

## GUIDELINES FOR DEATH AS AN ENDPOINT

The OLAW *Institutional Animal Care and Use Committee Guidebook (NIH Publication No. 92-3415)* states, "Endpoints other than death must always be considered and should be used whenever the research objective makes it possible." Death as an endpoint does not include euthanasia at the end of a study. Death as an endpoint implies that the study results in death of the animal without investigator intervention.

The Institutional Animal Care and Use Committee (IACUC) of the University of Rhode Island discourages the use of death as an endpoint and instead encourages the use of alternative endpoints. Some examples of alternative endpoints include the following, as determined by type of experimental application (tumor study, toxicity testing, surgical procedure, etc.):

- a. Tumor load > 10% of normal body weight.
- b. Weight loss of > 20% of normal body weight (due to anorexia, physical inability to obtain food and/or water, or severe diarrhea or vomiting).
- c. CNS signs such as circling, blindness, convulsions.
- d. Hematological parameters indicative of end-stage organ failure.

Animals should be humanely euthanized at the time the alternative endpoint is reached, or if they demonstrate signs of being moribund. *Moribund* is defined as "in a dying state" (<http://www.mercksource.com>). Animals are considered to be moribund if they manifest any of the following clinical signs:

- a. Inability to maintain an upright position.
- b. Prolonged (greater than 48 hours) physical inability to obtain food and/or water.
- c. Prolonged (greater than 48 hours) anorexia and/or clinical dehydration.
- d. Uncontrollable diarrhea, vomiting or constipation.
- e. Agonal breathing and cyanosis.
- f. Unconsciousness with no response to external stimuli (e.g., toe-pinch withdrawal test).

If death as an endpoint must be used (i.e., killing a moribund animal would invalidate the study) the following stipulations must be met:

- a. Scientific justification for using death as an endpoint must be provided in writing as part of the animal care protocol and must be approved by the IACUC. The following points must be discussed/explained in the justification:
  - i. What alternatives were considered and why morbidity can't be used in place of death?
  - ii. What additional information is gained in the interval between the moribund condition and death?

- iii. The number of animals in survival duration protocols should be clearly stated, as well as the statistical techniques used to estimate the numbers in the study groups.
  
- b. Moribund animals must be monitored a minimum of twice daily (in the early morning and late afternoon, including weekends and holidays).
- c. Written records must be made of all monitoring sessions indicating the time and date of the observation, the person performing the observation, and any findings (such as number of animals demonstrating clinically abnormal behavior, number of animals found dead, etc.). These records must be kept on file and made available to the CLAF personnel or the Attending Veterinarian upon request.
- d. Moribund animals must be removed from group housing and housed individually with easy access to food and water.
- e. The minimum number of animals necessary to achieve statistical significance must be used.
- f. Drugs or techniques to alleviate pain or distress preceding death must be used unless they would interfere with the scientific objectives of the study.
- g. Proposals foregoing the use of anesthetics, analgesics or tranquilizing drugs must be extensively justified in writing as part of the animal care protocol and approved by the IACUC. Additionally, proposals which utilize death as an endpoint and which forego the use of anesthetics, analgesics or tranquilizing drugs to alleviate pain and distress in experimental animals will be assigned the highest pain level category, "E," on all protocol forms and regulatory papers.

**CHECK ONE:**

I agree to comply with the following guidelines.

I have attached written justification for deviation from these guidelines.

\_\_\_\_\_  
Principal Investigator

\_\_\_\_\_  
Date

**APPROVED:**

\_\_\_\_\_  
IACUC Chair

\_\_\_\_\_  
Date