

Institutional Animal Care and Use Committee		UNTHSC
Title: Analgesics in Laboratory Animals		
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A. BACKGROUND INFORMATION

- a. In general, procedures which cause pain in humans should be expected to cause pain in animals.
- b. Appropriate analgesics must be used unless withholding such agents is scientifically justified in the animal use protocol.

B. RESPONSIBILITIES

- a. It is the responsibility of the Principal Investigator (PI):
 - i. To list appropriate analgesics when performing potentially painful procedures on animals. The PI must consult with the Attending Veterinarian for information on which analgesic(s) to use if the PI is unsure.
 - ii. To procure the analgesics listed on an approved protocol unless arrangements are made with DLAM (Department of Laboratory Animal Medicine) ahead of time. Some analgesics are controlled substances and will require a DEA license. It is the responsibility of the PI to have this license.
- b. It is the responsibility of the Principal Investigator and other research personnel who will administer analgesics to have completed the applicable CITI training module.
- c. It is the responsibility of the Principal Investigator or designated lab staff and/or students to administer the analgesics listed in the approved protocol unless arrangements are made ahead of time for DLAM staff to do so.
- d. It is the responsibility of IACUC to assure that this SOP is followed.

C. PROCEDURES

- a. Determining which procedures require analgesia and which ones may be useful, several factors should be considered:
 - i. The invasiveness of the procedure that was performed:
 - 1. Are body cavities invaded?
 - 2. Are especially sensitive tissues involved (e.g. bones or teeth)?
 - 3. Is significant tissue destruction or inflammation produced?
 - ii. The degree or severity of pain that is expected:
 - 1. Comparison to similar procedures in people: would a reasonably stoic human be able to tolerate the postoperative period without analgesics?
 - 2. Behavior of the animal during postoperative period; e.g., level of activity, appetite, etc. when compared to sham (anesthetized) control animals.
 - iii. Duration of the postoperative pain or discomfort expected:

1. Postoperative analgesia is desirable for most surgical procedures involving penetration deeper than the skin and subcutaneous tissues.
 2. For procedures involving invasion of bones, joints, teeth or significant destruction or inflammation in other tissues, it is the responsibility of the PI to make sufficient justification in their animal use protocol if postoperative analgesics cannot be used.
- b. **No post-operative analgesia required:**
- i. Injections that will cause mild or no pain or discomfort. Examples such as injections of low irritation potential substances, non-invasive catheter or electrode placement, skin incisions, or sutures.
- c. **Short-term postoperative analgesia desired:**
- i. Procedures likely to cause mild to moderate pain or discomfort of short duration (12-24 hours). Examples include:
 1. Castrations, including ovariectomies
 2. Invasive electrode or catheter placement
 3. Adrenalectomy and hypophysectomy in rodents
 4. Extraocular surgery
- d. **Prolonged postoperative analgesia required:**
- i. Procedures likely to result in severe or prolonged pain or discomfort. Examples include:
 1. Extensive dissection of soft tissues
 2. Major entry into the pleural or peritoneal cavity
 3. Intraocular surgery
 4. Orthopedic or dental surgery
- e. **Types of analgesics:**
- i. Opioids - These are controlled substances. The Principal Investigator must have a DEA license.
 - ii. NSAIDs - Non-steroidal anti-inflammatory drugs. These are not controlled substances.
 - iii. Local analgesics – act only at the site of application
- f. **Points to remember when using analgesics:**
- i. Always use the analgesic that is listed in protocol.
 - ii. Calculate the dose by body weight.
 - iii. Drugs under the control of the Drug Enforcement Agency (DEA) must be stored in a locked cabinet in a secure area.
 - iv. A written record is required when controlled drugs under the control of the DEA are used (how much of the drug you have, how much was used and for what purpose).
 - v. An inventory list of analgesics should be kept.
- g. The following listings of analgesics and the corresponding doses for each species must be considered for use by the Principal Investigator. If another drug not on this list is to be used, the Attending Veterinarian must be consulted.

Mouse

Drug	Dose and Route	Frequency	Notes
Opioid analgesia			
Buprenorphine (Recommended)	0.05-0.1 mg/kg SC or IP	Pre-operatively for preemptive analgesia and post-operatively every 4 – 12 hours	When used as sole analgesic, typical regimen is: once at time of procedure, second dose will be administered 4-6 hours later. Additional doses every 8-12 hrs as needed. Consider multi-modal analgesia with NSAID and local analgesic.
Buprenorphine SR	0.5-1.0 mg/kg SC	Give once for 72 hours	
Non-steroidal anti-inflammatory analgesia (NSAID) – Note that prolonged use may cause renal, gastrointestinal, or other problems.			
Carprofen (Recommended)	5-10 mg/kg SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hour	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Meloxicam (Recommended)	5-10 mg/kg PO, IM or SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hour	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Ketoprofen	2-5 mg/kg SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hour	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Ketorolac	5-7.5 mg/kg ORAL or SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hour	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Flunixin Meglumine	~2 mg/kg SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hour	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Local anesthetic/analgesics (Lidocaine and bupivacaine may be combined in one syringe for rapid onset and long duration analgesia)			
Lidocaine Hydrochloride	Dilute to 0.5% do not exceed 7	Use locally before making surgical incision, or before	Faster onset than bupivacaine but short (< 1 hour) duration of action

	mg/kg total dose, SC or intra-incisional	final skin closure	
Bupivacaine	Dilute to 0.25 %, do not exceed 8 mg/kg total dose, SC or intra-incisional	Use locally before making surgical incision, or before final skin closure	Slower onset than Lidocaine but longer (~4-8 hour) duration of action.

Rat

Drug	Dose and Route	Frequency	Notes
Opioid analgesia			
Buprenorphine	0.01-0.05 mg/kg IM or SC	Pre-operatively for preemptive analgesia and post-operatively every 4 – 12 hours	Takes 1 h to be effective so should be given preemptively Duration of effect is 4-6 h NSAID is recommended for continued pain relief
Non-steroidal anti-inflammatory analgesia (NSAID) – Note that prolonged use may cause renal, gastrointestinal, or other problems.			
Carprofen	5-10 mg/kg SC, PO	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hour	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Meloxicam	1-2 mg/kg PO, SC	Once daily for up to 3 days	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Local anesthetic/analgesics (Lidocaine and bupivacaine may be combined in one syringe for rapid onset and long duration analgesia)			
Lidocaine	Dilute to 0.5%, should not exceed 7 mg/kg SC or intra-incisional	Use locally before making surgical incision, or before final skin closure	Use as local anesthetic, fast onset but duration of action is less than 1 h.
Bupivacaine	Dilute to 0.25%, should not exceed a total dose of 8 mg/kg SC or intra-incisional	Use locally before making surgical incision, or before final skin closure	Use as a local anesthetic, slow onset but duration of action is 4-8 h. Do not give IV.

Hamster

Drug	Dose and Route	Frequency	Notes
Opioid analgesia			
Buprenorphine	0.05-0.1 mg/kg SC	Every 8-12 hours	
Butorphanol	1-5 mg/kg SC	Every 2-4 hours	
Non-steroidal anti-inflammatory analgesia (NSAID) – Note that prolonged use may cause renal, gastrointestinal, or other problems.			
Aspirin	240 mg/kg PO	Every 24 hours	
Flunixin	2.5 mg/kg SC	Every 12 – 24 hours	Consult with Vet regarding repeated administration
Local anesthetic/analgesics (Lidocaine and bupivacaine may be combined in one syringe for rapid onset and long duration analgesia)			
Bupivacaine	1-2mg/kg max dose, mixed with Lidocaine at 1-4 mg/kg Lidocaine	Before incision is made	Use as a local anesthetic, slow onset but duration of action is 4-8 h. Do not give IV.
Lidocaine	1-4 mg/kg max dose, mixed with bupivacaine at 1-2 mg/kg bupivacaine	Before incision is made	Use as local anesthetic, fast onset but duration of action is less than 1 h.

Rabbit

Drug	Dose and Route	Frequency	Notes
Opioid analgesia			
Recommended: Buprenorphine	0.05 – 0.1 mg/kg SC or IP	Used pre-operatively for preemptive analgesia and post-operatively every 4-12 hrs	When used as sole analgesic, typical regimen is: once at time of procedure, second dose will be administered 4-6 hours later. Additional doses every 8-12 hrs as needed. Consider multi-modal analgesia with NSAID and local analgesic.
Buprenorphine SR	1.0-2.0 mg/kg SC	Give once for 72 hours	
Non-steroidal anti-inflammatory analgesia (NSAID) – Note that prolonged use may cause renal, gastrointestinal, or other problems.			
Recommended: Carprofen	4-5 mg/kg SC	Used pre-operatively for preemptive analgesia and post-operatively	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.

		every 12-24 hours	
Meloxicam	0.1-0.3 mg/kg PO, IM or SC	Used pre-operatively for preemptive analgesia and post-operatively every 24 hour for up to 4 days	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Ketorolac	0.3-0.5 mg/kg PO or SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hour	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Ketoprofen	2-5 SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hour (4-8 hour) duration of action	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Local anesthetic/analgesics (Lidocaine and bupivacaine may be combined in one syringe for rapid onset and long duration analgesia)			
Lidocaine Hydrochloride	Dilute to 0.5%, do not exceed 7 mg/kg total dose, SC or intra-incisional	Use locally before making surgical incision	Faster onset than bupivacaine but short (< 1 hour) duration of action
Bupivacaine	Dilute to 0.25%, do not exceed 8 mg/kg total dose, SC or intra-incisional	Use locally before making surgical incision	Slower onset than Lidocaine but longer (~ 4/8 hour) duration of action

Swine

Drug	Dose and Route	Frequency	Notes
Opioid analgesia			
Recommended: Buprenorphine	0.005 – 0.1 mg/kg SC (Usually use .05 – 0.1 for major surgery)	Used pre-operatively for preemptive analgesia and post-operatively every 4-12 hrs	When used as sole analgesic, typical regimen is once at time of procedure, second dose will be administered 4-6 hours later. Additional doses every 8-12 hrs as needed. Consider multi-modal analgesia with NSAID and local analgesic.

Butorphanol	0.1 – 0.5 mg/kg SC	Used pre-operatively for preemptive analgesia and post-operatively every 4-6 hour	For major procedures, require more frequent dosing than 12 hour intervals. Consider multi-modal analgesia with a NSAID
Oxymorphone	0.01 – 0.2 mg/kg	Used pre-operatively for preemptive analgesia and post-operatively every 3-4 hour, or for 'rescue analgesia' when buprenorphine is not potent enough	More potent but shorter duration than buprenorphine or butorphanol.
Fentanyl patch	50 ug/hr	Place patch 24 hours in advance of surgery and maintain for up to 3 days	When severe post-surgical pain is anticipated. Should not be used as sole analgesic.
Non-steroidal anti-inflammatory analgesia (NSAID) – Note that prolonged use may cause renal, gastrointestinal, or other problems.			
Recommended: Carprofen	2 – 4 mg/kg SC or PO	Used pre-operatively for preemptive analgesia and post-operatively every 24 hours for up to 4 days (Page 2)	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Ketoprofen	10. – 2.0 mg/kg SC	Used pre-operatively for preemptive analgesia and post-operatively every 24 hour for up to 4 days	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Ketorolac	5 – 1.0 mg/kg SC	Used pre-operatively for preemptive analgesia and post-operatively every 24 hour for up to 4 days	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Local anesthetic/analgesics (Lidocaine and bupivacaine may be combined in one syringe for rapid onset and long duration analgesia)			
Lidocaine Hydrochloride	May dilute to 0.5 – 1% (=10mg/ml).	Use locally before making surgical incision	Faster onset than bupivacaine but short (< 1 hour) duration of action

	May be mixed in same syringe with bupivacaine SC or intra-incisional		
Bupivacaine	May dilute to 0.25-0.5%, May be mixed in same syringe with lidocaine. SC or intra-incisional	Use locally before making surgical incision	Slower onset than Lidocaine but longer (~4-8 hour) duration of action.