UNIVERSITY STANDARD

Title

UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL
STANDARD ON PAIN IDENTIFICATION AND POST-OPERATIVE
ANALGESIA

Introduction

PURPOSE
The standards and procedures described below provide guidance to all researchers and
animal handlers for appropriate post-operative analgesia for prevention of pain and
proper identification of pain in animals if present.

SCOPE OF APPLICABILITY
All personnel engaged in the care and husbandry of animals and laboratory members
administering post-operative analgesia and/or performing post-operative monitoring.

The UNC-CH IACUC expects that anyone involved in animal work at the University will
comply with this Standard. Requests for exceptions to this Standard must be reviewed
and approved by the IACUC.

Standard

In order to alleviate pain and/or distress post-operatively, the IACUC requires the
administration of analgesics for all survival surgeries. Selection of the appropriate
analgesic agent(s) should be based on the type of surgical procedure, be provided for a
minimum of 24 hours (minor surgery) to 48 hours (major surgery), and continued longer
if the animal is displaying any symptoms associated with pain. Those in contact with
animals post-operatively should be familiar with the potential signs associated with pain
or distress to ensure analgesia is provided as needed (please refer to table and links at
the end of this standard).

Dependent on the procedure, different forms of anesthesia may be utilized to alleviate
pain. A major surgery may require the administration of a narcotic agent such as
Buprenorphine (Buprenex®) for adequate pain control and/or relief. Non-steroidal anti-
inflammatory agents such as carprofen or meloxicam may be suitable for major or minor
surgeries. Combinations of analgesics may be recommended, in order to provide
multimodal analgesia, particularly for major surgeries. Depending on the procedure,
administration of a local anesthetic may aid in pain reduction (eg: Marcaine® (local anesthetic agent able to reduce pain), Lidocaine® (local anesthetic agent for relief of itching, burning and pain due to skin inflammation)).

Note: Sedatives (able to reduce irritability / excitement) and anxiolytics (able to prevent or reduce anxiety) do not relieve pain. However, they may be used in conjunction with appropriate analgesics.

The USDA and PHS policies require proper documentation of animal care and use to assess compliance with research protocols and clinical care procedures. UNC Chapel Hill specifically requires the use of the pink ‘Post-Operative Monitoring/Analgesia’ cards on all post-operative cages receiving monitoring or analgesia. Cards must be kept on the cage during the specified monitoring or analgesia period described within the protocol. The lab may utilize these cards as the required documentation for all observations and treatments performed during the post-operative period. Dates and times (including AM/PM) of all time-sensitive observations or treatments (post-operative evaluations, pain medication) must be recorded. If these cards are the only documentation of the post-operative analgesic administration, they must be kept with the lab’s surgery records for review.

Written records are a standard form of documentation which verify experimental procedures and protocol compliance. As part of an effective animal care and use program, research personnel working with animals must develop and maintain accurate study records. Specific parameters (body weight measurements, clinical signs, tumor size, etc.) outlined in an approved protocol must be documented with attention given to the type of monitoring, frequency and duration outlined in the approved protocol (e.g., the statement in the approved protocol ‘We will monitor the animal daily after surgery,’ requires written documentation of the daily observation.)

Regulatory and accrediting agencies expect proper documentation of animal care and use as a means for the institution to ensure compliance with research protocols and clinical care procedures. The extent of records varies based on the nature of the procedure. However, at a minimum, records of the procedure must consist of: Animal /cage/group ID, date of procedure, type of procedure, anesthetics/analgesics used (dose, route, and time), anesthesia chart (verification of toe pinch), drugs given (dose, time), general procedures (e.g., intubation, beginning and end of surgery, etc.).

EXCEPTIONS
Requests for exceptions to this Standard must be reviewed and approved by the IACUC and/or DCM Management.

Definitions, Table and Links for Reference

IACUC: Institutional Animal Care and Use Committee
DCM: Division of Comparative Medicine
University Standard: The minimum acceptable limits or rules used to achieve Policy implementation, enforceable by the IACUC.
AWA: Animal Welfare Act
ACLAM: American College of Laboratory Animal Medicine
ILAR: Institute for Laboratory Animal Research
NIH: National Institutes of Health
Distress: the biological responses an animal exhibits in an attempt to cope with a threat to its homeostasis.
Non-survival Surgery: Surgical procedure where an animal is euthanized before recovery from anesthesia.
Major Survival Surgery: Surgical procedure that penetrates and exposes a body cavity. This also includes procedures that induce substantial impairment of physical or physiologic functions (such as laparotomy, thoracotomy, joint replacement, and limb amputation), or involves extensive tissue dissection or transection.
Minor survival surgery: does not expose a body cavity and causes little or no physical impairment.
Pain: A result from stimuli that damages tissue or has the potential to damage tissue.

Table 1: Potential Signs Associated with Pain or Distress in Rats, Mice, and Rabbits:

<table>
<thead>
<tr>
<th></th>
<th>Mice</th>
<th>Rats</th>
<th>Rabbits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased Food and Water Consumption</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Weight Loss/ decreased body condition</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Self-Imposed Isolation/Hiding</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Self-Mutilation, Gnawing at Limbs</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Rapid Breathing</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Open Mouth Breathing</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Abdominal Breathing</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Grinding Teeth</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>Biting/Growling/Aggression</td>
<td></td>
<td>X</td>
<td>X</td>
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<tr>
<td>Increased/Decreased Movement</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Unkempt Appearance (Erected, Matted, or Dull Haircoat)</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>Abnormal Posturing/Positioning (e.g., Head-Pressing, Hunched Back)</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td>---------------------------------------------------------------</td>
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<tr>
<td>Restless Sleep</td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td>Tearing (Including Porphyria), Lack of Blinking Reflex</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>Dilated Pupils</td>
<td></td>
<td></td>
<td>X</td>
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<tr>
<td>Muscle Rigidity, Lack of Muscle Tone</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Dehydration/Skin Tenting/Sunken Eyes</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Twitching, Trembling, Tremor (non-seizure-related)</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Vocalization (Rare)</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Redness or Swelling Around Surgical Site</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Increased Salivation</td>
<td></td>
<td></td>
<td>X</td>
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</tbody>
</table>

The following links provide pictorial examples of pain in rats, mice & rabbits:

**Links:**
- The Mouse Grimace Scale
- The Rat Grimace Scale
- The Rabbit Grimace Scale

**Related Requirements**

**EXTERNAL REGULATIONS AND CONSEQUENCES**

- Animal Welfare Act: Page 58, §2.31(d)(iv)(A)
- Guide for the Care and Use of Laboratory Animals (8th ed.), Veterinary Care: Pages 120, 121, 122, 123

**UNIVERSITY POLICIES, STANDARDS, AND PROCEDURES**

- Analgesia and Anesthesia Formulary - Mice
- Analgesia and Anesthesia Formulary - Rats
- Analgesia and Anesthesia Formulary - Other Species

For more detailed guidance, please refer to the University Policy on the Care and Use of Vertebrate Animals for Research, Training and Teaching Purposes.
Contact Information

<table>
<thead>
<tr>
<th>Subject</th>
<th>Contact</th>
<th>Telephone</th>
<th>Email</th>
</tr>
</thead>
<tbody>
<tr>
<td>Veterinary Consult</td>
<td>DCM Vet Services</td>
<td>919-966-2609</td>
<td></td>
</tr>
<tr>
<td>IACUC Protocol</td>
<td>OACU</td>
<td>919-966-5569</td>
<td><a href="mailto:iacuc@med.unc.edu">iacuc@med.unc.edu</a></td>
</tr>
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</table>

Important Dates

- Effective Date and title of Approver: January 2011; UNC IACUC
- Revision and Review Dates, Change notes, title of Reviewer or Approver: April, 2014, June 2018; UNC IACUC

Approved by: UNC IACUC

Dr. Roland Tisch 06/2018

UNC IACUC Chair