	IV CRI	Short-acting opioid useful for intra-operative pain management during major invasive procedures; Required as balanced anesthesia for procedures such as sternotomies that are expected to cause severe pain
Analgesics		
Meloxicam 1mg/kg	IM or PO	NSAID – generally no more than 3-5 days, may provide analgesia for up to 72hrs
Flunixin (Banamine) 1.1mg/kg	IM or IV SID-BID	NSAID – generally no more than 3-5 days
Buprenorphine 0.005-0.01mg/kg	IV or IM TID	Opioid

AMPHIBIAN FORMULARY

Drug and Dose Range	Route	Comments
Anesthetics		
Isoflurane 3-5% induction to effect; 2-3% maintenance	Inhalation	
Tricaine methane sulfonate (MS-222) 50-200 mg/kg ---------- 0.5-2.0 g/l (frogs/salamanders)	Intracoelomic ---------- Water bath to effect	Buffer to a pH of 6-7 with sodium bicarbonate
Ketamine 50-150 mg/kg	SQ, IM, IV or dorsal lymph sac	
Analgesics		
Drug and Dose Range	**ROUTE and FREQUENCY**	**Notes**
Buprenorphine 38-75 mg/kg	Dorsal lymph sac; Not less than every four hours	
Carprofen 2-4 mg/kg 1st dose 1-2 mg/kg 2nd dose	PO, SQ or IM; Every 24-72 hours	
Meloxicam 0.1-1.0 mg/kg	PO, SQ or intracoelomic; Every 24 hours	
Morphine 38-42 mg/kg	SQ; No less than every few hours	
Bupivicaine <2 mg/kg	Infiltrate or apply topically; Redose as needed	not to exceed a total dose of 2 mg/kg)
Lidocaine/Bupivicaine <2 mg/kg	Infiltrate or apply topically; Lasts 1-4 hours; Redose as needed	(not to exceed a total dose of 2 mg/kg)

Directions for Adding Acetaminophen Liquid to Water and MediGel Sucralose for Mouse Analgesia

Acetaminophen can reach a therapeutic level when given to mice in both drinking water and MediGel Sucralose together. The correct concentrations and instructions for making them up are described here.

https://www.urmc.rochester.edu/animal-resource/sr-buprenorphine.aspxhttps://www.urmc.rochester.edu/animal-resource/sr-buprenorphine.aspx

Materials

- Hydropacs (420 ml) or sterile bottles of water (400 ml) for mouse MIT cage Children's' liquid acetaminophen – cherry or grape flavored – confirm that the concentration is 160mg/5ml (1 teaspoon)
- MediGel Sucralose
- Sterile needles and syringes
- tape

For Hydropacs, spray Hydropac with Rescue™. Using sterile technique, insert needle and withdraw 15 ml of water. Replace with 15 ml of liquid acetaminophen. Place tape over hole from needle.
For water bottles, remove cap and withdraw 14 ml of water. Replace with 14 ml of liquid acetaminophen.

For MediGel Sucralose, warm the containers in a water bath until the gel becomes liquid. Spray top of container with Rescue™. Inject 2.5 ml of the acetaminophen liquid through the lid using an 18g needle. Place tape over the hole in the lid to prevent contamination. Shake for ~10 seconds, then place in refrigerator so gel can solidify. To use, spray with Rescue™, remove lid and place in mouse cage. Replace when most of the gel has been eaten.

MediGel Sucralose can be ordered through the Animal Resource. If enough investigators are interested in administering acetaminophen by this method, it is recommended that you order a box (96 gels) as a group to prevent wastage.

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