IACUC GUIDELINE
MOUSE ANESTHESIA AND ANALGESIA RECOMMENDATIONS

The University of Pennsylvania Institutional Animal Care and Use Committee (IACUC) has developed the following recommendation to help research investigators with updated practice standards for rodent anesthesia and analgesia, related to changes in literature and updated information in the field of laboratory animal medicine.

When writing the IACUC protocol, it is encouraged to include dose ranges to allow for appropriate flexibility. Specific doses drawn from the suggested ranges may be procedure-, strain-, gender-, and age-specific; please consult with ULAR or OAW veterinary staff if needed.

This recommendation document concentrates on the following topics regarding the use anesthesia and analgesia in mice:

- Definitions
- Anesthesia
    - Non-painful procedures
    - Minor surgical procedures
    - Major surgical procedures
- Analgesia

DEFINITIONS

Sedation—The animal has suppressed spontaneous movement and decreased agitation, curiosity and aggression. The animal can respond to external stimuli (including pain) if the stimulus is of adequate intensity. The state is not associated with any analgesic effect.

Surgical plane of anesthesia—The animal is unconscious and does not move in response to a noxious stimulus. The animal should not respond to external stimuli (including pain).

Minor surgery—Minor survival surgery does not expose a body cavity and causes little or no physical impairment (e.g. wound suturing, peripheral vessel cannulation, percutaneous biopsy, routine agricultural animal procedures such as castration). These procedures are routinely done on an "outpatient" basis in veterinary clinical practice.

Major surgery—Major survival surgery (e.g. laparotomy, thoracotomy, joint replacement, and limb amputation) penetrates and exposes a body cavity, produces substantial impairment of physical or physiologic functions, or involves extensive tissue dissection or transection. (Guide)

Analgesia—Relief of pain to a normally painful stimulus.

Pre-emptive analgesia—Analgesia delivered before the painful stimulus. Provision of pre-emptive analgesia is consistent with standard veterinary practice.

ANESTHESIA

The use of ***ISOFLURANE*** inhalant anesthesia for rodent procedures is recommended, due to its wide safety margin, reliability, ease of administration, and rapid return to consciousness for animals after exposure has ended. Use of anesthetic regimens other than isoflurane may be chosen if required for the specific research model. Scientific justification for other anesthetic protocols may be required by the IACUC.

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Non-painful procedures (e.g., imaging, restraint)
Recommendations include:

1. ***Isoflurane***: 3-4% for induction and 1-3% for maintenance.
2. ***Ketamine/xylazine***: intraperitoneal dose at 70-100 mg/kg ketamine + 5-12 mg/kg xylazine. If animals appear to be responding to touch or awakening, redose with 50% of the initial dose of ketamine.

Minor surgical procedures (e.g., skin biopsies, device implantation in the subcutaneous space)
Recommendations include:

1. ***Isoflurane +/- local anesthetic***: 3-4% for induction and 1-3% for maintenance. Administer the local anesthetic, prior to the procedure, at the incision site.
2. ***Ketamine/xylazine + Local anesthetic***: dose at 70-100 mg/kg ketamine (IP) + 5-12 mg/kg xylazine (IP) and administer the local anesthetic, prior to the procedure, at the incision site.

Major surgical procedures (e.g., thoracotomies, laparotomies, craniotomies, head caps)
Recommendations include:

1. ***Isoflurane + Bupivacaine***: 3-4% for induction and 1-3% for maintenance. Administer the local anesthetic bupivacaine, prior to the procedure, at the incision site.
2. ***Ketamine/xylazine/acepromazine + Bupivacaine***: dose at 80-100 mg/kg Ketamine (IP) + 8-12 mg/kg Xylazine (IP) + 1-3mg/kg acepromazine (IP). Administer the local anesthetic bupivacaine, prior to the procedure, at the incision site.

For other procedures that require individualized anesthesia protocols or questions about selection of dosing within the ranges presented, please consult with a ULAR or OAW veterinarian.

ANALGESIA

As with anesthesia, the recommendations for analgesics will depend upon the procedure being performed. Pre-emptive analgesia refers to providing the analgesics prior to the painful event and is recommended unless scientifically justified. The first dose of the analgesic should be administered PRIOR TO the surgical procedure, i.e. before the "first cut" is made. Use of analgesic protocols may be chosen if required for the specific research model—all surgical protocols require anesthesia and analgesia, unless specifically justified by the PI and approved by the IACUC.

Table 1. Recommendations for types of analgesics for different procedures and expected pain levels.

Type of pain	Severity	Examples of procedure	Duration#	Recommended analgesics
Surgical	mild	Punch biopsy, vascular cutdown	Once	Local +/- NSAID
Surgical	moderate	Head cap, craniotomy, subcutaneous procedure	1 full day	Local with either NSAID or Narcotic
Surgical	Severe	Thoracotomy, laparotomy	3 full days	Local with both NSAID and Narcotic
Chronic	Mild-moderate*	Arthritis	long term	NSAID

*Severe chronic pain will not be permitted without strong scientific justification and full committee review of the procedure.
Duration for the various procedure types can be entered into ARIES, as written.

Please see the Rodent Survival Surgery guideline for requirements regarding post-operative monitoring and recordkeeping. Analgesic administration must continue until the animal is not longer painful.

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Table 2. Recommended analgesic drugs.

Drug#	Dose# and route#	Frequency#	Comments
Narcotics			
• Monitor for respiratory depression (during anesthesia) • May cause decreased GI motility (long term recovery)			
Buprenorphine	0.05 - 0.1 mg/kg SC or IP	Every 4-6 hours	– May be administered either pre-operatively or post-operatively.
Sustained-release buprenorphine (ZooPharm)	1.0 mg/kg SC	Single dose prior to the time of surgery	– Use buprenorphine SR-LAB formulation to prevent injection site reaction – Veterinary license required to purchase drug
Sustained-release buprenorphine (Animalgesic)	3.25 mg/kg SC	Single dose prior to the time of surgery	
Non-steroidal anti-inflammatory analgesia (NSAID)			
• prolonged use my cause renal, gastrointestinal, or other problems			
Injectable NSAIDs			
Meloxicam	5-10 mg/kg SC	12-24 hours	Preferred
Carprofen	5-10 mg/kg SC	12-24 hours	
Oral NSAIDs			
• Use only on the days after surgery, not immediately post op, as ingestion may be unreliable			
Meloxicam	5-10 mg/kg	12-24 hours	Preferred
Carprofen	0.5 mg / mouse / day	24 hours	– ¼ of 2 mg tablet per day – http://www.bio-serv.com/product/RRMD.html
Local anesthetic/analgesics			
• Administer after mouse is under general anesthesia			
Lidocaine	Dilute to 0.5% and inject # ml SC or intra-incisional	Use locally before making surgical incision, or before final skin closure	– Faster onset (2 minutes) than bupivacaine but short (<1 hour) duration of action – Do not exceed 7 mg/kg total dose
Bupivacaine	Dilute to 0.25% and inject # ml SC or intra-incisional	Use locally before making surgical incision, or before final skin closure	– Slower onset (15 minutes) than lidocaine but longer (4-8 hour) duration of action – Do not exceed 8 mg/kg total dose