



STANDARD OPERATING PROCEDURE #102 RABBIT ANALGESIA

1. PURPOSE

The intent of this Standard Operating Procedure (SOP) is to describe methods of assessing pain in rabbits and mitigating pain by administration of analgesic medications.

2. RESPONSIBILITY

Principal investigator (PI) and their research staff, veterinary care staff.

3. GENERAL CONSIDERATIONS

- 3.1. A procedure which would be expected to be painful if it were done on humans must be considered painful to the animal.
- 3.2. When there is a question of whether or not a procedure is painful, the animal should receive the benefit of analgesia.
- 3.3. Analgesia should be provided at an appropriate dose and frequency to control pain.
- 3.4. Any deviation from this procedure must be justified by the investigator and approved by the appropriate Facility Animal Care Committee (FACC).

4. PAIN RECOGNITION AND ASSESSMENT

- 4.1. Adapt the frequency of observation to the invasiveness of the procedure (minimum once a day).
 - 4.2. Start by observing the animal from a distance so the animal's behavior is not altered by the presence of the observer. Then proceed to observe the animal more closely.
 - 4.3. Look for any changes in the behavior. Report animals which appear to be in pain to the veterinary care staff.
 - 4.4. Common clinical signs indicative of pain or distress include:
 - 4.4.1. Avoidance, teeth grinding, vocalization and aggressiveness (mainly if the animal cannot escape)
 - 4.4.2. Spontaneous activities are reduced. The animal is isolated from the social group
 - 4.4.3. Altered gait
 - 4.4.4. Hunched posture
 - 4.4.5. Piloerection
 - 4.4.6. Reduced grooming; dark-red stain around the eyes and at nostrils
 - 4.4.7. Reduced appetite and subsequent weight loss
- Note:** The most reliable signs of pain and distress are the changes in behavior. This implies a good knowledge of species and individual normal behavior by the observer.

4.5. Rabbit Grimace Scale (Keating et al. 2012)

The rabbit grimace scale is a standardized behavioral coding system that demonstrates facial expressions which can be used to assess pain in the laboratory rabbit.



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The Rabbit Grimace Scale

Research has demonstrated that changes in facial expression are associated with changes in pain intensity. The specific facial action units shown below comprise the Rabbit Grimace Scale. These action units increase in intensity in response to pain. These action units should only be used in awake animals. Each animal should be scored at least once to avoid scoring brief changes in facial expression as part of a clinical assessment alongside other validated techniques.

	Action units		
	Not present	Moderately present	Obviously present
Orbital tightening <ul style="list-style-type: none"> • Closing of the eyelid (narrowing of orbital fissure) • A wrinkle may be visible around the eye 			
Cheek flattening <ul style="list-style-type: none"> • Flattening of the cheeks. When 'obviously present', cheeks have a sunken look • The face becomes more angular and less rounded 			
Nostril shape <ul style="list-style-type: none"> • Nostrils (nares) are drawn vertically forming a 'V' rather than 'U' shape • Nose tip is moved down towards the chin 			
Whisker shape and position <ul style="list-style-type: none"> • Whiskers are pushed away from the face to 'stand on end' • Whiskers shorten and lose their natural, downward curve • Whiskers increasingly point in the same direction. When 'obviously present', whiskers may 'pave downwards' 			
Ear shape and position <ul style="list-style-type: none"> • Ears become curled (more cylindrical) in shape • Ears rotate from facing towards the source of sound to facing towards the hindquarters • Ears may be held up or sides of the body 			

Read the original paper: [Yonas AA, Fickelmeil PA, Leach M, et al. \(2012\) Changes in physiological, behavioural and facial expression responses. PLOS ONE 7\(9\): e44437. doi:10.1371/journal.pone.0044437](#)

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For guidance on using the Rabbit Grimace Scale to assess pain in research papers that underpin this technique, and for information on other grimace scales in other species, visit: www.nc3rs.org.uk/grim

The Rabbit Grimace Scale would not have been developed without the continued work of the [Rabbit Grimace Scale Development Team](#).

8. REFERENCES

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- 8.2. Keating SCJ, Thomas AA, Flecknell PA, Leach MC (2012) Evaluation of EMLA Cream for Preventing Pain during Tattooing of Rabbits: Changes in Physiological, Behavioural and Facial Expression Responses. *PLoS ONE*7(9): e44437. <https://doi.org/10.1371/journal.pone.0044437>
- 8.3. Plumb, DC. (2005). *Plumb's veterinary drug handbook*. Stockholm, Wis. : Ames, Iowa :PhrmaVet ; Distributed by Blackwell Pub.
- 8.4. Delk KW, Carpenter JW, KuKanich B, Nietfeld JC, Kohles M. Pharmacokinetics of meloxicam administered orally to rabbits (*Oryctolagus cuniculus*) for 29 days. *Am J Vet Res.* 2014 Feb;75(2):195-9. [doi: 10.2460/ajvr.75.2.195](https://doi.org/10.2460/ajvr.75.2.195). PMID: 24471756.

SOP REVISION HISTORY

DATE	NEW VERSION
2015.04.22	6.1 Use lidocaine HCl 2% (20mg/ml) injectable solution.
2015.04.22	6.1 Use bupivacaine HCl 0.50% (5mg/ml) injectable solution.
2015.04.22	6.1 Lidocaine-bupivacaine mixture: Discard mixture after 3 months.
2016.09.02	7. Carprofen, ketoprofen and meloxicam: Ensure good water intake and monitor hydration status. Suspend water restriction prior to administration.
2016.09.06	7. Buprenorphine route of administration:-SC-Preferred: IM, IV, sublingual, gingival Other: SC
2017.01.27	7.1. Administration of non-steroidal anti-inflammatory drugs (NSAIDs): 7.1.1. NSAIDs include carprofen, ketoprofen and meloxicam. 7.1.2.