



Institutional Animal Care and Use Committee Guidelines and Policies

GUIDELINES FOR HUMANE ENDPOINTS FOR ANIMALS IN STUDY: (MAKING THE DECISION TO EUTHANIZE AN ANIMAL)

These guidelines are meant to assist PIs in their choice of humane endpoints in animal studies that will assist them in making reasonable decisions about timely euthanasia of animals and about *early termination* of an animal's enrollment in a study. Ultimately, these guidelines should help to minimize the degree of pain or distress experienced by research animals. Both the USDA regulations and the *Guide for the Care and Use of Laboratory Animals* state that investigators must be qualified by training or experience to accomplish experimental manipulations in a humane manner. All personnel who will be working with animals must be trained to recognize the signs of pain and distress in animals. Observations of experimental animals must be of adequate frequency depending on the severity of the animal's condition (sometimes once/day is adequate and at other times 3x/day is required). Weekend and holiday observations should not be overlooked. Investigators should request veterinary technical support when they are uncertain or it is unclear whether an animal is experiencing pain or distress.

Suggested Endpoints:

Moribund is defined as: *being in the state of dying : approaching death*. The PI or designee(s), in conjunction with the attending veterinarian, are responsible for evaluating animals with adverse clinical findings and making a decision as to when euthanasia is necessary. Clinical signs should be observed as predictors of lethality, if possible before the animal becomes moribund, to assure essential data collection while minimizing animal suffering. A combination of 2 or more clinical signs (see below), particularly intermediate or severe signs, or sometimes even one severe sign, should be enough to warrant medical intervention and possibly euthanasia of an animal (see Table 1 below, for reference of clinical signs). Please refer to tumor guidelines for humane endpoints specifically related to animals in tumor studies.

Euthanasia Decision: If the PI or designee cannot be located in a reasonable length of time, the attending veterinarian will use their best clinical judgment regarding whether or not euthanize an animal.

Additional Considerations Each experiment may need to be evaluated on an individual basis related to variables such as:

1. Pharmacological effects of test material
2. Expected survival time – if it appears that an animal will not survive for more than 24 hours, then it should be humanely euthanized.
3. Length of study time remaining.
4. Potential modification of study (for example decrease doses in future)



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SIGNS FOR EVALUATING MORIBUND CONDITION

The following guidelines can be used as objective parameters of a moribund condition. An animal might exhibit one of these signs without being considered moribund, but two or more are usually indicative, and sometimes one severe sign may be sufficient to conclude that the animal is near death, dying.

1. Impaired ambulation (unable to reach food and water easily) whether due to a large mass or poor body condition (weakness).
2. Evidence of muscle atrophy or other signs of body emaciation. Note that due to tumor growth an animal's body weight is not always proportionate.
 - a. rapid weight loss (15-20% within a few days)
 - b. extended period of weight loss
3. Obvious signs of illness including but not restricted to:
 - a. prolonged inappetence
 - b. central nervous system signs (head tilt, hydrocephalus, tremors, seizures, circling, paresis)
 - c. chronic diarrhea or constipation
 - d. rough haircoat, hunched or rounded posture, distended abdomen
 - e. dyspnea (obvious difficulty breathing which may occur with metastatic models which seed the lungs or due to infection)
 - f. paleness (indicating anemia, this most easily visualized in nude animals)
 - g. marked discolored urine
 - h. ocular discharge
4. Paralysis
5. Inability to remain upright
6. Frank bleeding from any orifice
7. Trauma
8. Non-healing or extensive skin lesions/wounds/ulcerations
9. Distended urinary bladder with difficulty expressing
10. Distended abdomen due to ascites or neoplasia



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TABLE 1: CLINICAL SIGNS THAT THE ANIMAL IS ADVANCING TOWARDS THE MORIBUND CONDITION

Minor	Ocular discharge - in rodents
	Ruffled, dull, or unkempt fur/hair coat
	Weight loss of less than 10%
Intermediate	Ataxia - uncoordinated movements
	Dehydration of 5-10%; visualized by an animal being smaller than cage mates, shriveled/ shrunken appearance
	Hunched back - protective posture or painful stance; distended abdomen; constipation
	Lethargy - no energy reserves
	CNS signs: tremors; head tilt
	Impaired ambulation
	Weight loss of 10 - 20%
Severe	Anorexia - inability to eat or drink
	Dehydration of >10% this may be consistent with diarrhea (bedding pasted around anus)
	Anemia evidenced by pale mucous membranes
	Marked discolored urine
	Diarrhea (bedding pasted around anus)
	Cyanotic - inadequate oxygenation, blue - tinged mucous membranes; difficulty breathing
	Hypothermia - cold to the touch
	Moribund - lack of a righting reflex
	Emaciation: weight loss of >20%; muscle wasting
	Painful lesion(s) or conditions
	CNS signs: hydrocephalus, seizures, circling
	Frank bleeding from any orifice
	Paresis/Paralysis - inability to ambulate.

Note: These guidelines must be combined with sound judgment. A veterinarian should always be consulted if there are questions about any case.