



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.
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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**)

SOP 801 HUMANE INTERVENTION POINTS

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Approved by the BGU Animal Policy and Welfare Oversight Committee