 <p>Institutional Animal Care and Use Committee Guiding Principles and Procedures</p>	<p>Effective: 10/17/2013</p> <p>Revised: 1/17/2019, 10/15/2020</p>
<p>Title: Humane Endpoints-Criteria for Premature Euthanasia</p>	<p>Page 1 of 19</p>

Guiding Principle

The use of animals in research and teaching is a privilege granted to institutions, investigators, staff and students that commit to meeting high ethical and regulatory standards. In accordance with federal regulations and guidelines, NDSU requires investigators to identify humane endpoints in projects that involve pain and distress.

Requirements

Guide for the Care of and Use of Laboratory Animals, ILAR, NAS, Eighth Edition 2011, pg 27 Experimental and Humane Endpoints “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.” “Determination of humane endpoints should involve the PI, the veterinarian, and the IACUC, and should be defined when possible before the start of the study. Information that is critical to the IACUC’s assessment of appropriate endpoints consideration in a protocol includes precise definition of the humane endpoint (including assessment criteria), the frequency of animal observation, training of personnel responsible for assessment and recognition of the humane endpoint, and the response required upon reaching the humane endpoint.”

The Public Health Service (PHS) Policy, 2002, IV.C. 1a.“Procedures with animals will avoid or minimize discomfort, distress and pain to the animals, consistent with sound research design”. IV. C. 1e “Medical care for animals will be available and provided as necessary by a qualified veterinarian.”

U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training, IRAC, 1985, Principle IV “Proper use of animals, including the avoidance or minimization of discomfort, distress, and pain when consistent with sound scientific practices, is imperative.” **Principle VI.** “Animals that would otherwise suffer severe or chronic pain or distress that cannot be relieved should be painlessly killed at the end of the procedure, or if appropriate, during the procedure.”

Introduction

The experimental endpoint of a study occurs when the scientific aims and objectives have been reached. This may involve the euthanasia or other final disposition of animals at a predetermined endpoint even when they may be clinically healthy. The humane endpoint is the point at which pain or distress in an animal is prevented.

Animals that become ill, debilitated, or experience unrelieved pain or distress, either as a result of spontaneous disease or as a result of experimental procedures, must be provided standard veterinary treatment or be immediately euthanized. Withholding pain relief (treatment or euthanasia) is only permitted if specifically reviewed and approved by the IACUC.

In the event that an animal exhibits clinical signs of disease, illness, or unrelieved pain or distress, reasonable attempts will be made to contact the PI for consultation. If the PI is unavailable, the AV or designee has the authority to use appropriate treatment measures including euthanasia if necessary.

Special Statement Regarding Wildlife Species - If Principal Investigators find wild animals in the field that meet the criteria for a humane endpoint (e.g. injuries, disease, congenital abnormalities, etc) that have occurred naturally or outside of the research project, the animals are not required to be euthanized. The NDSU Attending Veterinarian and/or North Dakota Game and Fish Department Veterinarian may be used for consultation if needed.

The criteria below are clinical signs of illness or disease that indicate a humane endpoint has been reached. The Attending Veterinarian must be consulted when assessing criteria for endpoints. Exceptions to the following endpoints are only approved by the IACUC as part of the protocol review process.

Humane Endpoints: The following clinical signs of illness or disease that constitute a humane endpoint include but are not limited to:

- **Weight loss.** Loss of 15% body weight compared to the pre-study weight or to age-matched controls. With some disease processes or in growing animals, body weight is a poor indicator, thus body condition scoring (e.g. muscle atrophy or emaciation) may be more useful (see species specific humane endpoint documents).
 - In production animal species, during early lactation a drop in body condition score (BCS) of as much as 1 point may be acceptable provided the dam went into the periparturient period in a satisfactory BCS
- **Anorexia.** Complete anorexia for 24 hours in rodents or for up to 5 days in livestock, OR partial anorexia (less than 50% of caloric requirement) for 3 days in

rodents or for up to 7 days in livestock. Anorexia may be “normal” for immediate post-surgical patients.

- **Inability to obtain food/water.** Inability to ambulate to reach food or water; lesions that interfere with eating or drinking or reluctance to stand which persists for 24 hours.
- **Infection.** Infection involving any organ system (either clinical or as indicated by laboratory testing) which fails to respond to antibiotic therapy and is accompanied by systemic signs of illness.
- **Tumors.** Tumors which interfere with the ability to eat, drink, or move normally. Tumors that exhibit necrosis, ulceration, and/or infection. Tumors that interfere with a vital physiological function such as respiration, mastication, swallowing, urination, and/or defecation regardless of size of tumor. Tumor that exceed 2 cm in any direction in mice or 4 cm in any direction in rats.
- **Marked change in behavior/depression.** Lethargy, abnormal vocalization, aggression, recumbency, rough hair coat/hunched posture.
- **Fluid accumulation in body cavities/subcutaneous tissue.** Distended abdomen in conjunction with other clinical signs or conditions that lead to debilitation (e.g. neoplasia, liver failure)
- **Signs of severe organ system dysfunction.** Non-responsive to treatment or with a poor prognosis as determined by a clinical veterinarian in consultation with the Attending Veterinarian. Examples include but are not limited to:
 - **Respiratory.** Labored breathing, cyanosis, persistent coughing
 - **Cardiovascular.** Marked dehydration, blood loss or anemia, bleeding from any orifice, cardiac failure
 - **Gastrointestinal:** severe vomiting or diarrhea
 - **Urogenital:** renal failure, urinary tract obstruction
 - **Neurological symptoms.** e.g. circling, head tilt, seizures, paresis, paralysis
 - **Musculoskeletal:** muscle damage or bone fracture resulting in inability to use limb, muscle atrophy
 - **Integumentary:** non-healing wounds, repeated self –trauma, progressive dermatitis
- **Moribund state** (in a dying state; in a clinically irreversible condition leading inevitably to death) Extreme depression, body temperature significantly below normal, nonresponsive or unconscious with no response to external stimuli such as handling or the toe-pinch withdrawal test.

Species Specific Humane Endpoint Criteria

- [Equine](#) (Appendix A)
- [Ruminants](#) (Appendix B)

- [Swine](#) (Appendix C)
- [Birds/Poultry](#) (Appendix D)

Death as an Endpoint

While it is preferable to use the earliest endpoints compatible with the scientific requirements of each study, there are studies that require moribundity or death as an endpoint. In these studies, animals are permitted to become moribund or die, as a result of the experimental procedures. The continuation of an experimental study to the point where an animal dies, without the benefit of intervention or euthanasia, is not acceptable without strong scientific justification and review and approval by the IACUC.

PROCEDURE FOR DETERMINING ENDPOINT CRITERIA

1. A plan outlining specific criteria, is required to follow animal care and monitoring procedures.
 - 1.1. The plan must identify personnel responsible for evaluation, record keeping, and notification of the PI and/or AV.
 - 1.1.1. The PI and/or AV should be notified as soon as animals show clinical signs of illness. An assessment of the animal's condition is made and appropriate action taken as soon as possible.
 - 1.2. The plan includes observation and intervention as designated in the study protocol.
 - 1.2.1. Negative aspects of an animal's condition are to be recorded on the score sheets and reported to the PI and/or AV. [Scoring Criteria](#) examples can be found in Appendix E.
 - 1.2.2. Animals will be observed daily.
 - 1.2.3. Animals will be weighed weekly.
 - 1.2.4. The frequency of observations will be increased to twice daily and hands-on monitoring including weights will be increased to twice weekly once any clinical signs are noted.
 - 1.2.5. Score sheets will be kept in the animal facility.
 - 1.2.6. Deceased animals must be promptly removed, reported to the PI and/or AV and either taken to the NDSU Veterinary Diagnostic Laboratory for necropsy or held in a refrigerator until a necropsy can be performed.
2. Selection of an endpoint should be made with the following considerations:
 - 2.1. Trained observations of the animals
 - 2.2. Assigning objective assessment values to those observations
 - 2.3. Recognition of significant indicators of pain and distress
3. To obtain IACUC approval for exceptions to the above defined endpoints, provide the following on the Animal Care and Use Application form:
 - 3.1. Indicate which criteria for which you are requesting an exception.

- 3.2.** Scientific justification for the requested exception.
- 3.3.** Supportive care that will be given to minimize discomfort, distress, or pain.
- 3.4.** The endpoint that will be used for euthanasia.
- 4.** To obtain IACUC approval for the use of moribundity or death as an endpoint, provide the following on the Animal Care and Use Application form:
 - 4.1.** Why morbidity (i.e. affected with disease or illness) as an endpoint cannot be used?
 - 4.2.** Whether animals will be euthanized when moribund (i.e. in the state of dying or clinically irreversible condition leading inevitably to death) and if not, what scientific information is to be gained in the interval between moribundity and death, or how it will jeopardize the scientific validity of the study?
 - 4.3.** Will pain relieving measures be used? If not, provide scientific justification for withholding pain relief.
- 5.** When moribundity or death is approved as an endpoint, the PI must comply with the following:
 - 5.1.** A cage card must be placed on every cage at the onset of the experiments indicating “moribundity or death as an endpoint” as applicable.
 - 5.2.** Animals will be monitored daily by research personnel trained in recognizing signs of pain, distress, and morbidity. The frequency of observation will be increased to at least twice daily when animals exhibit signs of pain or distress.
 - 5.3.** If signs of pain or distress are detected, designated personnel, including a veterinarian, should be notified promptly to assess the animals’ condition and establish a plan of action.
 - 5.4.** Animals are to be removed from group housing to individual cages when their condition deteriorates to the point that injury from other animals is likely, and/or access to food and/or water becomes difficult.
 - 5.5.** Promptly remove animals upon death.
 - 5.6.** Written records must be made of monitoring sessions indicating the protocol number, the date, and time of observation, the person performing the observation, any interventions performed, and any findings such as number of animals demonstrating pain and/or distress, number of animals dead, etc. These records must be kept on file and available for review by regulatory bodies.

Equine Humane Endpoint Guidelines

Adapted from: Euthanasia Guidelines (AAEP)

The criteria below are clinical signs of conditions or diseases that indicate a humane endpoint has been reached. The Attending Veterinarian must be consulted when assessing criteria for endpoints. Exceptions to the following endpoints may be approved by the IACUC as part of the protocol review process.

- A horse should not have to endure continuous or unmanageable pain from a condition that is chronic and incurable.
- A horse should not have to endure a medical or surgical condition that has a hopeless chance of survival.
- A horse should not have to remain alive if it has an unmanageable medical condition that renders it a hazard to itself or its handlers.
- A horse should not have to receive continuous analgesic medication for the relief of pain for the rest of its life.
- A horse should not have to endure a lifetime of continuous individual box stall confinement for prevention or relief of unmanageable pain or suffering.

Special Considerations for the Insured Horse and Cases Involving Multiple Practitioners:

Each insurance policy for a horse is a contract between the horse owner and the insurance company and will dictate the specific terms and conditions concerning the payment of a mortality claim. Careful consideration should be given to possible “conflicts of interest” as referenced in the Ethical and Professional Guidelines in the AAEP Resource Guide and Membership Directory. The attending, consulting and referring veterinarians should follow the Ethical and Professional Guidelines contained within the AAEP Resource Guide & Membership Directory.

Reviewed by the AAEP board of directors in 2016.

Body conditioning scoring of horses for evaluation of general condition

condition score 1 - 3



poor neck

condition score 4 - 6

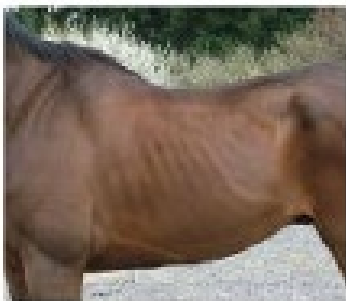


moderate neck

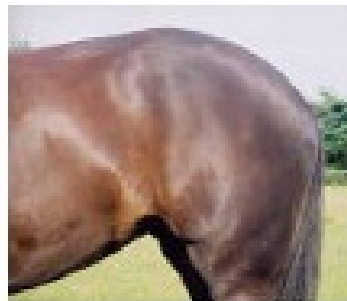
condition score 7 - 9



fat neck



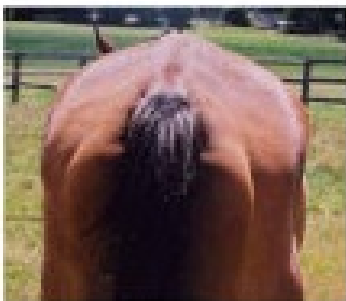
poor middle



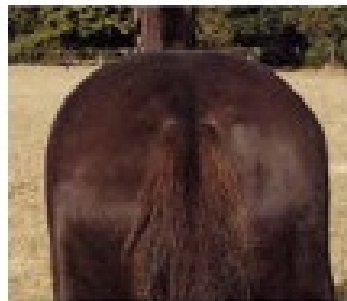
moderate middle



fat middle



poor rear



moderate rear



fat rear

Humane Endpoints for Ruminants (beef cattle, dairy cattle, and sheep)

The criteria below are clinical signs of conditions or diseases that indicate a humane endpoint has been reached. The Attending Veterinarian must be consulted when assessing criteria for endpoints. Exceptions to the following endpoints may be approved by the IACUC as part of the protocol review process.

1. A body condition score (BCS) of 2 or less requires immediate action. No animal with BCS of less than 2 may be transported or leave the farm unless for veterinary treatment.
 - a. Causes
 - i. Poor dentition
 - ii. Parasites
 - iii. Chronic disease
 - iv. Poor nutrition
 - b. See BCS charts below
2. Congenital abnormalities
3. Lameness

As an aid to assessing the status of lameness in the herd, locomotion scoring may be utilized.

 - Locomotion scores:
 - No unevenness of gait, no apparent tenderness
 - Uneven gait, slightly tender
 - Slight obvious lameness, but not affecting behavior
 - Obvious lameness, behavior pattern affected, some weight loss
 - Extreme difficulty in rising, difficulty in walking, adverse effects on behavior pattern, noticeable weight loss.
 - [Manson & Leaver 1988]
4. No live animal can leave the farm or be transported unless it is able to walk unassisted (except for veterinary care).
5. Long-standing illness such as chronic pneumonia, hardware disease, chronic bloat
6. Acute injury which compromises normal life functions
7. Cancer -Some types of bovine cancer (i.e. squamous cell carcinoma of the eye) may allow for localized surgical intervention and salvage of the animal. These cases should be considered on an individual basis by the AV and PI.

Body Condition Score Chart for Beef Cattle



Body Condition Score	Vertebrae at the middle of the back	Rear view (cross-section) of the hook bones	Side view of the line between the hook and pinbones	Cavity between tailhead and pinbone	
				Rear view	Angled view
1 Severe underconditioning					
2 Frame obvious					
3 Frame and covering well balanced					
4 Frame not as visible as covering					
5 Severe overconditioning					

Body Condition Score Chart for Dairy Cattle

ELANCO
ANIMAL HEALTH

Body Condition Scoring in Dairy Cattle



2.0



2.5



2.75



3.0



3.25








3.5



3.75

Body Condition Score Chart for Sheep

 <p>Condition Score 1</p>	<p>No fat and very little muscle on the backbone and ribs. Seriously low body condition. Quite unacceptable – prone to disease and at risk of death.</p>
 <p>Condition Score 2</p>	<p>A small amount of muscle along the backbone but no fat. The least acceptable condition for thrift. Perhaps acceptable for dry sheep when the feed is short but a clear indication that nutrition requires attention.</p>
 <p>Condition Score 3</p>	<p>Good level of fat and muscle with rounded ends of ribs and top of backbone. A good level for Merino ewes from joining to lambing and an ideal condition for young sheep.</p>
 <p>Condition Score 4</p>	<p>Over-round across backbone – lots of muscle and fat. Tending towards over-fat.</p>
 <p>Condition Score 5</p>	<p>Can't feel the backbone or ribs. Definitely over-fat. Too fat for slaughter.</p>

Humane Endpoints for Swine

The criteria below are clinical signs of conditions or diseases that indicate a humane endpoint has been reached. The Attending Veterinarian must be consulted when assessing criteria for endpoints. Exceptions to the following endpoints are may be approved by the IACUC as part of the protocol review process.

1. Body condition score 2 or less
2. Lameness/joint lesions
3. Recumbency with inability to rise
4. Hernia (umbilical or scrotal) should be evaluated as presented below

DO NOT transport an animal that has a hernia that meets one or more of the following criteria:

- a. impedes movement (includes conditions in which the hind legs of the animal touch the hernia when the animal is walking),*
- b. is painful on palpation; indicated by vocalization, a change in the animal's mood (aggression), behaviors by the animal directed at the painful area, escape reaction and increased respiratory rate*
- c. touches the ground when the animal is standing in its natural position, and/or*
- d. includes an open skin wound, ulceration or obvious infection.*

Assessment 1 - smaller hernias



Assessment: Transport direct to slaughter. These pigs have hernias that do not touch the ground, do not impede movement and are not open or bleeding.

Assessment 2 - larger hernias

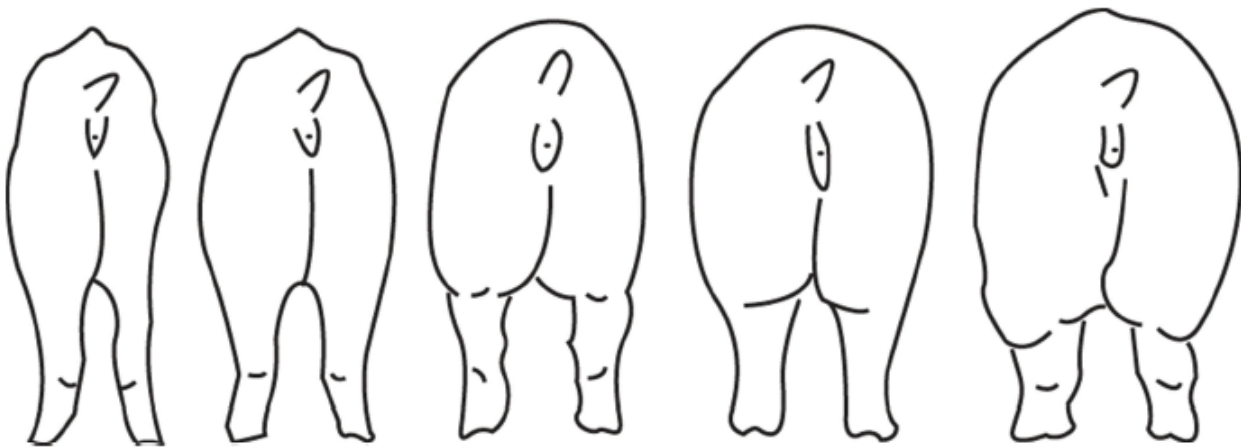


Assessment: Not suitable for transport. These hernias should have been addressed sooner. The pigs must be promptly and humanely destroyed.

<http://www.omafra.gov.on.ca/english/livestock/swine/facts/13-075.htm>

7. External abscesses (debilitating)
8. Signs of central nervous system disease (nystagmus, paralysis/paresis, head tilt)
9. Lesions or behavior consistent with infectious disease (difficulty breathing, dermatitis, etc.)
10. Traumatized, infected or irreparable rectal/vaginal prolapses
11. Congenital abnormalities

Body Condition Scoring of Swine



Body Condition Scores (BCS). Scores are arranged from 1 (left) which is assigned to emaciated sows to 5 (right) which is reserved for excessively fat sows. A score of 3 is ideal.

Taken from "Assessing Sow Body Condition" by R.D. Conffey, G.R. Parker, and K.M. Laurent (ASC-158); 1999).



BCS Score 1

BCS Score 2

BCS Score 3

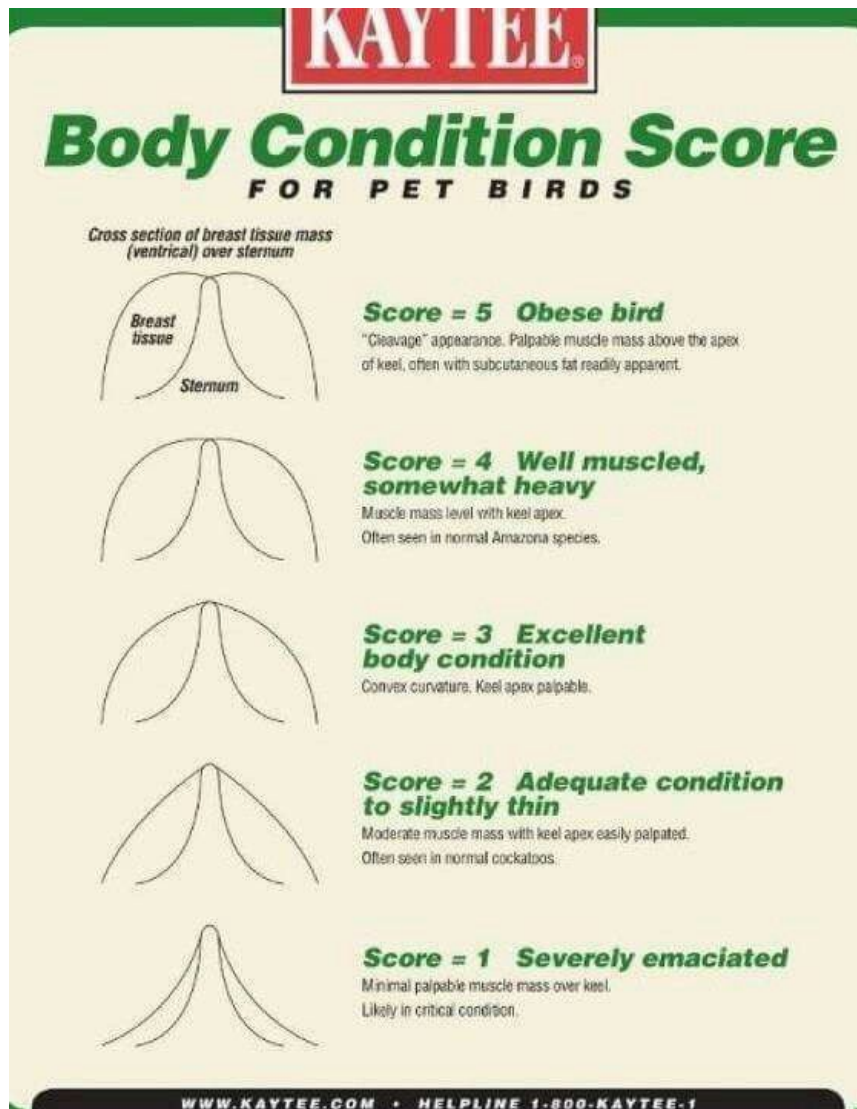
BCS Score 4

BCS Score 5

Photo credit: Dr. Ken Stalder and the National Hog Farmer magazine

Score	Last rib backfat depth (in.)	Condition	Body Shape
1	<.6	Emaciated	Hips, spine prominent to the eye
2	.6 - .7	Thin	Hips, spine easily felt without pressure
3	.7 - .8	Ideal	Hips, spine felt only with firm pressure
4	.8 - .9	Fat	Hips, spine cannot be felt
5	>.9	Overfat	Hips, spine heavily covered

Body Condition Scoring of Birds/Poultry



Scoring systems for poultry humane endpoint evaluation

1. Gait abnormalities*

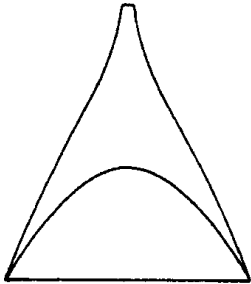
0 – No impairment. Can walk at least 5 ft with a balanced gait.

1 – Obvious impairment. Can walk at least 5 ft but with a clear limp or awkward gait.

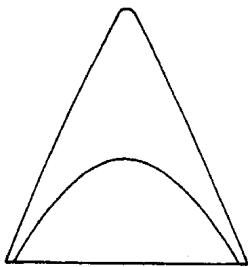
2 – Severe impairment. Will not walk 5 ft. May shuffle on shanks or hocks with assistance of wings.

*Webster, AB et al. Validation of a three-point gait-scoring system for field assessment of walking ability of commercial broilers. *J Appl. Poult. Res.* 2008. 17:529-539.

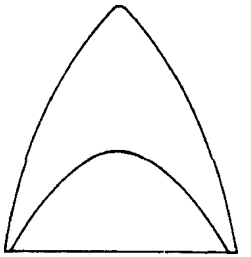
2. Keel*



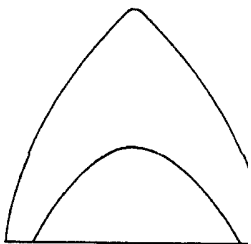
Score= 0 Protruding keel bone and depressed contour to breast muscles



Score= 1 Prominent keel bone with poorly developed **breast** muscles



Score=2 Less prominent **keel** bone and moderate breast muscle development



Score= 3 Plump breast muscles which provide a smooth contour with the keel

Fig. I Diagrammatic cross-sections of the breast muscle and ventral abdominal cavity for the 4 body condition scores. Each score has been standardized to the same body cavity dimensions.

*Gregory NG and JK Robbins. **A body condition scoring system for layer hens.** *New Zealand Journal of Agricultural Research.* 1998. 42:555-559

Birds with a keel score of 0 to 1 and/or a gait score of 1 to 2 require further assessment by the PI and AV leading to decisions regarding medical intervention, nutritional supplementation or euthanasia.

Additional Resources:

Poultry Health Assessment:

<https://www.merckvetmanual.com/exotic-and-laboratory-animals/backyard-poultry/physical-examination-of-backyard-poultry>

Broiler chicken welfare

http://www.oie.int/fileadmin/Home/eng/Health_standards/tahc/current/chapitre_aw_broiler_chicken.pdf

Scoring criteria #1

***Body Weight**

- < 10% weight loss = 1
- 10 – 20% weight loss = 2
- >20% weight loss = 3

• Physical appearance

- Normal = 0
- Lack of grooming = 1
- Rough coat, nasal/ocular discharge = 2
- Very rough coat = 3

• Behavior

- Normal = 0
- Minor changes = 1
- Inactive = 2
- Unresponsive – 3

Breathing: R= Rapid; S = Shallow; L = Labored; N = Normal

Body Condition Score: 0 = Normal; 3 = Emaciated

When a total score of three or more is reached, the PI is to be notified. When a score of 3 in any one category or a total of 6 is reached, the animal will be euthanized.

Scoring criteria #2

Score 0 to 3 with 0 = normal

Weight loss: <10% = 1; 10-20% = 2; >20% = 3

Grooming: Lack of grooming = 1; rough coat, nasal discharge = 2; very rough coat=3

Ulceration: Loss of hair, skin intact = 1; ulceration size of a dime or less = 2; ulceration larger than a dime = 3

Activity: Normal = 0; minor changes = 1; inactive = 2; unresponsive = 3

Breathing: R= Rapid; S = Shallow; L = Labored; N = Normal; present = 2

Dehydration, Tremors, Circling: present = 2

Body Condition Score: Normal = 0; Emaciated = 3

Once Total Score is 3, monitor twice a day.

Euthanize when weight loss is greater than 20% or when cumulative score of 6 or greater