1. PURPOSE

This Standard Operating Procedure (SOP) provides instructions for setting humane intervention points in animal research models.

2. RESPONSIBILITY

Principal investigator (PI) and their research staff.

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 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 determine intervention points where the course of the 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 Ethical committee 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 protocol.
   3.4.3. Ensure all personnel responsible for animal observations have been adequately trained to observe and recognize the intervention points in the approved animal protocol.

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 veterinary care staff on study refinements designed to minimize pain and distress.

4.1.3. Schedule regular animal observations at an appropriate frequency to detect signs of pain and discomfort early.

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 or natural control body weight. For young animals, failure to maintain average weight gain within 15% of age-matched control animals.

4.2.2. The body condition score (BCS) is less than 2.

4.2.3. Uncontrolled seizures.

4.2.4. Impaired mobility 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: 15mm in longest diameter or 1500mm³ or 10% of the baseline body weight
   4.2.7.2. Rats: 35mm in longest diameter or 5% of the baseline body weight

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 extremities (rodents) or mucous membranes

4.2.13. Uncontrolled hemorrhaging

4.2.14. Self-mutilation

4.2.15. Specific organ failure is 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 802.

4.4. Recommended intervention point for rodent cancer models:

4.4.1. Refer to SOP 803.

4.5 Record HUMANE INTERVENTION POINTS in MONITORING LOG (File SOP801-A)