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UC Davis
Institutional Animal Care and Use Committee (IACUC)

Title: Humane Endpoints for Laboratory Animals

I. 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 Campus 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.

II. 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 CAMPUS 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 topic[1].

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 Campus Veterinary Services or the facility clinical veterinarian(s).

III. 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 Campus 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 Campus 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 Campus 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 total tumor burden is greater than or equal to 10% of the animal's normal body weight, or any single tumor 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.

IV. References:

1. ILAR Journal V41(2) 2000.
2. 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.
3. United Kingdom Coordinating Committee on Cancer Research (UKCCCR). Guidelines for the Welfare of Animals in Experimental Neoplasia (2nd ed). Br J Cancer 77:1-10, 1998.

Attachment 1: Mouse Body Condition Scores

Notes

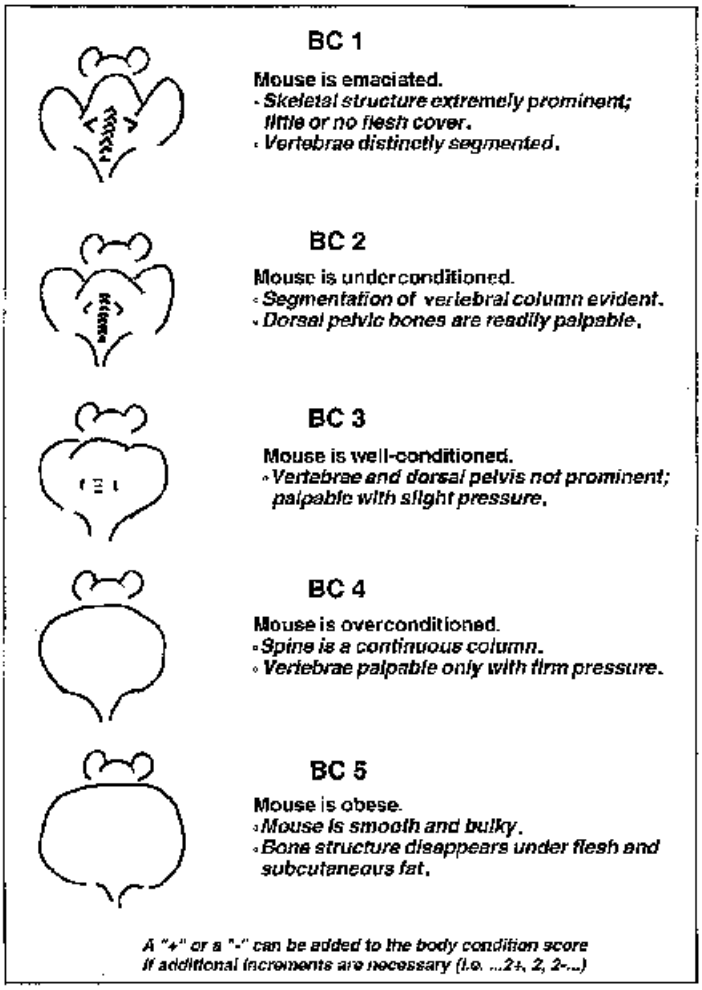


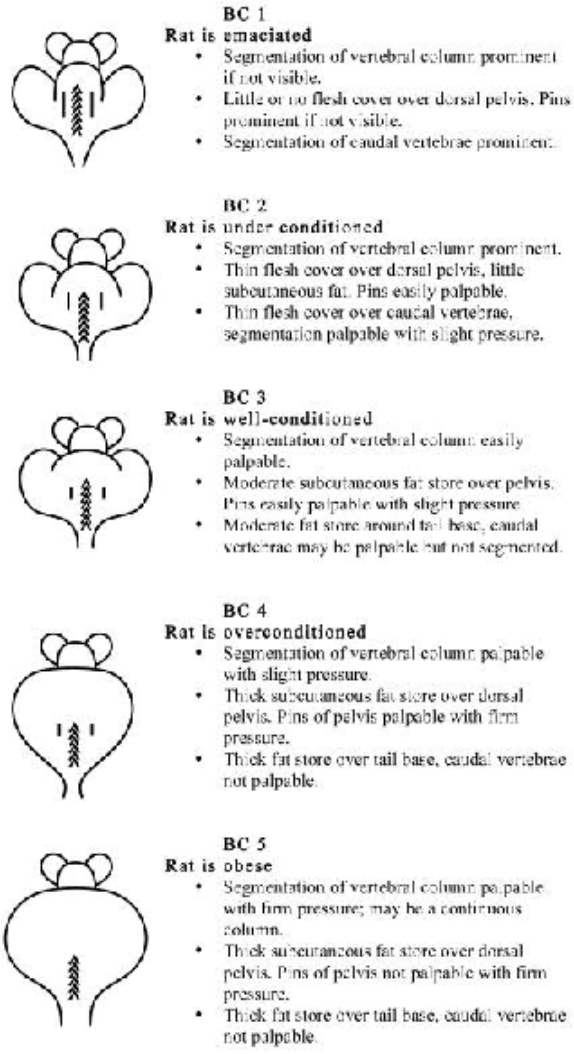
Figure 1. Line drawings and descriptions of body condition (BC) scoring.

32.1

Source: Journal of the American Association for Laboratory Animal Science 1999

Attachment 2: Rat Body Condition Scores

Figure 2. Rat Body Condition Score



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 underconditioned
- 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.

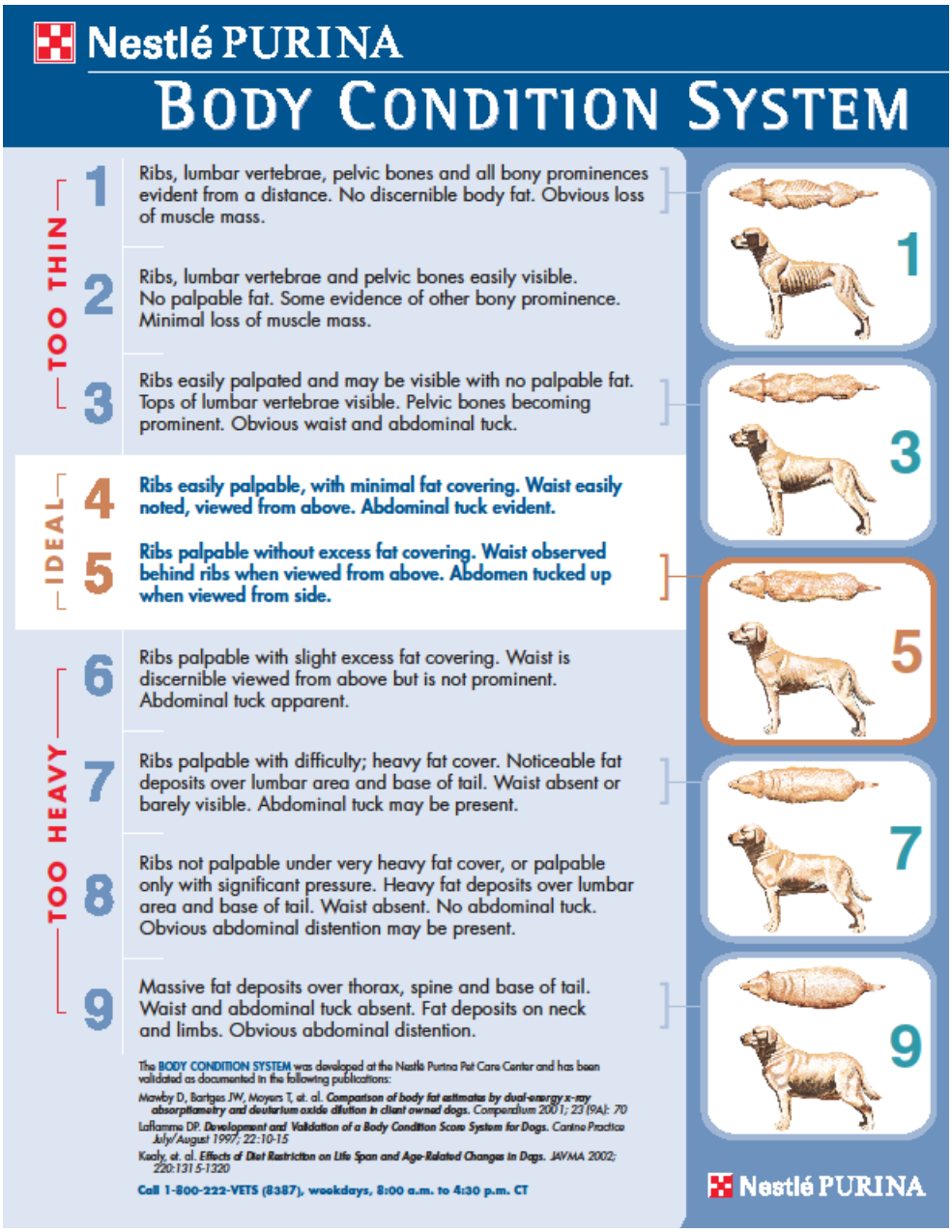
BC 4
Rat is overconditioned
- Segmentation of vertebral column palpable with slight pressure.
- Thick subcutaneous fat store over dorsal pelvis. Pins of pelvis palpable with firm pressure.
- Thick fat store over tail base, caudal vertebrae not palpable.

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.

From: J Am Assoc Lab Anim Sci. 2010 March; 49(2): 155–159.

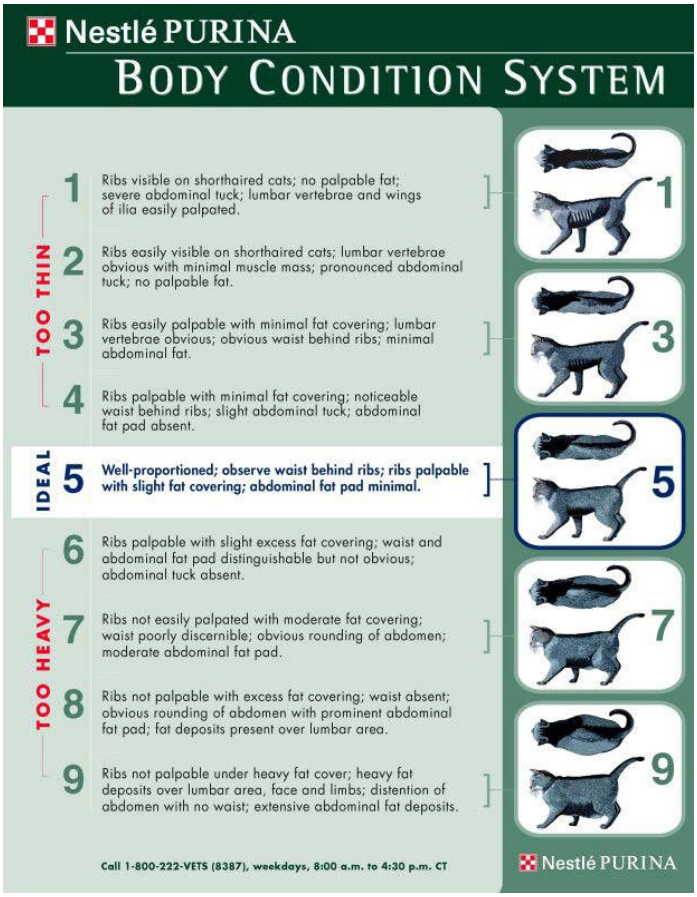
Source: Journal of the American Association for Lab Animal Science 2010

Attachment 3: Dog Body Condition Scores



Source: Nestle Purina

Attachment 4: Cat Body Condition Scores



Attachment 5: Non-Human Primate Body Condition Scores

Body Condition Scoring of Nonhuman Primates Using Macaca mulatta as a Model.

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** – Very little or no muscle loss, but only mild fat reserves. Hip bones and spinous processes are readily palpable, but not prominent. Body is less angular as there is a thin layer of subcutaneous fat.	
3	**OPTIMUM** –Hip bones, ribs and spinous processes are readily palpable with gentle pressure but generally not visible. Bony prominences are smooth due to adequate subcutaneous fat layer and muscle mass.	
3.5	**SLIGHTLY OVERWEIGHT** – Hip bones and spinous processes palpable but well covered with sufficient amounts of muscle and mildly excessive fat. Subcutaneous fat layer easily palpable, may have small abdominal fat pad.	
4	**HEAVY** – 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 either 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.	
5	**GROSSLY OBESE** – Disproportionate fat/muscle ratio. Pronounced fat deposits may alter posture/ambulation. Severe cases may have inspiratory stridor due to excessive fat deposits in neck and chest. Hip bones and spinous processes only palpable with deep palpation	

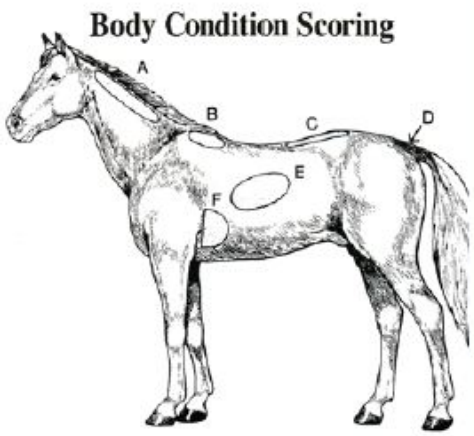
Source: Journal of the American Association of Laboratory Animal Science 2012

Attachment 6: Horse Body Condition Scores

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 e 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.

Source: University of California, Davis. Center for Equine Health Horse Report, July 2012.