

# GUIDELINES FOR HUMANE ENDPOINTS IN ANIMAL STUDIES

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## Background

According to the Guide for the Care and Use of Laboratory Animals (8<sup>th</sup> edition), “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.” The humane endpoint is defined as “the point at which pain or distress in an experimental animals is prevented, terminated or relieved.” Preemptive euthanasia can help prevent unnecessary pain and distress and also provides advantages to the researcher, including easier collection of tissues and blood for postmortem analysis, as well as eliminating the collection of non-useful data that may show severe and unexpected physiologic derangements.

## Guidelines for Humane Endpoints

Researchers should euthanize animals at the earliest possible stage that allows for collection of the necessary data points.

When creating humane endpoints, researchers should consider the following parameters:

Parameter	What to look for
General Appearance	Dehydration (sunken eyes, skin tenting), decreased body weight or loss of body condition, missing anatomy, abnormal posture, hypothermia, fractured appendage, swelling, tissue masses, prolapse, paraphimosis (prolapsed penis)
Fur/Skin	Urine stain, pallor, redness, cyanosis, icterus, wound, sore,

	abscess, ulcer, alopecia, ruffled fur
Eyes	Exophthalmos, ptosis, reddened eye, lacrimation, discharge, opacity
Nose, Mouth, and Head	Head tilt, nasal discharge, malocclusion, salivation
Respiration	Sneezing, dyspnea, tachypnea, rales
Urine	Discoloration, blood in urine, polyuria, anuria
Feces	Discoloration, blood in the feces, softness/diarrhea
Locomotor/Hyperactivity	Hyperactivity, coma, ataxia, circling, muscle tremors, paralysis, paresis

Animals showing pain or distress that is not approved in the AUP MUST be euthanized or must be treated in consultation with OLAC to avoid unapproved pain and distress. If treatment would invalidate experimental results, the animals must be euthanized, and a revision to the AUP describing the unrelieved pain and distress must be approved before continuing the experiment.

### **Moribund Animals**

Moribundity is “the clinically irreversible condition leading inevitably to death.” If the moribund state is to be used as an endpoint, the AUP must consider possible alternatives, why measures cannot be taken to relieve pain and distress, and why animals cannot be euthanized at an earlier state. All moribund animals must be euthanized unless death as an endpoint is approved in the AUP. If moribundity is approved as an endpoint and animals show signs of pain/distress, but have not reached the moribund state, animals must be monitored at least once daily (including weekends and holidays) with appropriate documentation, or more often depending on the model and progression of disease.

Moribund animals are defined as the following:

- Inability to right itself or lie in a sternal position
- Inability to eat or drink or any condition that interferes with the ability to eat or drink
- Inappetance or severe dehydration (prolonged skin tenting) greater than 48 hours
- Respiratory distress, agonal breathing, cyanosis
- Paralysis/paresis
- Uncontrollable hemorrhage
- Unrelievable, progressive hypothermia Unresponsiveness to stimuli
- BCS < 2/5 or Irreversible weight loss (15%) compared to normal control animals

## References

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Hawkins P. (2002) Recognizing and assessing pain, suffering and distress in laboratory animals: a survey of current practice in the UK with recommendations. Lab Anim. 36(4):378-95.

Montgomery CA. (1990) Oncological and toxicological research: Alleviation and control of pain and distress in laboratory animals. Cancer Bulletin. 42:230-237.

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