IACUC Approved on 2/19/2025

University of Southern California

Institutional Animal Care and Use Committee

Humane Endpoint Criteria

A. Background

The purpose of this document is to clearly define humane endpoints for laboratory animals at USC. The guidelines herein may aid researchers in making ethical decisions that minimize animal pain and/or distress.

B. Definitions

BCS: Body Condition Score, typically assigned as a numerical value out of 5

Dystocia: Difficult birth, marked by prolonged labor and inability to pass pups

Humane endpoint: The point at which pain or distress is prevented, terminated, or relieved in an experimental animal (via the *Guide*)

Ulceration: Exposure of deep tissues underneath the surface of the skin/tumor

C. Applicability

The General Humane Endpoints listed below apply to all animals involved in research studies at USC.

The Tumor Endpoint Guidelines section below applies to all studies that involve tumor development in mice and rats. This includes, but is not limited to, spontaneous, transplanted, and chemically induced tumors. Genetically modified animals that are more prone to develop neoplasia are also included.

D. Policy

General Humane Endpoints:

- Animal appears to be in distress (lethargy, abnormal respiration, cyanosis or pallor, diarrhea, paralysis, uncontrolled bleeding, pain unrelieved with analgesics, etc.)
- Weight loss exceeding 20% of the original body weight

- Body Condition Score (BCS) of <2/5 (see Appendix 1)
- Inability to eat and/or drink
- Moribund or unresponsive to stimuli

Breeding-Related Humane Endpoints:

- Dystocia
- Failure to thrive
- Paraphimosis (penile prolapse)
- Runted pups

Tumor Endpoint Guidelines:

Criteria of humane endpoints for subcutaneous tumors:

- If the tumor, regardless of size, becomes ulcerated or necrotic beyond the area of a pinpoint (unless allowed in the protocol).
  - If ulcerated tumors are approved in the protocol, use the Tumor Ulceration Scoring Guide (see Appendix 2) to help determine the timing of euthanasia.
- Multiple tumors are counted as a single tumor if their borders touch.
- The following maximum size endpoints apply:

Size Endpoints for Subcutaneous Tumors

	Mouse	Rat
Diameter (in any direction)	1.5 cm	2.5 cm
Volume	1800 mm^3	8000 mm^3

Criteria of humane endpoints for internal tumors:

- Since the volume of an internal tumor cannot be accurately assessed without imaging, the humane endpoints for internal tumors are based on the animals' overall condition.
- Use the General Humane Endpoints or Paster Scale (see Appendix 3) to help determine the timing of euthanasia.

E. References

1. Committee for the Update of the Guide for the Care and Use of Laboratory Animals, et al. (2011). *Guide for the Care and Use of Laboratory Animals*. 8th ed., National Academies Press. https://www.ncbi.nlm.nih.gov/books/NBK54050/

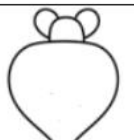
2. Paster, Eden V., Villines, Kimberly A., and Hickman, Debra L. (2009). "Endpoints for Mouse Abdominal Tumor Models: Refinement of Current Criteria." Comp. Med., 59(3): 234-241. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2733284/

3. Ullman-Culleré, M. H., Foltz, C. J. (1999). "Body condition scoring: a rapid and accurate method for assessing health status in mice." Lab Anim. Sci., 49(3): 319-23. https://pubmed.ncbi.nlm.nih.gov/10403450/

F. Appendix

1. Body condition scoring chart for mice (via Ulman-Cullere and Foltz, 1999; Burkholder et al, 2012; UC San Francisco IACUC; UC Davis IACUC)

Body Condition Score Chart

		*BC 1* *Mouse is emaciated* • *Skeletal structure extremely prominent; little or no flesh cover* • *Vertebrae distinctly segmented*
		*BC 2* *Mouse is under conditioned* • *Segmentation of vertebral column evident* • *Dorsal pelvic bones are readily palpable*
		*BC 3* *Mouse is well-conditioned* • *Vertebrae and dorsal pelvis not prominent; palpable with slight pressure*
		*BC 4* *Mouse is over conditioned* • *Spine is a continuous column* • *Vertebrae palpable only with firm pressure*
		*BC 5* *Mouse is obese* • *Mouse is smooth and bulky* • *Bone structure disappears under flesh and subcutaneous fat*

2. Tumor Ulceration Scoring Guide

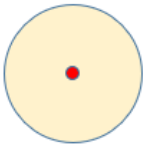
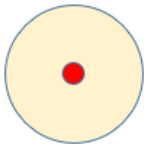
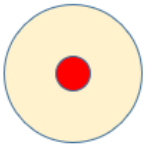
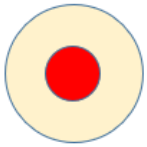
The Tumor Ulceration Scoring Guide is used for tumor-bearing rodents on protocols that have mild tumor ulceration approved (score of 1-3 on chart). A score of 4 indicates that the humane endpoint has been reached and euthanasia is indicated.

Tumor Ulceration Scoring Guide

If an animal has an ulcerated tumor, regardless of the size of the ulceration, the **Animal Score** is the HIGHEST number (1-4) which contains ANY of the signs that the animal is showing.

When an ulceration is discovered on an animal, a **Monitoring Cage Card** should be placed on the front of that cage for each animal with an ulcerated tumor. This can be done by vet staff, care staff, or the lab.

If an animal has a score of 1-3 for 7 consecutive days, the animal must be euthanized within 24 hours.
If an animal has a score of 4 at any point, the animal must be euthanized within 24 hours.

Animal Score	1	2	3	4 (Humane Endpoint)
Ulceration Size	"Pinpoint" 	5-10% surface area 	10-20% surface area 	>20% surface area 
Appearance of Ulceration	-Small, smooth pink/red spot on surface of skin	-Dry, scab	-Moist without significant discharge	-Any cavitation in the tumor surface -Pus -Discoloration -Signs of necrosis -Active bleeding
Inflammation or Infection	-No hair loss or inflammation	-Minor hair loss and/or redness	-Moderate redness -Minor swelling or inflammation	-Significant redness Significant swelling or inflammation -Signs of necrosis
Scratching	-No scratching	-Occasional scratching	-Frequent scratching	-Evidence of self-mutilation -Constant scratching
Behavior & Appearance	Normal		-Slightly abnormal gait -Minor ruffling of the fur -Decreased activity -Abnormal behavior	-Lethargic -Significantly hunched/ruffled - >20% weight loss
Pain & Discomfort	No signs of pain		-Minor signs of pain without analgesia -No signs of pain with analgesia	Moderate to major signs of pain with or without analgesia

3. Paster scale (via Paster et al., 2009)

Note: The Paster scale was developed to aid in the assessment of mice with abdominal tumors. Therefore, the Paster scale may not assess other important metrics relevant to non-abdominal tumor studies.

Parameter	Description	Score
Appearance (Also note if abdominal distention is present)	N: bright eyes; shiny, well-groomed hair coat	2
	Abn: Unkempt hair coat, dull fur	1
	Abn: Hunching, piloerection	0
Natural behavior	N: Active; interactive in environment	3
	Slight decrease in activity; less interactive	2
	Abn: Pronounced decrease in activity; isolated	1
	Abn: Possible selfmutilation; hyperactive or immobile	0
Provoked behavior	N: Quickly moves away	3
	Slow to move away or exaggerated response	2
	Abn: Moves away after short period of time	1
	Abn: Does not move or reacts with excessively exaggerated response	0
Body condition score	1, emaciated; 2, thin; 3, normal; 4, overweight; 5, obese	1–5
Total score		1–13

(Abn = abnormal, N = normal)

Paster scoring system: 11-13: Healthy
6-10: Declining in condition, increased morbidity
≤ 5: Poor condition, consider euthanasia