
1. PURPOSE

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

2. RESPONSIBILITY

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

3. GENERAL CONSIDERATIONS

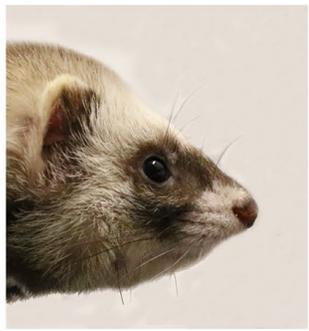
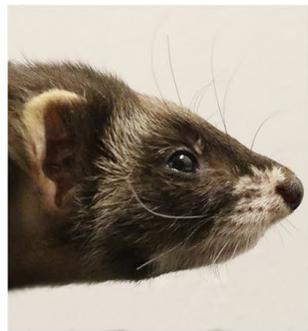
- 3.1. A procedure which would be expected to be painful if it were done on humans must be considered painful to the animal.
- 3.2. When there is a question of whether or not a procedure is painful, the animal should receive the benefit of analgesia.
- 3.3. Analgesia should be provided at an appropriate 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, 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. 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. Ferret Grimace Scale (Reijgwart et al. 2017)

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

	Not present (0)	Moderately present (1)	Obviously present (2)
<p>Orbital tightening</p> <ul style="list-style-type: none"> ▪ The eyelids close (orbital area narrows) ▪ A wrinkle may be visible around the eye 			
<p>Nose bulging</p> <ul style="list-style-type: none"> ▪ The nose is pulled down ▪ The nose rounds off ▪ The nostrils point down ▪ The bridge of the nose bulges 			
<p>Cheek bulging</p> <ul style="list-style-type: none"> ▪ The cheek muscles bulge ▪ The contour of the cheeks become visible ▪ the cheek may be pulled up at the side of the ear 			
<p>Ear changes</p> <ul style="list-style-type: none"> ▪ The ears are pulled back against the body ▪ The ears may form a pointed shape ▪ The ears may fold over 			
<p>Whisker retraction</p> <ul style="list-style-type: none"> ▪ The whiskers are pulled back against the cheek ▪ The whisker follicles converge caudally ▪ The whiskers clump together 			

5. ANALGESIA PLAN

- 5.1. If possible, provide analgesia before the painful stimulus, as it is more effective in preventing pain (e.g. give analgesic before surgery).
- 5.2. Use a combination of analgesics, which is often more effective than using a single agent. For example, a combination of opioid, non-steroidal anti-inflammatory drug (NSAID), and infiltration of a local analgesic.
- 5.3. For surgical procedures, extend analgesia from pre-op to 72 hours post-op, unless otherwise specified in the Animal Use protocol (AUP) and approved by the FACC.

6. LOCAL ANALGESIA

- 6.1. Infiltrate or apply local analgesic to areas where a painful stimulus may be induced. Repeat application of local agent 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. Diluted solution is as effective but induction of analgesia is slightly prolonged. * Dilution with sodium bicarbonate is not necessary if lidocaine is to be administered to an anesthetized animal.
Bupivacaine	< 2 mg/kg	SC, Infiltration of surgical wounds	3–4 hr.	Use bupivacaine HCl 0.50% (5mg/ml) injectable solution. Same comment as for lidocaine.
* Lidocaine- bupivacaine mixture	< 2 mg/kg	SC, Infiltration of surgical wounds	30min.-4 hr.	Same comment as for lidocaine. Combining both drugs allows for rapid induction and prolonged effect. Use a 1:1 mixture of lidocaine HCl 2% (20mg/ml) injectable solution and bupivacaine HCl 0.50% (5mg/ml) injectable solution. Discard mixture after 3 months.
EMLA cream	Thick spread	Topical	30–60 min.	Shave or pluck the fur and apply a thick layer of cream ideally 10 minutes before the painful procedure. Use only on intact skin.

*most commonly used

7. GENERAL ANALGESIA

Ferret

Analgesic	Dose	Route	Frequency	Note
*Buprenorphine	0.01–0.5 mg/kg	IM, SC	8–12 hr.	Mild to moderate pain. Controlled drug.
*Carprofen	1-4 mg/kg	SC, PO	12–24 hr.	Mild to moderate pain.
*Ketoprofen	1-2 mg/kg	SC, IM, PO	24 hr.	Mild to moderate pain.
*Meloxicam	0.2 mg/kg	SC, IM, PO	12-24 hr.	Mild to moderate pain.
Butorphanol	0.1-0.4 mg/kg	SC, IM, IV	2-6 hr	Moderate to severe pain. Controlled drug.

*most commonly used

- 7.1. Administration of non-steroidal anti-inflammatory drugs (NSAIDs):
 - 7.1.1. NSAIDs include carprofen, ketoprofen and meloxicam.
 - 7.1.2. Ensure good water intake and monitor hydration status during the treatment period.
 - 7.1.3. To minimize chances for adverse drug interactions, a washout period of 5-7 days is recommended before switching between NSAIDs.

8. REFERENCES

- 8.1. Plumb, DC. Plumb's Veterinary Drug Handbook. Stockholm, Wis. : Ames, Iowa :PhrmaVet ; Distributed by Blackwell Pub., 2005.
- 8.2. Reijgwart ML, Schoemaker NJ, Pascuzzo R, Leach MC, Stodel M, de Nies L, et al. (2017) The composition and initial evaluation of a grimace scale in ferrets after surgical implantation of a telemetry probe. PLoS ONE 12(11): e0187986

SOP REVISION HISTORY

DATE	NEW VERSION
2021.11.04	5.2. Try to Use a combination of analgesics, which is often more effective than using a single agent. For example, a combination of buprenorphine opioid, carprofen non-steroidal anti-inflammatory drug (NSAID), and local infiltration of lidocaine/bupivacaine a local analgesic.
2021.11.04	7.1.3. Suspend water restriction prior to administration of NSAIDs.