

Humane Endpoints for Laboratory Animals

Purpose

The purpose of this document is to provide guidelines for selecting an endpoint that reduces animal pain and/or distress, while still meeting research objectives when animals are used for biomedical research, teaching, and testing. These guidelines are provided to assist investigators in fulfilling their ethical responsibilities to minimize animal pain and/or distress. Investigators are expected to consult with TRACS Veterinary Services or a clinical veterinarian affiliated with the facility to assist with developing these endpoints, and for additional information or questions. In this document “endpoint” refers to one or a combination of physical (e.g., body weight), behavioral (e.g., grooming activity), or other signs of disease or distress that are used, typically during a longitudinal experimental procedure in which animal health may deteriorate (e.g., inoculation with an infectious agent), and to decide when an intervention will be terminated or an animal may be euthanized to minimize pain or distress.

Background

Although it is crucial to minimize the level of pain and distress experienced by laboratory animals, it is also important that the scientific objectives of experimental studies are achieved. The criteria that provides the basis for terminating experimental procedures in order to minimize or alleviate any actual or potential pain, distress, or discomfort is made by choosing the earliest endpoint that is compatible with the scientific objectives; these criteria are referred to as humane endpoints. Selection of such endpoints by the investigator involves consultation with TRACS Veterinary Services or the facility clinical veterinarian(s), and the endpoints chosen must be approved by the IACUC. For additional reference material, the ILAR Journal, volume 41, is devoted to this topic¹.

The principles of humane endpoints apply to all species. Humane endpoints for species or specific projects that may not be covered in this document are determined on a case-by-case basis in consultation with TRACS Veterinary Services or the facility clinical veterinarian(s).

Guidelines

A. General Humane Endpoints

The following are general humane endpoints that require euthanasia.

1. The inability to reach food or water for approximately 12 hours.
2. A 20% decrease in optimal body weight

3. A Body Condition Score (attachments 1-6) typically less than a 2 on a 5-point scale or less than a 3 on a 9-point scale **for adult animals**.

4. Development of conditions that result in significant pain that cannot be alleviated by analgesics.

Prior approval from the IACUC is required if an investigator wishes to maintain an animal on study when endpoints meet the above criteria. Obtaining such approval requires scientific justification.

General observations for assessing pain and distress include change in body weight, external physical appearance, clinical signs (e.g., inability to reach food and water, lethargy or decreased mental alertness, labored breathing, inability to remain upright), significant changes in behavior, and responses to external stimuli. Sick animals should be identified as early as possible prior to a moribund state (e.g., near death). Laboratory personnel must carefully observe the animals for changes in health status, appearance, and behavior, and have knowledge of the animal treatment(s) and procedures that are part of the approved IACUC protocol. Animals should be weighed and the weight documented on a frequency to ensure the animals to not exceed 20% weight loss.

During periods when morbidity and mortality are expected to increase, animals must be evaluated a minimum of two times daily (approximately 6 hours apart including an AM and PM observation during the vivarium's lights on cycle). Those animals that are not expected to survive until the next scheduled evaluation should be humanely euthanized.

Humane endpoints will vary depending on the nature of the study. Protocols may include more specific criteria. Investigators requesting departures from these standard endpoints must discuss with TRACS Veterinary Services or the facility clinical veterinarian(s). Identifying the initial signs that occur prior to a moribund state in order to avoid additional pain and suffering is key to developing humane endpoints. Criteria with a scoring system provide an excellent, objective method for identifying the appropriate time for euthanasia, and can be developed with the assistance of TRACS Veterinary Services or the facility clinical veterinarian(s) for individual projects. Objective criteria are best when they can be uniformly applied by a variety of personnel. A Body Condition Score is one example of the type of assessment for inclusion in such a scoring system. The attached references are general guidelines for Body Condition Score assessment. Should an animal appear ill or unthrifty TRACS Veterinary Services or the facility clinical veterinarian(s) must be contacted for further assessment.

Pilot studies will provide an opportunity to evaluate humane endpoints and assure the scientific objectives are met before proceeding to large scale projects.

UC Davis facilities, such as non-human primate facilities, have more specific criteria and guidelines for euthanasia that must be approved by the IACUC prior to implementation.

B. 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". Death as an endpoint is not typically necessary for research protocols but may be required in some situations, including acute toxicity testing, assessment of virulence of pathogens, and neutralization tests for toxins.

Death as an endpoint requires scientific justification and documentation in the IACUC protocol that the above humane endpoints cannot be used. Such justifications may include reference to the requirements of regulatory agencies (e.g., EPA, FDA).

C. Tumor Burden

General guidelines regarding tumor burden should be followed. Euthanasia is indicated if the tumor burden is greater than or equal to 10% of the animal's normal body weight, exceeds 2 cm in size in any direction for mice or 4 cm for rats, a diminished Body Condition Score, the tumor prevents ambulation or ability to reach food and water, the tumor is ulcerated, necrotic or infected, or the tumor is causing significant pain and distress. Certain tumor therapies under investigation may result in an expected progression of tumor necrosis, ulceration, and/or healing; this must be addressed in the approved IACUC protocol. If the tumor is infected the clinical veterinary service will recommend either euthanasia or antibiotic treatment based on the animal's health status and study needs.

Premature euthanasia may result in the loss of valuable information regarding the success of novel studies and therapies. Pilot studies may be used to establish individual humane endpoints for therapeutic studies for cancer-related research.

D. Euthanasia

If the veterinary staff has examined an animal and determined that it will not survive until the next scheduled examination, a reasonable effort will be made to contact the Principle Investigator (P.I.) or their designee to obtain permission to treat or euthanize the animal. If the veterinary staff is unable to contact the P.I. or designee, the clinical veterinarian, clinical veterinary service, or Attending Veterinarian will be contacted to obtain permission to euthanize the animal.

It is important for investigators to promptly respond to all veterinary communications. If immediate euthanasia is not indicated and an animal is deemed stable by the clinical veterinarian(s) then a plan for further monitoring or intervention (such as implementing analgesics, antibiotics, diagnostics, etc.) as needed will be instituted.

References

- ILAR Journal V41(2) 2000.
- Ullman-Cullere MH, Foltz CJ. Body condition scoring: a rapid and accurate method for assessing health status in mice. *Lab Anim Sci* 49:319-323, 1999
- United Kingdom Coordinating Committee on Cancer Research (UKCCCR). Guidelines for the Welfare of Animals in Experimental Neoplasia (2nd ed). *Br Cancer* 77: 1-10, 1998



BC 1

- Mouse is emaciated.
- *Skeletal structure extremely prominent; little or no flesh cover.*
 - *Vertebrae distinctly segmented.*



BC 2

- Mouse is underconditioned.
- *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 overconditioned.
- *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.*

A "+" or a "-" can be added to the body condition score if additional increments are necessary (i.e. ...2+, 2, 2-...)

Attachment 1



BC 1

Rat is emaciated

- Segmentation of vertebral column prominent if not visible.
- Little or no flesh cover over dorsal pelvis. Pins prominent if not visible.
- Segmentation of caudal vertebrae prominent.



BC 2

Rat is under conditioned

- Segmentation of vertebral column prominent.
- Thin flesh cover over dorsal pelvis, little subcutaneous fat. Pins easily palpable.
- Thin flesh cover over caudal vertebrae, segmentation palpable with slight pressure.



BC 3

Rat is well-conditioned

- Segmentation of vertebral column easily palpable.
- Moderate subcutaneous fat store over pelvis. Pins easily palpable with slight pressure.
- Moderate fat store around tail base, caudal vertebrae may be palpable but not segmented.



BC 4

Rat is overconditioned

- Segmentation of vertebral column palpable with slight pressure.
- Thick subcutaneous fat store over dorsal pelvis. Pins of pelvis palpable with firm pressure.
- Thick fat store over tail base, caudal vertebrae not palpable.



BC 5

Rat is obese

- Segmentation of vertebral column palpable with firm pressure; may be a continuous column.
- Thick subcutaneous fat store over dorsal pelvis. Pins of pelvis not palpable with firm pressure.
- Thick fat store over tail base, caudal vertebrae not palpable.

Attachment 2

BODY CONDITION SYSTEM

TOO THIN 1 Ribs, lumbar vertebrae, pelvic bones and all bony prominences evident from a distance. No discernible body fat. Obvious loss of muscle mass.



2 Ribs, lumbar vertebrae and pelvic bones easily visible. No palpable fat. Some evidence of other bony prominence. Minimal loss of muscle mass.



3 Ribs easily palpated and may be visible with no palpable fat. Tops of lumbar vertebrae visible. Pelvic bones becoming prominent. Obvious waist and abdominal tuck.



IDEAL 4 Ribs easily palpable, with minimal fat covering. Waist easily noted, viewed from above. Abdominal tuck evident.

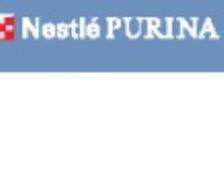
5 Ribs palpable without excess fat covering. Waist observed behind ribs when viewed from above. Abdomen tucked up when viewed from side.



6 Ribs palpable with slight excess fat covering. Waist is discernible viewed from above but is not prominent. Abdominal tuck apparent.



TOO HEAVY 7 Ribs palpable with difficulty; heavy fat cover. Noticeable fat deposits over lumbar area and base of tail. Waist absent or barely visible. Abdominal tuck may be present.



8 Ribs not palpable under very heavy fat cover, or palpable only with significant pressure. Heavy fat deposits over lumbar area and base of tail. Waist absent. No abdominal tuck. Obvious abdominal distention may be present.



9 Massive fat deposits over thorax, spine and base of tail. Waist and abdominal tuck absent. Fat deposits on neck and limbs. Obvious abdominal distention.

The BODY CONDITION SYSTEM was developed at the Nestlé Purina Pet Care Center and has been validated as documented in the following publications:
 Mowbray D, Borjesson JW, Moyers T, et al. Comparison of body fat estimates by dual-energy x-ray absorptiometry and deuterium oxide dilution in client-owned dogs. *Compendium* 2001; 23 (9A): 70
 Luffness DF. Development and Validation of a Body Condition Score System for Dogs. *Canine Practice* July/August 1997; 22:10-15
 Kuczy, et al. Effects of Diet Restriction on Life Span and Age-Related Changes in Dogs. *JAVMA* 2002; 220:1315-1320

Call 1-800-222-VETS (8387), weekdays, 8:00 a.m. to 4:30 p.m. CT



BODY CONDITION SYSTEM

TOO THIN

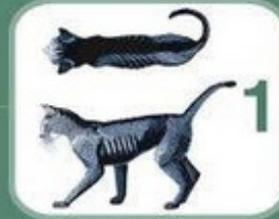
- 1** Ribs visible on shorthaired cats; no palpable fat; severe abdominal tuck; lumbar vertebrae and wings of ilia easily palpated.
- 2** Ribs easily visible on shorthaired cats; lumbar vertebrae obvious with minimal muscle mass; pronounced abdominal tuck; no palpable fat.
- 3** Ribs easily palpable with minimal fat covering; lumbar vertebrae obvious; obvious waist behind ribs; minimal abdominal fat.
- 4** Ribs palpable with minimal fat covering; noticeable waist behind ribs; slight abdominal tuck; abdominal fat pad absent.

IDEAL

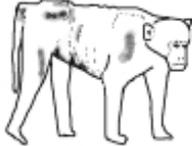
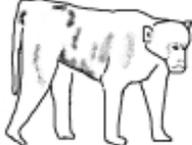
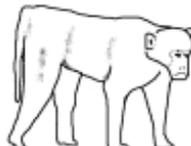
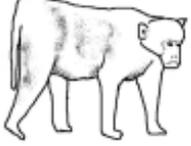
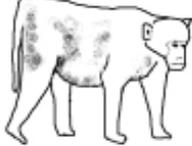
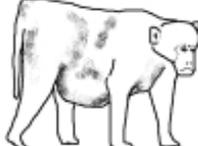
- 5** Well-proportioned; observe waist behind ribs; ribs palpable with slight fat covering; abdominal fat pad minimal.

TOO HEAVY

- 6** Ribs palpable with slight excess fat covering; waist and abdominal fat pad distinguishable but not obvious; abdominal tuck absent.
- 7** Ribs not easily palpated with moderate fat covering; waist poorly discernible; obvious rounding of abdomen; moderate abdominal fat pad.
- 8** Ribs not palpable with excess fat covering; waist absent; obvious rounding of abdomen with prominent abdominal fat pad; fat deposits present over lumbar area.
- 9** Ribs not palpable under heavy fat cover; heavy fat deposits over lumbar area, face and limbs; distention of abdomen with no waist; extensive abdominal fat deposits.



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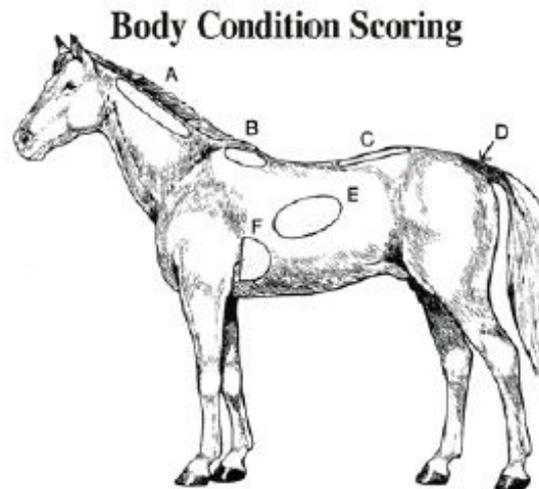
		Ambulating	Right Lateral Viewed from Back
1	EMACIATED – Very prominent hip bones (easily palpable and likely visible), prominent facial bones, spinous processes and ribs. Minimal to no muscle mass is palpable over ileum or ischium. Anus may be recessed between ischial callosities. Body is very angular, no subcutaneous fat layer to smooth out prominences.		
1.5	VERY THIN – Hips, spinous processes, and ribs are prominent. Facial bones may be prominent. There is very little muscle present over the hips and back. Anus may be recessed between ischial callosities. Body is angular, no subcutaneous fat to smooth out prominences		
2	THIN – Very minimal fat reserves, prominent hip bones and spinous processes. Hips, spinous processes and ribs are easily palpable with only a small amount of muscle mass over hips and lumbar region.		
2.5	LEAN – Overlying muscle gives hips and spine a more firm feel. Hip bones and spinous processes are readily palpable, but not prominent. Body is less angular because there is a thin layer of subcutaneous fat.		
3	OPTIMUM – Hip bones, ribs and spinous processes are palpable with gentle pressure but generally not visible. Well developed muscle mass and subcutaneous fat layer gives spine and hips smooth but firm feel. No abdominal, axillary or inguinal fat pads.		
3.5	SLIGHTLY OVERWEIGHT – Hip bones and spinous processes palpable with firm pressure but are not visible. Bony prominences smooth. Rib contours are smooth and only palpable with firm pressure. Small abdominal fat pad may be present.		
4	HEAVY – Bony contours are smooth and less well defined. Hip bones, spinous processes and ribs may be difficult to palpate due to more abundant subcutaneous fat layer. May have fat deposits starting to accumulate in the axillary, inguinal or abdominal areas.		
4.5	OBESE – This animal will often have prominent fat pads in the inguinal, axillary or abdominal region. Abdomen will be pendulous when animal sitting or ambulating. Hip bones and spinous processes difficult to palpate. Bony contours smooth and poorly defined.		
5	GROSSLY OBESE – Obvious, large fat deposits in the abdominal, inguinal and axillary regions. Abdominal palpation is very difficult due to large amount of mesenteric fat. Pronounced fat deposits may alter posture/ambulation. Hip bones, rib contours and spinous processes only palpable with deep palpation.		

Attachment 5

Henneke Body Condition Scoring System

Body condition, or the measure of fat cover, can be evaluated by visual appraisal and palpation. A scoring system in horses uses six areas of the body to assign scores of 1 (extremely emaciated) to 9 (obese). The six areas are: (A) along the neck, (B) withers, (C) crease down back, (D) tailhead, (E) ribs, and (F) behind the shoulder. Note that a long hair coat or a winter hair coat may "hide" skeletal protrusions or fat deposits. Thus, it is best to evaluate the animal from several different angles and palpate (feel) the appropriate areas of the body to determine the proper body condition score.

A score between 5 and 7 is considered ideal for healthy horses. Horses scoring in the 1 and 2 category should be evaluated further for causes such as medical conditions, dental problems, or the lack of proper nutrition. **Individual body condition scores (1-9) are as follows:**



1— Poor. Animal extremely emaciated; spinous processes, ribs, tailhead, hip joints and lower pelvic bones projecting prominently; bone structure of withers, shoulders and back easily noticeable; no fatty tissue can be felt.

2— Very Thin. Animal emaciated; slight fat covering over base of spinous processes; transverse processes of lumbar vertebrae feel rounded; spinous processes, ribs, tailhead, hip joints and lower pelvic bones prominent; withers, shoulders and back structure faintly discernible.

3— Thin. Fat buildup about halfway on spinous processes; transverse processes cannot be felt; slight fat cover over ribs; spinous processes and ribs easily discernible; tailhead prominent, but individual vertebrae cannot be identified visually; hip joints appear rounded but easily discernible; lower pelvic bones not distinguishable; withers, shoulders and neck accentuated.

4— Moderately Thin. Slight ridge along back; faint outline of ribs discernible; tailhead prominence depends on conformation, fat can be felt around it; hip joints not discernible; withers, shoulders and neck not obviously thin.

5— Moderate. Back is flat (no crease or ridge); ribs not visually distinguishable but easily felt; fat around tailhead beginning to feel spongy; withers appear rounded over spinous processes; shoulders and neck blend smoothly into body.

6— Moderately Fleshy. May have slight crease down back; fat over ribs spongy; fat around tailhead soft; fat beginning to be deposited along the side of withers, behind shoulders and along sides of neck.

7— Fleshy. May have crease down back; individual ribs can be felt, but noticeable filling between ribs with fat; fat around tailhead soft; fat deposited along withers, behind shoulders and along neck.

8— Fat. Crease down back; difficult to feel ribs; fat around tailhead very soft; area along withers filled with fat; area behind shoulder filled with fat; noticeable thickening of neck; fat deposited along inner thighs.

9— Extremely Fat. Obvious crease down back; patchy fat appearing over ribs; bulging fat around tailhead, along withers, behind shoulders and along neck; fat along inner thighs may rub together; flank filled with fat.

Attachment 6

Procedure: IACUC-28

Date: January 12, 2017

Enabled By: PHS

Supersedes: February 11, 2016

Source URL (modified on 02/14/18 07:17pm): <https://safetyservices.ucdavis.edu/article/humane-endpoints-laboratory-animals>