1. PURPOSE
This Standard Operating Procedure (SOP) provides instruction on how to set humane intervention points for animal research models.

2. RESPONSIBILITY
Principal investigator (PI) and their research staff, veterinary care staff, Facility Animal Care Committee (FACC).

3. INTRODUCTION
3.1. Humane intervention points are clear criteria set to prevent or relieve unnecessary pain or distress to a research animal.

3.2. Humane interventions are defined as actions or instructions including, but not limited to, the following:
   3.2.1. Adequate veterinary treatment, analgesia and/or supportive therapy to the animal(s)
   3.2.2. Termination of painful procedures
   3.2.3. Removal of the animal(s) from the study
   3.2.4. Modification of the experimental procedures to minimize the discomfort to the animal(s)
   3.2.5. Increasing the frequency of animal observations
   3.2.6. Modification to the housing and husbandry practices to improve the comfort of the animal(s)
   3.2.7. Euthanasia

3.3. Pilot studies can be used to determine intervention points in cases where the course of disease, the experimental effects or the indicators of discomfort are otherwise unknown.

3.4. Ensuring appropriate intervention points involves the combined efforts of the PI, the veterinary care staff and the FACC to carry out the following instructions:
   3.4.1. Determine the humane intervention points that are appropriate for the study.
   3.4.2. Ensure that humane intervention points are clearly defined in the Animal Use Protocol (AUP).
   3.4.3. Ensure all personnel responsible for making animal observations have been adequately trained to observe and recognize the intervention points in the approved AUP.

4. PROCEDURES
4.1. Establishing intervention points:
   4.1.1. Review literature and perform web-based searches of established models and alternative methods. Implement the alternatives whenever possible.
   4.1.2. Consult with veterinary care staff on study refinements designed to minimize pain and distress.
   4.1.3. Schedule regular animal observations at an appropriate frequency to ensure early detection of signs of pain and discomfort.
   4.1.4. 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.
   4.1.5. Keep records of all observations including specific measurements or data (e.g., body weight).

4.2. Recommended general intervention points:
   4.2.1. Weight loss exceeding 20% of baseline bodyweight. For young animals, failure to maintain normal weight gain within 15% of age-matched control animals.
4.2.2. Body condition score (BCS) less than 2.
4.2.3. Uncontrolled seizures.
4.2.4. Impaired mobility which interferes with normal eating, drinking, ambulating or grooming.
4.2.5. No or weak response to external stimuli.
4.2.6. Hypothermia.
4.2.7. Mass that is ulcerated, necrotic or impairing normal function (e.g., eating, drinking) or exceeding acceptable size endpoints:
   4.2.7.1. Mice: 2cm³ or 10% of the baseline bodyweight
   4.2.7.2. Rats: 5cm³ or 5% of the baseline bodyweight
4.2.8. Respiratory distress: labored breathing, increased or decreased respiratory rate, cyanosis
4.2.9. Hunched posture, lethargy and lack of grooming.
4.2.10. Incoordination, paralysis
4.2.11. Abnormal vocalizations
4.2.12. Pale eyes and/or extremities (rodents) or mucous membranes
4.2.13. Uncontrolled hemorrhaging
4.2.14. Self-mutilation
4.2.15. Specific organ failure assessed by physical examination and, where possible, ancillary tests (hematology, biochemistry, imagery, etc).

4.3. Recommended intervention points for aging rodents (over 18 months of age):
   4.3.1. Refer to SOP 412.

4.4. Recommended intervention point for rodent cancer models:
   4.4.1. Refer to SOP 415.