

| University Animal Care Committee Standard Operating Procedure | | |
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| Document No: 10.2 | Subject: Humane Interventions (Rat) | |
| Date Issued: July 7, 2011 | Revision: 4 | Page No: 1 |

Location: Queen's University

Responsibility: Principal Investigators, Research Staff, Veterinary Staff

Purpose: This Standard Operating Procedure (SOP) outlines the steps that must be taken to establish humane interventions and possible treatment for rodent research models. These interventions are to be determined and described on each Animal Use Protocol.

1. Introduction and Definitions: Humane interventions are clear criteria set a priori to define the point at which an experimental animal's pain and/or distress is terminated, minimized or reduced, by taking appropriate actions such as terminating a painful procedure, giving treatment to relieve pain and/or distress, or euthanizing the animal.

In experiments involving animals, any actual or potential pain, distress, or discomfort should be minimized or alleviated by choosing the earliest intervention that is compatible with the scientific objectives of the research.

Humane interventions are defined as actions or instructions including but not limited to:

- a. Providing adequate veterinary treatment, analgesia and/or supportive therapy to the animal(s).
- b. Termination of painful procedures.
- c. Removal of the animal(s) from the study.
- d. Modification of the experimental procedures to minimize the discomfort to the animal(s).
- e. Increasing the frequency of animal observations.
- f. Modification to the housing and husbandry practices to improve the comfort of the animal(s).
- g. Euthanasia.

The role of the UACC is vital in establishing the structure to ensure that the earliest interventions consistent with producing reliable data are considered, identified, and used. Ensuring appropriate interventions involves the combined efforts of the PI, the veterinary care staff, Animal Care Services Staff and the UACC to carry out the following instructions:

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- a. Determine the humane interventions that are appropriate for the study.
- b. Ensure that humane intervention points are clearly defined in the Animal Use Protocol (AUP).
- c. Ensure all personnel responsible for making animal observations have been adequately trained to observe and recognize the interventions in the approved AUP.

The investigator should consider the following questions, to ensure that appropriate interventions will be in place:

- What are the scientific justifications for using the proposed endpoint?
- What is the expected time course for the animals, from initial treatment to first signs of pain/distress, to the death of the animal, based on previous information with the specific model under study?
- When are the effects to the animal expected to be the most severe?
- If the course of the disease and expected signs of the adverse effects are unknown, could an initial (pilot) study, under close observation by the investigator and/or veterinary staff, answer these questions?
- Has a checklist of observations (Animal Welfare Assessment), on which the interventions will be based, been established?
- Who will monitor the animals (identify all responsible) and keep records?
- Has a clear chain for reporting observations been established?
- What will be the frequency of animal observations:
 - during the course of the study; and
 - during critical times for the animals?
- Do the investigators, animal care and technical staff have the training and expertise to monitor the animals adequately?
- What provisions have been made to deal with any animals that show unexpectedly severe signs and symptoms?
- For toxicological studies, has existing toxicological data been evaluated?

Abbreviations: Animal Care Services **ACS**, Principal Investigator **PI**, subcutaneous **SC**, intravenous **IV**, intraperitoneal **IP**, intramuscular **IM**, per os **PO**, per rectum **PR**

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2. Materials:

- Animal Welfare Assessment Sheet
- Scale
- Weight Loss chart
- Body Condition Scoring chart
- Logbook / Record sheets
- 0.9% sodium chloride
- Sterile needles (26-27g)
- Sterile 1ml syringes
- Ensure or Boost ***check with PI to confirm use, could alter microbiome***
- Small petri dishes
- Moist chow
- Meloxicam injectable

3. Procedures:

Establishing Intervention and Final Endpoints:

- a. Review literature and perform web-based searches of established models and alternative methods. Implement the alternatives whenever possible.
- b. Consult with veterinary care staff on study refinements designed to minimize pain and distress.
- c. Schedule regular animal observations at an appropriate frequency to ensure early detection of signs of pain and discomfort.
- d. Increase the frequency of observations and measurements in response to a decline in the animal's condition and during pre-determined critical periods during the study.
- e. Keep records of all observations including specific measurements or data (e.g., body weight).

Recommended General Interventions and Final Endpoints






- In the event that a model specific Animal Welfare Assessment has not been developed, the following general interventions should be used:
 - a. Weight loss exceeding 15% of baseline bodyweight. For young animals, failure to maintain normal weight gain within 15% of age-matched control animals.
 - b. Body condition score (BCS) less than 2.
 - c. Uncontrolled seizures.
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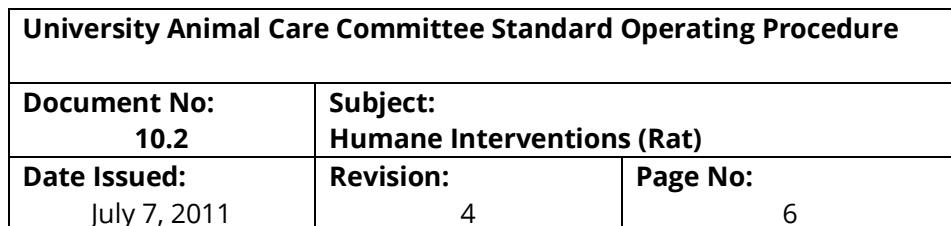
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- d. Impaired mobility which interferes with normal eating, drinking, ambulating or grooming.
 - e. No or weak response to external stimuli.
 - f. Hypothermia.
 - g. Mass that is ulcerated, necrotic or impairing normal function (e.g., eating, drinking) or exceeding acceptable size endpoints:
 - Rats: 5cm³ or 5% of the baseline bodyweight
 - h. Pale eyes and/or extremities and/or mucous membranes.
 - i. Uncontrolled hemorrhaging.
 - j. Self-mutilation.
 - k. Specific organ failure assessed by physical examination and, where possible, ancillary tests (hematology, biochemistry, imagery, etc.).
 - l. Respiratory distress: labored breathing, increased or decreased respiratory rate, cyanosis.
 - m. Hunched posture, lethargy and lack of grooming.
 - n. Incoordination, paralysis.
 - o. Abnormal vocalizations.
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Body Condition Scoring for Rats:

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|  | <p>BCS 1 - Rat is emaciated</p> <ul style="list-style-type: none"> Segmentation of vertebral column prominent if not visible. Little or no flesh cover over dorsal pelvis. Pins prominent if not visible. Segmentation of caudal vertebrae prominent. |
|  | <p>BCS 2 - Rat is under conditioned</p> <ul style="list-style-type: none"> Segmentation of vertebral column prominent. Thin flesh cover over dorsal pelvis, little subcutaneous fat. Pins easily palpable. Thin flesh cover over caudal vertebrae, segmentation palpable with slight pressure. |
|  | <p>BCS 3 - Rat is well-conditioned</p> <ul style="list-style-type: none"> Segmentation of vertebral column easily palpable. Moderate subcutaneous fat store over pelvis. Pins easily palpable with slight pressure. Moderate fat store around tail base, caudal vertebrae may be palpable but not segmented. |
|  | <p>BCS 4 - Rat is overconditioned</p> <ul style="list-style-type: none"> Segmentation of vertebral column palpable with slight pressure. Thick subcutaneous fat store over dorsal pelvis. Pins of pelvis palpable with firm pressure. Thick fat store over tail base, caudal vertebrae not palpable. |
|  | <p>BCS 5 - Rat is obese</p> <ul style="list-style-type: none"> Segmentation of vertebral column palpable with firm pressure; may be a continuous column. Thick subcutaneous fat store over dorsal pelvis. Pins of pelvis not palpable with firm pressure. Thick fat store over tail base, caudal vertebrae not palpable. |



1. Guidelines for Assessing the Health and Condition of Mice. Charmaine J. Foltz and Mollie Ullman-Cullere. *Lab Animal*. April 1999. Vol 28, No. 4, pps. 28-32.
2. CCAC Guidelines: Identification of scientific endpoints, humane intervention points, and cumulative endpoints.
3. Body Condition Scoring: A Rapid and Accurate Method for Assessing Health Status in Mice *Lab Animal Science*, Vol 49 (3) 319-323, 1999

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