1. Purpose

The purpose of this guideline is to provide criteria for identifying and utilizing the earliest endpoints that are compatible with the scientific objective of research studies while preventing, minimizing, or alleviating any actual or potential pain, distress or discomfort to study animals.

1. Scope

This applies to all animal users working under an IACUC approved protocol. Principal Investigators are responsible for ensuring staff are trained on the humane endpoints listed in the protocol.

1. Definitions

Humane Endpoint: Humane endpoints refer to one or more predetermined physiological or behavioral signs that define the point at which an experimental animal’s pain and/or distress is terminated, minimized or reduced by taking actions such as euthanizing the animal, terminating a painful procedure or giving treatment to relieve pain and/or distress.([CCAC](https://www.ccac.ca/Documents/Standards/Guidelines/Appropriate_endpoint.pdf))

Experimental Endpoint: When the scientific aims and objectives are reached.

1. Guidance

A. Animal Welfare Regulations and Policies require: Animals exhibiting signs of pain, discomfort, or distress are to receive appropriate relief unless written scientific justification has been provided in the protocol and approved by the IACUC. Additional points of guidance include:

1. Certain animal use protocols include procedures or approaches that require special consideration during the IACUC review process due to their potential for unrelieved pain or distress or other animal welfare concerns.
2. The IACUC is obliged to weigh the objectives of the study against potential animal welfare concerns. By considering opportunities for refinement, the use of appropriate non-animal alternatives, and the use of fewer animals, both the institution and the principal investigator (PI) can begin to address their shared obligations for humane animal care and use.
3. Use of humane endpoints contributes to refinement by providing an alternative to experimental endpoints that result in unrelieved or severe animal pain or distress, including death.
4. The PI should identify, explain, and include in the animal use protocol an experimental endpoint that is both humane and scientifically sound.
5. Critical information that should be included in defining experimental endpoints 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.
6. Guiding Principles
   1. The earliest possible humane endpoints that meet the scientific aims and objectives must be used for studies in which it is anticipated that animals may experience more than mild pain or distress.
   2. The number of animals that may experience more than momentary pain or distress must be clearly described and scientifically justified. If humane endpoints that allow for greater degrees of pain and/or distress per experimental group are used (e.g., a sepsis study in which some groups of animals are euthanized within 24 hours and other groups are followed for up to 5 days), the number of animals for each endpoint must be clearly described and justified.
   3. If analgesics interfere with the scientific aims and objectives and cannot be used, written justification must be provided in the approved IACUC protocol.
   4. Animals must be monitored at a frequency acceptable by the IACUC and described in the protocol by personnel trained and experienced in recognizing signs of illness, injury, or abnormal behavior. At a minimum, monitoring must include the following:
7. Abnormal appearance: abnormal posture or reluctance, rough coat, head tucked into abdomen, exudate around eyes and/or nose, skin lesions, abnormal breathing, neurological deficits, weight loss, dehydration.
8. Abnormal activity: abnormal movement or reluctance to move, decreased food or water intake, self-mutilation.
9. The frequency of observation of the entire cohort must be increased when one animal or more animals in a cohort are observed to be in unrelieved or severe animal pain or distress, including death.
10. Personnel with training to determine humane endpoints must make an assessment as soon as possible if notified of an adverse health event. If personnel directly responsible for the project cannot be contacted for some reason, ARC staff responsible for emergency veterinary care should provide care for or euthanize the animals in a timely manner. The Attending Veterinarian must be promptly notified that animals are showing clinical signs of disease.

C. Examples of conditions where intervention, including euthanasia, where appropriate include:

* + 1. Weight loss of >20% of body weight

1. Persistent dehydration, non-responsive to medical intervention
2. Chronic uncontrollable emesis or diarrhea
3. Decrease in food consumption (less than 50% of food offered) for more than one day
4. Secondary infections subsequent to immunosuppression, not responsive to treatment
5. Persistent hypothermia/hyperthermia of +/-4C normal range, nonresponsive to remedial action
6. Persistent severe anemia with respiratory distress, pale membranes
7. Extended period of weight loss, progressing to emaciated state
8. Surgical complications unresponsive to medical intervention
9. Combination of the following:
   * + 1. Poor Physical Appearance
          1. Very rough hair coat
          2. Abnormal posture
       2. Abnormal Behavior
          1. Reduced mobility
          2. Unconsciousness
          3. Unsolicited vocalizations
          4. Self-mutilation
       3. Abnormal or exaggerated responses to external stimuli
       4. Abnormal clinical signs
     1. Severe respiratory distress, unresponsive to treatment
     2. Severe anaphylaxis, unresponsive to treatment
     3. Vascular Access Port(VAP) associated infections; migration of catheter; unalleviated by corrective actions.
     4. Occurrence of a serious injury or trauma from which recovery is unlikely
     5. Neurological signs that interfere with eating and drinking and from which recovery is unlikely
10. Trauma to eye, ulceration/vascularization of cornea, unresponsive to treatment
11. Protrusion of the eye with inability to blink and maintain lubrication.
12. Continuous frank bleeding from any orifice, which is unresponsive to treatment
13. Swollen painful joints, interfering with mobility and nonresponsive to medical intervention
14. One or more skin ulcers that do not heal, depending upon the species and severity of the ulcers
15. Mass with a size or location that interferes with normal function, greater than 15% of normal body weight, or that ulcerates with no evidence of healing
16. Score Sheets /Pain & Distress forms
    1. Score sheets are important tools that may be used for identifying and recording clinical signs and laboratory results (e.g., hematology, clinical chemistries, biomarkers etc.,) indicative of impact on pain or distress that can be used for timely decision-making for humane intervention.
    2. The clinical signs/laboratory results included in the score sheet should be relevant to the potential responses anticipated for the age, species, strain and breed of animal being used.
    3. When established animal models are used, the score sheets should include a progression of increasing severity of clinical signs typical for that model.
    4. Observations should be based on monitoring the animals both at rest and after gentle stimulation.
    5. The signs can be scored as present (+) or absent (-) or given a numerical value.
    6. The cumulative score for the presenting signs may give an overall impression of animal well-being.
    7. Persistence of a combination of two or three minor signs over a specific time period or a single major sign may be sufficient to indicate the need for immediate euthanasia.
    8. Written records of monitoring sessions should indicate the identity of the animals including the protocol number, time of observations, initials of the person performing the observations, the number of animals exhibiting clinically abnormal behavior or death, and any intervention performed to alleviate pain and/or distress. These records should be maintained in the animal housing room, to serve as a method of communication with the ARC staff and AV, until the conclusion of the experiment and should be made available to the IACUC upon request.
17. Pilot Studies
    1. When novel studies are proposed and information on a procedure’s effect on animals is limited or unavailable, or humane endpoints cannot be identified or defined, a pilot study may be recommended or required by the IACUC.
    2. When such pilot studies are approved by the IACUC, the IACUC must be informed of outcomes (e.g., morbidity/mortality) as described in the approved protocol, and the protocol must be amended to include requirements related to animal monitoring and humane endpoints determined by the pilot study.
    3. Regular observations of the animals throughout a pilot study are required to identify critical periods during the experiment when the animals’ well-being will be especially at risk.
18. References

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