ACC-2-Endpoints and Intervention for Laboratory Mammals Species

1. Purpose:

The purpose of this policy is to establish guidelines for the development of endpoints and define required interventions (including euthanasia) when humane endpoints specified in this document have been met. The guidelines are consistent with the Ontario Animals for Research Act, R.S.O. 1990, c.A22, the Canadian Council on Animal Care, Guide to the Care and Use of Laboratory Animals, 2nd Edition and Guidelines on Choosing an Appropriate Endpoint in Experiments Using Animal For Research, Teaching and Testing.

2. General:

Careful consideration should be given at the project planning stage to the fate of the animals at the end of the research or teaching project. The fate of the animals needs to be described in the animal use protocol.

The decision to reuse an animal needs to be carefully considered so that animals are used wisely but within reason. For teaching or training projects, the release of animals and their reuse needs to be considered based on the procedures performed and must be approved by the Animal Care Committee. Animals which undergo minimally invasive procedures (e.g. blood collection, injection of saline or a vehicle) could be reused for another project.

In the event that animals become ill, debilitated, or experience unrelieved pain or distress, either as a result of spontaneous disease or as a result of experimental procedures, the criteria described below must be utilized in deciding whether euthanasia is the most humane option or if another treatment option is warranted. Diagnostic tests may be used to define endpoints (e.g. vital signs, hematology, serum chemistry, and imaging).

2.1 Definitions:

A. Humane endpoint: Point at which an experimental animal's pain and/or distress is terminated, minimized or reduced, by taking actions such as euthanasia, terminating a painful procedure, or giving treatment to relieve pain and/or distress.

B. Experimental endpoint: Most experimental animal use protocols involve the euthanasia of study animals at a predetermined endpoint even when the animals may be clinically healthy. These endpoints can include, but are not limited to the need for cells or tissue for in vitro research, for the collection of blood, tissue or other biological samples, for diagnostic purposes, or to retire animals from their respective breeding programs.

C. Euthanasia: Act of inducing humane death in an animal

3. Humane Endpoints:

3.1 Humane endpoints should be selected based on their ability to accurately and reproducibly predict or indicate unjustifiable pain and/or distress, imminent deterioration, or death. Specific humane endpoints must be clearly defined in animal protocols and should be determined in consultation with the Animal Care and Veterinary Service.

3.2 The decision to authorise the euthanasia of an animal is based on:

A. **The general condition of the animal**: When this is considered to indicate signs of severe pain or distress or indicates a high probability of imminent death.

B. **The animal as an experimental model:** When the animal is no longer an acceptable experimental model, or would not give additional information for the purpose of the study, or when an animal has clinical evidence of an infectious disease which could compromise the health status of the colony.

Several factors are used when the animal's condition is evaluated. The following signs are not all inclusive but if present; the severity of these signs, their duration and the coincidence of more than one of these signs would prompt the decision to euthanize an animal for humane reasons and should be considered when developing humane endpoints for an experiment:

- Seriously impaired ambulation (unable to reach food or water easily) and/or inability to remain upright

- Lack of responsiveness to manual stimulation
- Rapid weight loss or net weight loss of more than 20% of the body weight
- Prolonged inappetence
- Evidence of muscle atrophy/marked loss of body condition
- Neurological signs: lethargy, weakness, non-coordination, head tilt, unconsciousness, seizures, circling, ataxia, stereotypic behavior and paresis or paralysis that would prevent the animal from eating, drinking or standing normally.
- Respiratory signs: difficult or abnormal respiration, coughing, nasal discharge, cyanosis
- Jaundice and/or anemia
- Unexplained/uncontrollable bleeding from any site on the body
- Persistent vocalization, self-mutilation
- Increased aggression
- Any obvious prolonged illness including such signs as chronic diarrhea or constipation, markedly discolored urine, polyuria or anuria, markedly abnormal body temperature, pale mucous membranes, hunched posture, severe dehydration, erected and neglected fur (rodent).
- Any diagnostic result that indicates a painful or distressing pathology for which treatment is impossible, impracticable or unacceptable for experimental purposes.

In addition, the following species specific signs are useful when establishing humane endpoints as they are indicators of pain/or distress:

- **Rodents:**
  - facial grimace demonstrating severe pain
  - hunched, abnormal stance or arched back
  - severe piloerection and/or severe skin tent
  - severe porphyrin staining in rats
  - withdrawal from cagemate, unresponsiveness
  - Size or condition of a mass: ulceration, necrosis, discharge, bleeding, persistent self-induced trauma. The mass should not significantly interfere with normal bodily functions (e.g. eating, drinking, and movement) or cause pain or distress due to its location. The acceptable upper limit of a mass burden should be evaluated based on the clinical condition of the individual animal. The adverse effect on the animal, the site, the condition and the development of the mass should be considered. As a guideline, an animal with a mass of greater than 5% of its normal body weight for routine tumor passage or 10% for animals involved in therapeutic experiment (i.e. 17 mm in a 25g mouse or 35mm in a 250g rat) will be considered for euthanasia.

- **Rabbits**
  - head pressing
  - teeth grinding
  - reluctant to move
  - hunched posture
  - excessive licking and scratching, excessive salivation

- **Swine**
  - changes in gait and posture
  - squeal and attempt to escape
  - reluctant to move
  - vomiting/diarrhea that is unresponsive to treatment

- **Cats**
  - hiding
  - growling/hissing
  - excessive licking
  - reluctant to move
  - haircoat appears rough, ungroomed
  - changes in posture (including irritable tail twitching, flattened ears)

- vomiting/diarrhea that is unresponsive to treatment

3.3 Monitoring Frequency

As the potential for pain and/or distress in animals rises, there should be an increasing intensity of monitoring and frequency of observations performed. The plan for scheduled monitoring of research animals as well as the provision of treatments and supportive care should be included in the protocol submission.

3.4 If the evaluation of the animal's condition requires a veterinary examination, the Veterinarian will perform an evaluation and will report and discuss his/her findings and recommendations with the Principal Investigator or designate. Should the evaluation of the animal's condition indicate that the animal is experiencing unacceptable pain or distress, the Veterinarian or designate may recommend:

- Terminating the procedure
- Modifying the procedure or animal's environment
- Treating the animal
- Euthanizing the animal

4. Euthanasia

4.1 Unless specified otherwise in the experimental protocol, the Principal Investigator or designate is responsible for authorising the euthanasia of experimental animals related with his/her project and adhering to this guideline. It is mandatory that the Principal Investigator or designate evaluates the status of an animal without undue delay when its welfare is in question.

4.2 In cases where the Principal Investigator or designate is unavailable or if the condition of the animal(s) is such that emergency measures must be taken, the Veterinarian or designate, on behalf of the Animal Care Committee, has the authority to treat, remove from the study or euthanize, if necessary, an animal according to his/her professional judgment in the animal's best interest.