UNIVERSITY OF TEXAS AT ARLINGTON

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE

ANALGESIA IN NON-USDA LABORATORY ANIMALS SOP

I. 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.

II. Responsibilities

A. It is the responsibility of the Principal Investigator (PI):
   1. To list appropriate analgesics when performing potentially painful procedures on animals. The PI must consult with the Attending Veterinarian (AV) for information on which analgesic(s) to use if the PI is unsure.
   2. To procure the analgesics listed on an approved protocol. Some analgesics are controlled substances and will require a DEA license.
   3. To assure that this SOP is followed.
   4. To make sufficient justification in their animal use protocol if postoperative analgesics cannot be used for any procedure with the potential to cause pain.
B. It is the responsibility of the PI and other research personnel who will administer analgesics:
   1. To complete the applicable training with the Animal Care Facility (ACF) Manager.
   2. To administer the analgesics listed in the approved protocol unless arrangements are made ahead of time for ACF staff to do so.
C. It is the responsibility of the ACF Manager and AV to verify qualifications of personnel.

III. Procedures

A. For determining which procedures require analgesia and which ones may be useful, several factors should be considered:
   1. The invasiveness of the procedure that was performed:
      a. Is penetration deeper than skin and subcutaneous tissues?
      b. Are body cavities invaded?
      c. Are especially sensitive tissues involved (e.g., bones or teeth)?
      d. Is significant tissue destruction or inflammation produced?
   2. The degree or severity of pain that is expected:
      a. Comparison to similar procedures in people: would a reasonably stoic human be able to tolerate the postoperative period without analgesics?
      b. Behavior of the animal during postoperative period, e.g., level of activity, appetite,

etc. when compared to sham control animals which were also anesthetized.

B. Pharmaceutical Interventions:
   1. Opioids - These are controlled substances. The PI may need a DEA license.
   2. NSAIDs - Non-steroidal anti-inflammatory drugs. These are not controlled substances.
   3. Local analgesics – These are not controlled substances. They act only at the site of application.

C. Requirements for Use of Analgesia:
   1. Always use the analgesic that is listed in protocol.
   2. Calculate the dose by body weight.
   3. Drugs under the control of the Drug Enforcement Agency (DEA) must be stored in a locked cabinet in a secure area. (http://www.deadiversion.usdoj.gov/pubs/manuals/sec/general_sec.htm#substantial)
   4. A written record is required when DEA controlled substances are used (how much of the drug you have, how much was used and for what purpose).
   5. An inventory list of analgesics should be kept.

D. The listings of analgesics beginning on page 4 and the corresponding doses for each species are approved by the IACUC. If another drug not on this list is to be used, the IACUC must review and approve it in the animal use protocol.

IV. Non-pharmaceutical interventions (Actions, apart from administering medicine, taken to mitigate pain and distress):

A. Gentle handling of the awake animal as well as gentle manipulation of the tissues intraoperatively to minimize tissue trauma
B. Appropriate wound closure including sufficiently spaced wound clips or suture with knots that are secure but not overly tight
C. A warm dry environment during recovery from anesthesia to prevent hypothermia
D. Maintaining a quiet environment during recovery to minimize external stress
E. Group housing for socially compatible animals following recovery from anesthesia
F. Ensuring enrichment such as a Nestlet is present, and utilizing a soft bedding material if a ventral incision is present
G. Ensuring the animal has easy access to food/water (rearing up to food bin may be difficult depending on the location of the surgical incision)
H. Moist food (food pellets + water in a petri dish) or other nutrient based support such as Boost diet gel® (Clear H2O products) placed on the cage floor in a dish and/or a water bottle with a long sipper tube

V. Examples

Analgesic Guidance Based on Anticipated Pain Level			
Level of Pain or Distress	**Mild** →	**Moderate** →	**Severe†**
Pharmacologic Analgesia Plan	Perioperative opioid for 24 hrs **OR** NSAID for 24 hrs	Perioperative opioid dose 24 hrs **AND** 2 days of NSAID analgesic	Opioid **AND** NSAID for 3 days **+/-** local analgesics

Examples of Procedures in Each Category	• Tail clipping at 21 days of age or greater‡
	• Trocar implantation > 16 gauge
	• Skin incision without deeper tissue manipulation
	• Subcutaneous mini-pump implant
		• Intracranial injection
		• Vascular cut down
		• Mild or moderate traumatic brain injury
		• Jugular/carotid catheter implantation
		• Minor abdominal surgeries
		  ▪ Ovariectomy/Castration
		  ▪ Mini-pump implantation in abdomen
		  ▪ Orthotopic injections/implantation
		• Skin biopsies/burn wounds (size dependent)
			• Intracranial implantation
			• Thoracotomy*
			• Orthopedic surgery
			• Neurologic surgery
			• Severe traumatic brain injury
			• Major abdominal surgeries
			  ▪ Partial or complete organ removal
			• Cecal ligation and puncture
			• Skin biopsies/burn wounds (size dependent)
			• Ischemia/reperfusion models

† Severe category surgeries may need to use the higher end of the analgesic dose range

‡ Tail clipping at 21 days of age or greater may not be performed without scientific justification in IACUC approved protocol

* Thoracic surgeries must use a local analgesic in conjunction with opioid and NSAID

When to Dose:

Most analgesics take 20-30 minutes to begin to take effect, and up to 60 minutes before reaching full potency. Analgesics should be given during surgical preparation, not post-operatively or during recovery as that will result in animals experiencing pain prior to analgesics taken effect.

Drug Formulary by Species

Mouse

Drug	Dose and Route	Frequency	Notes
Opioid analgesia (*preferred)			
Buprenorphine	0.05-0.1 mg/kg SC or IP	Pre-operatively for preemptive analgesia and post-operatively every 8 – 12 hours	Takes 1 h to be effective so should be given preemptively. Duration of effect is 4-6 h. Additional doses every 8-12 hrs as needed. Consider multi-modal analgesia with NSAID and local analgesic.
Buprenorphine SR (sustained release)	0.5-1.0 mg/kg SC	Give once every 72 hours	Takes 1 h to be effective so should be given preemptively. Duration of effect is 72 h. NSAID is recommended for balanced pain relief.
Ethiqa XR (extended release) *	3.25 mg/kg	Give once every 72 hours	Takes 1 h to be effective so should be given preemptively. Duration of effect is 72 h.
Non-steroidal anti-inflammatory analgesia (NSAID) – Note that prolonged use may cause renal, gastrointestinal, or other problems.			
Carprofen	5-10 mg/kg SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hours	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Meloxicam	3-5 mg/kg SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hours	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Local anesthetic/analgesics			
Lidocaine Hydrochloride	Dilute to 0.5% do not exceed 7 mg/kg total dose, SC or intra-incisional	Use locally before making surgical incision, or before final skin closure	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, or before final skin closure	Slower onset than Lidocaine but longer (~4-8 hour) duration of action. Do not give IV.
Lidocaine Hydrochloride and Bupivacaine Combination	Prepare a 50/50 mix of lidocaine 1-2% with 0.5% bupivacaine	Use locally before making surgical incision, or before final skin closure	May be combined in one syringe for rapid onset and long duration analgesia. Lidocaine and bupivacaine doses should not exceed 10 and 6 mg/kg respectively. Higher doses may lead to heart arrhythmias.

Rat

Drug	Dose and Route	Frequency	Notes
Opioid analgesia (* preferred)			
Buprenorphine	0.03-0.05 mg/kg IM or SC	Pre-operatively for preemptive analgesia and post-operatively every 8 – 12 hours	Takes 1 h to be effective so should be given preemptively. Duration of effect is 4-6 h. Additional doses every 8-12 hrs as needed. Consider multi-modal analgesia with NSAID and local analgesic.
Buprenorphine SR (sustained release)	0.6-1.2 mg/kg SC	Give once for 72 hours	Takes 1 h to be effective so should be given preemptively. Duration of effect is 72 h. NSAID is recommended for balanced pain relief. 1.2 mg/kg dose has been associated with pica in rats, so lower doses are recommended for most procedures.
Ethiqa XR (extended release) *	0.65 mg/kg SQ	Give once for 72 hours	Takes 1 h to be effective so should be given preemptively. Duration of effect is 72 h. NSAID is recommended for balanced 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	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hours	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Meloxicam	2-4 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.

Lidocaine Hydrochloride and Bupivacaine Combination	Prepare a 50/50 mix of lidocaine 1-2% with 0.5% bupivacaine	Use locally before making surgical incision, or before final skin closure	May be combined in one syringe for rapid onset and long duration analgesia. Lidocaine and bupivacaine doses should not exceed 10 and 6 mg/kg respectively. Higher doses may lead to heart arrhythmias.

USDA-Covered Species (Rabbits, Hamsters, Guinea Pigs, etc.)

Analgesia for USDA-covered species varies widely. Consult AV before protocol submission and refer to USDA SOP