ANIMAL EYE CONSULTANTS OF IOWA

Animal Eye Consultants of Iowa	
Institutional Animal Care and Use Committee	
Policy #8	**"Policy for Humane Endpoints"**
Approval Date: 1/13/2026 (Replacing Version 3/21/2024)	

A. Purpose

This policy outlines the requirements for developing and defining humane endpoints for all animals used in research, teaching or testing at AEC. While this policy is intended to provide guidance, the Principal Investigator (PI) must also work with the Office of the AEC Veterinary Staff (AEC) and the Institutional Animal Care and Use Committee (IACUC) to determine a humane endpoint that both minimizes animal distress and allows the study to meet its goals.

B. Definition

A humane endpoint is defined in the 8th 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." Many studies utilize "experimental endpoints," which involve the euthanasia or removal of animals from the study when scientific objectives have been met at a pre-determined timepoint. However, there are cases when an animal may become ill, debilitated, or experience unalleviated pain or distress, either as result of experimental procedures or spontaneous disease. Humane endpoints must be utilized in these cases. The use of humane endpoints contributes to the "Refinement" principle of the Three R's by providing an alternative to experimental endpoints that may be reached prior to completion of the experiment.

The PI must identify, describe, and include in the Animal Subject Approval Form (ASAF) endpoints that are both humane and scientifically sound. Humane endpoints must be

defined prior to the start of the study. Unanticipated adverse events may require modification of the endpoints.

C. Special Considerations

The Guide indicates that "while all studies should employ endpoints that are humane, studies that commonly require special consideration include those that involve:

- Tumor Models (For examples, please view Guideline #8: Tumor Burden)
- Infectious Diseases
- Vaccine Challenges
- Pain Modeling
- Trauma
- Production of Monoclonal Antibodies (addressed in AEC IACUC Policy #23)
- Assessment of Toxicological Effects
- Organ or System Failure
- Models of Cardiovascular Shock

These models often cannot utilize default humane endpoint guidelines and therefore should be developed on a case-by-case basis in conjunction with the IACUC and AEC.

Please contact AEC at animaleyeiowa@gmail.com and/or the Animal Welfare Program (AWP) Office at IACUC@animal-eye-iowa.com for assistance.

D. Protocol Components

The following items must be included when outlining humane endpoints in the IACUC protocol:

1. **Defining the Endpoint**:
   The endpoint(s) for the study must be clearly defined. This includes the anticipated time course and progression of the adverse effects, the justification for the endpoint to meet scientific requirements of the study, and the response when that point is reached. This response could entail removal from the study until the condition has adequately improved, clinical treatment sufficient to allow experimentation to continue, or euthanasia.

2. **Assessment Criteria**:
   Parameters that will be measured during a study that are indicative of an animal's general health, well-being, and/or clinical condition must be clearly described. Examples include but are not limited to: measuring body weight; food and water consumption; behavior; tumor size; imaging findings; blood chemistry results; and activity level. Research staff must be adequately trained in recognition of species-specific behavior and, in particular, species-specific signs of pain, distress, and morbidity (Please view the Indicators of Pain in Laboratory Animals chart for examples). Scoring systems are a recommended method of defining and implementing humane endpoints, as they may be developed or modified to fit individual protocols and animal models. An example scoring system may be viewed here, which was developed based on routine observations.

3. **Frequency of Monitoring**:
   It must be stated how frequently (e.g. number of times per day and week) responsible personnel will observe the animal and measure parameters identified as assessment criteria. Monitoring requirements may change during the study as a condition worsens over time or experimental manipulations change.

4. **Required Response**:
   The intervention that will occur when the defined endpoint(s) have been reached must be described. Intervention is most commonly medical treatment or euthanasia and may be performed by research or veterinary staff in compliance with pre-set arrangements described in the IACUC-approved protocol. Unanticipated adverse events must be reported to AEC and the IACUC in compliance with IACUC Policy #37: Reporting Adverse Events.

5. **Default Endpoints**:
   The following criteria may be considered standard, default endpoints for "low-risk" animal models, which would not generally be expected to have pain and distress under normal conditions but may experience adverse effects unpredictably.

a) Loss of ≥20% of body weight from baseline weight when assigned to the protocol (NOTE: A growth nomogram must be used to adjust the basal weight for young growing animals).
b) Major organ failure or medical conditions unresponsive to treatment.
c) Surgical complications unresponsive to intervention.
d) Failure to eat or drink or severe vomiting and/or diarrhea for 24-48 hours (species dependent), resulting in significant dehydration or rapid weight loss/emaciation.
e) Tumors arising from other than experimental means that grow in excess of 15% body weight (Or for rodents - mice ≥20mm and rats ≥40mm), impair movement, or ulcerate. Please view Guideline #8: Tumor Burden for additional information.
f) Clinical or behavioral signs of significant stress that are unresponsive to intervention.
g) Animal appears dull, depressed, and/or restless.
h) Difficult labored breathing/respiratory distress.
i) Persistent and severe abnormal posture, lameness, or weakness, including inability to ambulate or remain upright.
j) Unresponsive to stimuli or is moribund.
k) Body condition score of less than 2 (See the Body Condition Score Chart for guidance).

For models in which animals are expected to experience pain and distress, these default endpoints may not be considered sufficient and additional refinement of the endpoints to better suit the experiment may be required. It is recommended to consult with AEC (animaleyeiowa@gmail.com) in these cases, whether it be for an individual animal or a proposed study.

6. **Death as an endpoint**:
If an animal must be allowed to die without intervention in order to answer a scientific question, this is considered “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, including reasoning for why alternative endpoints and/or analgesics cannot be

used. PIs requesting death as an endpoint must also clearly detail plans for monitoring and supportive care, including monitoring frequency and record-keeping practices. These animals should be categorized as Distress Category E per IACUC Guideline #3.

7. **Veterinary Oversight:**
   The Attending Veterinarian (AV) has the responsibility for oversight of the health and welfare of animals used for research, teaching and testing. The AV and designated veterinary staff have the authority to euthanize or remove an animal from the study in the interest of animal welfare at any time. All attempts will be made to reach an agreement with the PI and research staff when these decisions must be made.

E. Required Documentation

Studies with defined monitoring parameters and humane endpoints are expected to maintain records and be able to provide those to the IACUC or AEC on request. Sample assessment/animal scoring documents are provided below and may be modified for individual studies.

- Representative Scoring System for Determining Humane Endpoints [DOC] [PDF]
- Tumor Burden Guidelines [PDF]
- Rodent Health Monitoring Sheet [DOC] [PDF]

Assessment of the animal for the parameters and at the frequency defined in the approved protocol must include the following. Records must be maintained for this data:

1. Animal Monitoring
   a. Parameters assessed
   b. Date of assessments
   c. Initials of the personnel assessing the animal
2. Intervention including the type (euthanasia, treatment, etc.), date and personnel identification.

F. References

1. *"The Guide for the Care and Use of Laboratory Animals, 8th Edition*." National Research Council of the National Academies. https://grants.nih.gov/grants/olaw/guide-for-the-care-and-use-of-laboratory-animals.pdf