



1. PURPOSE

This Standard Operating Procedure (SOP) intends to describe methods of assessing pain in rabbits and mitigating pain by administering analgesic medications.

2. RESPONSIBILITY

Principal investigator (PI) and their research staff.

3. GENERAL CONSIDERATIONS

- 3.1. A procedure expected to be painful in humans is considered painful in animals.
 - 3.2. When there is a question of whether a procedure is painful, the animal should benefit from 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 BGU ethical committee.
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4. PAIN RECOGNITION AND ASSESSMENT

- 4.1. Adapt the observation frequency to the procedure's invasiveness (minimum once a day).
- 4.2. Start by observing the animal from a distance, so the observer's presence does not alter the animal's behavior. Then proceed to observe the animal more closely.
- 4.3. Look for any changes in the behavior. Report animals that appear to be in pain to the vets.
- 4.4. Common clinical signs of pain or distress include (but are not limited to): avoidance, vocalization, aggressiveness, teeth grinding, isolation from the group, low spontaneous activity, hunched posture, lack of grooming, reduced appetite, and weight loss, and no feces in pen.

Note: *The most reliable signs of pain and distress are changes in behavior and no manipulation of enrichment materials.*

- 4.5. The Rabbit Grimace Scale (Keating et al. 2012): A poster demonstrating the scale is posted in Appendix 1.
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5. ANALGESIA PLAN

- 5.1. Specify the analgesia plan in your animal protocol.

- 5.2. Whenever possible, provide analgesia just before the painful stimulus, as it is more effective in preventing pain (e.g., give analgesic before surgery).
- 5.3. Use a combination of analgesics, often more effective than a single agent.
- 5.4. Extend analgesia from pre-op to 72 hours post-op for surgical procedures unless specified otherwise in the Animal Use protocol and approved by the BGU Ethical committee.

6. LOCAL ANALGESIA

- 6.1. Infiltrate or apply local analgesics to areas where a painful stimulus may be induced. Repeat the application of local agents at specified intervals to maintain analgesia. In some cases, a sedative is recommended when using local analgesia.

Analgesic	Dose	Route	Duration	Note
Lidocaine	< 2 mg/kg	SC, Infiltration of surgical wounds	30–60 min.	Use lidocaine HCl 2% (20mg/ml) injectable solution. Because this drug is acidic, it is recommended to dilute it 3:1 with sodium bicarbonate injectable solution (at 5 or 8.4%). Dilution must be prepared immediately before use and should not be stored. A diluted solution is as effective, but induction of analgesia is slightly prolonged. *Dilution with sodium bicarbonate is unnecessary if lidocaine is administered to an anesthetized animal.
EMLA cream	Thick spread	Topical	30–60 min.	Apply only to intact skin. Shave or pluck the fur. Ideally, 10 minutes before the painful procedure
Localine eye drops	1-2 drops	Ocular	30-60min	
Bupivacaine	< 2 mg/kg	SC, Infiltration of surgical wounds	3–4 hrs.	Use bupivacaine HCl 0.50% (5mg/ml) injectable solution. Same comment as for lidocaine.

7. GENERAL ANALGESIA


- 7.1. Administration of non-steroidal anti-inflammatory drugs (NSAIDs):
 - 7.1.1. NSAIDs include carprofen, ketoprofen, meloxicam, and dipyrone.
 - 7.1.2. Ensure good water intake and monitor hydration status during the treatment period.
 - 7.1.3. Suspend water restriction before administration of NSAIDs.
 - 7.1.4. Do not administer NSAIDs to neonatal rodents.

Rabbit


Analgesic	Dose	Route	Frequency	Note
Buprenorphine	0.1 mg/kg	SC, IP	4–8 hrs.	Mild to moderate pain. Controlled drug.
Carprofen	2 mg/kg	SC, PO	12–24 hrs.	Mild to moderate pain. Use carprofen 50mg/ml injectable solution. To prepare a 4mg/ml dilution: add 0.8ml of carprofen 50mg/ml to 9.2 ml of sterile water for injection. Administer 5µL/g of body weight. Store at room temperature. Discard dilution after one month.
Meloxicam	1.5 mg/kg	SC, PO	24 hrs.	Mild to moderate pain.
Ketoprofen	15 mg/kg	SC	12-24 hrs.	Mild to moderate pain.
Dipyrone	50 mg/kg	PO	In water bottle	Mild to moderate pain.

8. Appendix

Appendix 1: The Rabbit Grimace Scale



National Centre
for the Replacement,
Refinement & Reduction
of Animals in Research


















The Rabbit Grimace Scale

Research has demonstrated that changes in facial expression provide a means of assessing pain in rabbits.

The specific facial muscle units shown below comprise the Rabbit Grimace Scale. These are used to assess the intensity of pain or discomfort and can form part of a clinical assessment alongside other welfare indicators of pain.

The actions units shown only for dental (teeth) animals. Each animal should be observed for a short period of time to avoid any potential changes in those expression that are unrelated to the animal's welfare.

	Action units		
	Not present "0"	Moderately present "1"	Obviously present "2"
Orbital tightening <ul style="list-style-type: none"> • Closing of the eyelid • Flattening of orbital area • A wrinkle may be visible around the eye 			
Cheek flattening <ul style="list-style-type: none"> • Flattening of the cheeks • Flattening of the nostrils • Cheeks have a downturn look • The face becomes more angular and less rounded 			
Nostril shape <ul style="list-style-type: none"> • Nostril (pinna) are drawn vertically • Nostril is V rather than U shape • Nostril is in inward slant towards the eye 			
Whisker shape and position <ul style="list-style-type: none"> • Whiskers are tucked away from the face • Whiskers are held outwards • Whiskers differ and lose their radius, downward curve • Whiskers are curved upwards in the same direction when whiskers present • Whiskers are held downwards 			
Ear shape and position <ul style="list-style-type: none"> • Ears are erect (ears held) called (ears) erectability change • Ears are held back (ears) towards the ears of neck to bring towards the face • Ears may be held back to the back of the body 			

The Rabbit Grimace Scale (RGS) is a validated tool for assessing pain in rabbits. It is based on the observation of facial muscle units and is used to assess the intensity of pain or discomfort. The RGS is a validated tool for assessing pain in rabbits. It is based on the observation of facial muscle units and is used to assess the intensity of pain or discomfort.

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 Approved by the BGU Animal Policy and Welfare Oversight Committee