ACUP ID number: EP-1		
Approval date:	**	**GPS/ACUC**
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Revision by:		
Distribution		**All**

EP – 1: Guidelines on Analgesia for Rodent Surgeries

Objective: To establish the minimum required analgesic regimens for rodent survival surgeries.

Scope: This applies to all rodents under the Johns Hopkins University animal care and use program. Exemptions to the minimum requirements may be approved with appropriate scientific justification and must be described in the ACUC-approved protocol.

Pain Categorization: The following provides general guidelines in the determination of the severity of pain associated with surgical procedures in rodents.

- **Minimal to mild pain:** Includes procedures that cause momentary pain or pain of low intensity that does not have long-lasting consequences.
- **Mild to moderate pain:** Procedure that cause more than momentary pain, and are known to be painful in humans hours to days after the procedure/surgery is performed. Would cause rodents to be visibly painful by displaying any one of the following behaviors if no analgesics were given (weight loss, decreased grooming, decreased activity, dark red material around the eyes of rats, hunched posture).
- **Moderate to severe pain:** Any procedure that causes intense pain, or a moderate pain that last days to weeks after the procedure is completed. This may include any surgery that induces a chronic pain typically associated with degenerative diseases (e.g., osteoarthritis).

Guidelines:

1. Determine pain categorization and appropriate analgesic regimen of the surgical model using the table below, which is not intended as a comprehensive list of procedures that fall into these categories.
2. Upon conducting animal experiments, provide analgesics in addition to the minimum described in the table below considering factors such as a) personnel's surgical experience and technique, and
   b) intra-and post-operative complications. For example, aggressive tissue handling and complications like accidental organ perforation may elevate the pain level each animal experience.
3. Assess the animal at least daily for 7-10 days post-operatively, or at least until the sutures, wound clips, or staples are removed.
4. Manage post-operative complications (e.g., suture dehiscence and wound infection) as described in the ACUC-approved protocol, or upon veterinary consultation. Administer analgesics as appropriate.
5. Consider analgesic adjuvants such as sedatives and adjunct pain management approaches like using soft bedding material (e.g., paper vs. corncob) to further alleviate pain and distress.

MINIMUM ANALGESIA REQUIREMENTS[1]			
	Minimal to mild pain	**Mild to moderate pain**	**Moderate to severe pain**
Pre-emptive analgesia[2]	Single dose of systemic NSAID (e.g. meloxicam or carprofen) OR Opioid (e.g. buprenorphine) prior to surgery	Systemic NSAID (e.g. meloxicam or carprofen) OR Single dose of buprenophine SR[3] prior to surgery	Systemic NSAID (e.g. meloxicam or carprofen) AND Single dose of buprenorphine SR[3]
Intra-operative analgesia			Lidocaine and bupivacaine
Post-operative analgesia[4]	PRN	NSAID q 24h for 1 additional day (not necessary if buprenorphine SR[3] was administered pre-emptively) PRN after 1 day post-op	NSAID q 24h for 2 additional days PRN after 2 days post-op
EXAMPLES OF RODENT PROCEDURES			
	Subcutaneous osmotic pumps	Minor laparotomy (skin and muscle incision only - e.g., intra-peritoneal osmotic pump)	Major laparotomy (e.g., includes incising of viscera)
	Simple skin incision/biopsy	Craniotomy with significant tissue manipulation[5]	Middle cerebral artery occlusion
	Vascular cut-down	Ovariectomy	Meniscectomy
	Vasectomy	Orchidectomy	Carotid ligation
	Intracranial injection	Neural electrode implantation	Orthopedic procedures
			Hind limb transplant
			Thoracotomy

[1]Additional analgesics and other pain-relieving methods (e.g. local anesthetics) should be considered dependent on the expected outcome of the surgical procedure and/or in consultation with veterinary staff.

[2]Consider the surgery start time so as to reach therapeutic levels when animal recovers from anesthesia (e.g., 1h with injectable meloxicam [Chen et al., 2016], 2h with oral meloxicam or carprofen, and 12h with carprofen in drinking water [Ingrao et al., 2013]).

[3]The therapeutic duration of buprenorphine SR is 48h in mice and 72h in rats [Kendall et al., 2014; Foley et al., 2011]. Please note that meloxicam SR, carprofen-SR, fentanyl-SR, and

butorphanol-SR do not provide analgesia for more than 24 hours [Kendall et al., 2014].

[4]Animals must be assessed daily (see item Procedures 3 above) and analgesics given PRN (*pro re nata*; “as needed”).

[5]Craniotomy is defined as a surgical procedure used to temporarily open part of the skull to expose the brain. Examples of procedures that cause mild to moderate pain include cranial window and head cap
placement.

Select References:

1. Chen, P.H., Boyd, K.L., Fickle, E.K., Locuson, C.W. 2016. Subcutaneous meloxicam suspension pharmacokinetics in mice and dose considerations for postoperative analgesia. *J Vet Pharmaco Ther*. 39: 356-362.
2. Foley, P.L., Liang, H., Chrichlow, A.R. 2011. Evaluation of a sustained-release formulation of buprenorphine for analgesia in rats. *JAALAS*. 50: 198-204.
3. Ingrao, J.C., Johnson, R., Tor, E., Gu, Y., Litman, M., Turner, P.V. 2013. Aqueous stability and oral pharmacokinetics of meloxicam and carprofen in male C57BL/6 mice. *JAALAS*. 52: 553-559.
4. Kendall, L.V., Hansen, R.J., Dorsey, K., Kang, S., Lunghofer, P.J., Gustafson, D.L. 2014. Pharmacokinetics of sustained-release analgesics in mice. *JAALAS*. 53: 478-484.

I acknowledge that I have read and understand the JHU Animal Care and Use Program document "**Guidelines on Analgesia for Rodent Surgeries**" and I will follow this procedure. I agree to bring any deviations in this procedure to the attention of my supervisor/GPS Working Group.

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Name (Print)
Date

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Signature