

I. Introduction

The UIC Animal Care Committee (ACC) is charged with evaluating and ensuring that research projects are conducted in accordance with the Animal Welfare Act and the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals. These regulations and policies require that any research, testing and teaching that uses animals must be performed in such a way as to minimize discomfort, distress and pain consistent with sound research design.

The UIC-ACC recognizes that as a sequela of research or testing, laboratory animals may experience pain and/or distress. For certain studies the procedures may lead to the moribund condition or death. Therefore, the ACC has developed guidelines for establishing humane experimental endpoints to assist investigators with the process of completing the UIC Protocol for Animal Use and to insure that animal welfare issues are appropriately addressed. Since the diversity of research and testing protocols preclude the establishment of a rigid set of guidelines, the ACC reserves the right to evaluate each protocol on an individual basis.

Definitions

Humane Endpoint - The humane endpoint is the point at which 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.

Moribund Condition - The moribund condition is a severely debilitated state that precedes imminent death.

II. Institutional Guidelines

Investigators should identify humane experimental endpoints that minimize pain, distress, or discomfort by choosing the earliest endpoint that is compatible with the scientific objectives of the research project.

1. **The Moribund Condition** - Whenever possible, the moribund state should be used as an experimental endpoint instead of death, because it is assumed that euthanizing a moribund animal will avoid or reduce terminal distress. The following specific sequela should be considered:
 - a. The procedure should not interfere with the ability of the animal to ambulate, eat, drink, urinate and defecate.
 - b. The procedure should not result in a net weight loss of more than 20% of the body weight.
 - c. The procedure should be ended if the investigator has conclusive evidence that untreatable organ failure has occurred, and the animal exhibits signs associated with the failure of the organ system.
 - d. Animals should be euthanized if unrelated health conditions develop that make their experimental use of no value to the investigator.
 - e. Obvious signs of illness should serve as alternatives to death as an experimental endpoint. Examples of signs of illness in laboratory animals include:

1. Prolonged inappetance
 2. Evidence of muscle atrophy/marked loss of body condition
 3. Central nervous system disturbance - Head tilt, Seizures, Tremors, Circling, Spasticity, Paresis
 4. Chronic diarrhea or constipation
 5. Rough coat, hunching, distended abdomen
 6. Spreading area of alopecia caused by disease
 7. Coughing, rales, or respiratory distress
 8. Distinct jaundice and/or paleness (anemia)
 9. Markedly discolored urine, polyuria or anuria
 10. Inability to remain upright
 11. Frank bleeding from any orifice
 12. Persistent self-induced trauma
 13. Marked dehydration
- f. The use of death as an endpoint requires strong scientific justification in the Protocol for Animal Use.
2. **Monitoring Frequency** - The frequency of the observations should increase with the potential for increasing pain and/or distress. The interval between observations can vary greatly from weekly to several times each day. For some studies, initial observations may be made less frequently and then increase as the disease or condition progresses.
 3. **Pilot Study** - The selection of appropriate humane endpoints requires a detailed knowledge of the impact of the procedure on the animal. The ACC reserves the right to request a pilot study if these factors are unknown. For each scientific procedure, various parameters may be present that signify the moribund condition in the research animal and can be used to select a time point for euthanasia. A pilot study will help determine the time course and nature of any adverse effects on the animal and provide an indication of the variability of responses between treatment groups, which can then be used to estimate appropriate group sizes for the main study.
 4. **Score Sheet** - It may be difficult to assess the impact of certain procedures on an animal since the biological sequela of an experimental paradigm may be complex and are confounded by variations in responses by different species. Therefore, a score sheet system may be beneficial during a pilot study, and potentially throughout an experimental project. A score sheet system provides an objective format for deciding which observations are important, ensures that specific observations are not overlooked and provides a blueprint for training individuals involved in the research project. A sample of a score sheet system is provided in Appendix A. Further information regarding score sheet systems can be obtained by contacting a member of the BRL veterinary staff.
 5. **Cancer Research and Monoclonal Antibody Production** - Certain areas of research that are considered to have a high potential for producing pain and/or distress in laboratory animals are specifically addressed in the UIC-ACC Guidelines. These areas are 1) tumor growth or cancer research and 2) monoclonal antibody production.

III. Protocol for Animal Use

Protocols for all research or testing procedures that cause animals to experience a significant level of debilitation, disease or a pathological state will be subjected to a full-committee review. For these protocols, the items listed below should be addressed on the UIC Protocol for Animal Use.

1. Form A, item 8g, include a description of the experiment in its entirety, including a time course for the expected signs of disease or debilitation.
2. Form A, mark item 12a “Yes”. A response of “Yes” requires that Form A, item 13 as well as Form B be completed.
3. Form A, item 13 should include a justification for the procedure and a description of the resources used to determine that an appropriate alternative for the potentially painful or distressful procedure, including the use of an in vitro system, computer model or less sentient animal, is not available.
4. Form B, complete item 9, and include a description of the duration of the study, the monitoring frequency, the endpoint of the study and a justification for the model.
5. Form B, complete item 11 if death or a diseased/debilitated state is the endpoint.

Additional Reading:

- Tomasovic S.P., Coghlan L.G., Gray K.N., Mastromarino A.J., and Travis E.L.. (1988). *IACUC Evaluation of Experiments Requiring Death as an End Point: A Cancer Center's Recommendations. Lab Animal (Jan. B Feb.)* 31-34.
- Ullman-Cullere M.H., and Foltz C.J., (1999). *Body Condition Scoring: A Rapid and Accurate Method for Assessing Health Status in Mice. Laboratory Animal Science* 49(3): 319-323.
- *Canadian Council on Animal Care (1998). Guidelines on choosing an appropriate endpoint in experiments using animals for research, teaching and testing. Ottawa Ontario Canada: CCAC.*
- *National Research Council (2000). Humane endpoints for animals used in biomedical research and testing. Institute for Laboratory Animal Research Journal* 41(2).
- Toth L.A. (1997). *The moribund state as an experimental endpoint. Contemporary Topics* 36(3): 44-48.
- Danneman P.J. (1997). *Monitoring of Analgesia. In: Anesthesia and Analgesia in Laboratory Animals. Academic Press. p. 83-103.*
- Morton D.B. (1990). *Adverse effects in animals and their relevance to refining scientific procedures. ATLA* 18:29-39.
- Morton D.B., Griffiths P.H.M. (1985). *Guidelines on the recognition of pain, distress and discomfort in experimental animals and a hypothesis for assessment. Vet Rec* 116:431- 436.
- Morton D.B., Townsend P. (1995). *Dealing with adverse effects and suffering during animal research. In: Revised Version of Laboratory Animals - An Introduction for Experimenters. John Wiley. p. 215-231.*
- *Recognition of Alleviation of Pain and Distress in Laboratory Animals. 1992. National Research Council. National Academy Press.*
- *Institute for Laboratory Animal Research (ILAR) Journal (1999). 40:1.*

GUIDELINES – Humane Experimental Endpoints Appendix A**I. Scoring Systems**

For a given research protocol, several parameters may be present that signify the moribund condition in the research animal and can be used to select a time point for euthanasia. The use of a system for scoring the animal's condition provides an objective format for deciding which observations are important, ensures that specific observations are not overlooked and provides a blueprint for training individuals involved in the research project. A score sheet system allows each member of the research team to make and judge observations in a uniform manner. A checklist or score sheet system should be prepared specifically for each scientific procedure since the expected sequelae of experiments can vary greatly. For example, the effects of a failed skin graft will differ significantly from a failed kidney transplant. Qualitative signs such as limping may be assigned scores according to severity. Score sheets provide a method to obtain an overall impression of well-being.

Below is an example of a simple score sheet system. Depending on the research protocol, a more comprehensive score sheet system may be advantageous. Score sheet systems with increased complexity have been published by Morton and Griffiths 1985, Morton 1990, Morton and Townsend 1995, and Workman et. al., 1998. Further information on score sheets can be obtained by consulting with a member of the BRL veterinary staff.

Response variables and scoring system****Body weight changes*:**

- 0 - Normal
- 1 - <10% Weight loss
- 2 - 10-15% Weight loss
- 3 - >20% Weight loss

Body-condition score*:

- 0- Animal is well-conditioned. Vertebrae, pelvic or spinal bones are not prominent
- 1- Underconditioned, Segmentation of vertebral column evident. Pelvic bones are readily palpable.
- 2 - Animal is emaciated. Skeletal structures extremely prominent; little or no flesh cover.

Physical appearance:

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

Behavior:

- 0 - Normal
- 1 - Minor changes; limping
- 2 - Abnormal; reduced mobility, inactive
- 3 - Unsolicited vocalizations, self-mutilation, either very restless or immobile.

**Body weight is not always accurate as increases in abdominal fluid or tumor growth may mask weight loss. At times, body-condition scores may better reflect animal's actual condition.*

***When a total score of three or more is reached, based on the above checklist, the animal will be sacrificed.*