



## Humane Endpoints

**357.1 Purpose:** This policy outlines the requirements for developing and defining humane endpoints for all animals placed on an Emory IACUC protocol. A humane endpoint is defined in the 8<sup>th</sup> edition of *The Guide for the Care and Use of Laboratory Animals* as “the point at which pain or distress in an experimental animal is prevented, terminated, or relieved”. These are different from experimental endpoints, which occur when scientific objectives have been met, but the two can be closely linked. The use of humane endpoints contributes to refinement by providing an alternative to experimental endpoints that result in unrelieved or severe animal pain and distress, including death, and should be relevant and reliable. The PI, who has precise knowledge of both the objectives of the study and the proposed model, should identify, explain, and include in the animal use protocol a study endpoint that is both humane and scientifically sound. The final determination of humane endpoints should involve the PI, veterinarian and the IACUC, and should be defined when possible prior to the start of the study.

**357.2 Special Considerations:** The 8<sup>th</sup> edition of “*the Guide*” (page 27) indicates that “while all studies should employ endpoints that are humane, studies that commonly require special consideration include those that involve tumor models, infectious diseases, vaccine challenge, pain modeling, trauma, production of monoclonal antibodies, assessment of toxicologic effects, organ or system failure, and models of cardio-vascular shock”. These models often cannot utilize common default humane endpoint guidelines and therefore should be developed on a case-by-case basis in conjunction with the IACUC and veterinarians. The attached appendix provides sample humane endpoint guidelines for a number of common model systems (see Appendix A-B). Note also that the IACUC has separate policies for determining humane endpoints for tumor models and MPTP treatment as detailed in the appendix material below.

**357.3 Protocol components:** The following items must be included when outlining humane endpoints in the IACUC protocol:

- 357.3.1 Definition of endpoints.** Endpoints are thresholds that, when reached, require a response. This could entail removal from the study until the condition had adequately improved, clinical treatment sufficient to allow experimentation to continue, or more commonly euthanasia.
- 357.3.2 Assessment criteria.** These are the parameters that will be measured during a study that will be indicative of an animal’s general health and well-being or clinical condition, or that will indicate if an animal is experiencing pain or stress (either acute, or chronic). Examples include, but are not limited to, measuring body weight, food and water consumption, body temperature, tumor size, imaging findings, blood chemistry or hematology abnormalities, or assessing the ability to ambulate.
- 357.3.3 Frequency of monitoring.** This states the regularity, often number of times per day and per week, that responsible personnel will observe the animal or measure the parameters identified as assessment criteria. Monitoring requirements may change through the course of a study as a condition worsens over time or experimental manipulation
- 357.3.4 Required response.** This is the intervention that must occur when the defined endpoint(s) has been reached. The intervention will typically be medical treatment or euthanasia and may be performed by research or veterinary staff in compliance with pre-set arrangements in the IACUC-approved protocol and sometimes on other circumstances.

**357.4 Default Endpoints:** The following criteria may be considered standard, default endpoints for “low-risk” animal models which would not generally be felt to have pain and distress under normal conditions, but may experience untoward, potentially severe, effects unpredictably. For models in which animals are expected to have pain and distress, these default endpoints may not generally be considered to be sufficient and additional refinement of the endpoints on a case-by-case basis may be required.

- Loss of 25% of body weight from baseline weight when assigned to the protocol. **NOTE:** A growth nomogram must be used to adjust the basal weight for growing animals.
- Major organ failure or medical conditions unresponsive to treatment
- Surgical complications unresponsive to immediate intervention
- Non-rodent animals, other than Rabbits, that have complete anorexia for 4 days or are unable to consume sufficient nutrients without assistance for 7 days.
- Tumors arising from other than experimental means that grow in excess of 10% of body weight, impair movement, or ulcerate.
- Clinical or behavioral signs resulting in acute unrelievable stress, significant chronic stress or distress and unresponsive to appropriate intervention.
- In the case of rodents, the following abnormalities persisting for 24 hours and for rabbits, persisting for 48 hours would warrant euthanasia.
  - inactivity or hyper-activity
  - labored breathing
  - hunched posture
  - piloerection/matted fur
  - signs of dehydration
  - abnormal vocalization when handled
  - anorexia
  - one or more unresolving skin ulcers

**357.5 Death as an endpoint:** The use of death as an endpoint is generally discouraged. However, it is understood that in some special circumstances it is necessary or unavoidable and thus will be considered on a case-by-case basis. Approval requires adequate scientific justification for death as an endpoint including why alternative endpoints or stress or pain-relieving drugs cannot be used as well as detailed plans for monitoring and supportive care including frequency of monitoring and record-keeping practices.

**357.6 Veterinary Oversight:** The attending Veterinarian (AV) has the responsibility for oversight of the health and welfare of animals used for research. The AV and designated veterinary staff, has the authority to euthanize any animal in the interest of animal welfare regardless of approved humane endpoints. Note however, that a DAR/Yerkes veterinarian can determine that euthanasia is not required for an animal that meets the above criteria, provided that the animal is under veterinary care and the veterinarian determines that the animal is likely to respond to treatment. All attempts will be made to reach mutual agreement with the PI and research staff whenever possible when these decisions must be made.

### **357.7 Document Properties**

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## APPENDIX AND REFERENCE MATERIAL

### **RELATED IACUC ENDPOINT POLICIES:**

- 1) IACUC Policy 363: MPTP Guidelines: [http://www.iacuc.emory.edu/documents/MPTP\\_guidelines.pdf](http://www.iacuc.emory.edu/documents/MPTP_guidelines.pdf)
- 2) IACUC Policy 304- Tumor Burden Scoring Guidelines: [http://www.iacuc.emory.edu/documents/tumor\\_burden\\_scoring.pdf](http://www.iacuc.emory.edu/documents/tumor_burden_scoring.pdf)

### **Appendix A: Example humane endpoint guidelines for Transplant studies:**

#### Renal Transplant Studies:

Euthanasia will be performed if renal function ceases or becomes impaired such as a creatinine of greater than 8.0mg/dl or a BUN of greater than 100mg/dl sustained for 3 days, or if a creatinine greater than 4.0mg/dl or a BUN of greater than 80mg/dl sustained for more than 5days associated with decreased activity of the animal or severe anemia with a hematocrit of less than 20 for greater than a week or if in the opinion of the attending veterinarian or PI the animal is experiencing substantial, unrelievable pain or illness. In addition, the IACUC guideline for endpoints will be used for these studies.

#### Pancreatic Islet Cell Transplant Studies:

Animals with graft failure characterized clinically by persistently elevated blood sugars and resumption of exogenous insulin and confirmed by non-detectable c-peptide levels will be considered as transplant failures and will be euthanized. Additionally, animals that are severely ill (in the opinion of the Veterinary staff) will be euthanized. In addition, the IACUC guideline for endpoints will be used for these studies.

### **Appendix B: Example humane endpoint guidelines for rodent hind limb ischemia:**

1. Immediate euthanasia for animals with necrosis extending beyond the foot
2. Euthanasia seven days post-surgery for animals with necrosis extending beyond the toes.
3. Euthanasia of animals with toe necrosis that fail to recover functionality of the limb 10 days post-surgery noting that rodents typically lose ankle flexion after surgery, but recover mobility over 4-10 days. Functionality will be assessed by the ability to bend the ankle.