

TITLE: IACUC Guidelines, on Euthanasia as an Alternative to Death as an Endpoint in Rodents

PURPOSE: Provide guidelines for recognizing signs of morbidity and moribundity and recommended statements of Criteria for Moribundity.

REVIEW/REVISIONS: Permanent amendment/revisions to this policy must be presented to the IACUC for review before implementation and should be developed by the IACUC Membership and/or University Animal Care Veterinary personnel.

EFFECTIVE DATE: December 20, 1995; **Revised/Re-Approved:** 12/7/00, 11/2/06, November 1, 2007

PERSON(S) RESPONSIBLE: IACUC membership (review), University Animal Care personnel (monitoring), Research personnel (monitoring and establishment of criteria for moribundity)

POLICY/PROCEDURES:

The IACUC guidelines indicate that animals found moribund should receive euthanasia, but if experimental death itself is the required end point, the investigator may receive consideration for approval to conduct such studies by providing appropriate justification in a memorandum at the time the Animal Protocol Review Form is submitted to the Committee. Inconvenience or increased costs alone are not justifiable reasons, but the IACUC will otherwise generally accede to the scientific judgment of the investigator. Investigators are expected to make a good faith effort to justify their end points, or agree they can judge when to perform euthanasia on animals found moribund in a particular protocol. Moreover, all investigators are expected to continue to monitor experimental animals at least daily (including weekends and holidays), to euthanize any animals which they judge should receive euthanasia, to use alternative end points to death when possible, and to minimize animal numbers within statistical constraints in general, but especially in death-end-point protocols.

Suggested Signs and Symptoms for Judging Morbidity (disease/illness) in Rodents

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| 1. Rapid weight loss (>20% in 1 week) | 12. Paralysis |
| 2. Extended period of weight loss progressing to emaciation | 13. Persistent lateral recumbency |
| 3. Diarrhea or vomiting if debilitating or prolonged (more than 3 days). | 14. Impaired mobility or lesions interfering with eating, drinking, or ambulation. |
| 4. Rough hair coat, hunched posture, distended abdomen, or lethargy if debilitating or prolonged (more than 3 days). | 15. Tumors: |
| 5. Respiratory distress (dyspnea) or cyanosis. | a. That are >10% of the animal's original body weight |
| 6. Persistent cough, rales, wheezing, or nasal discharge. | b. With a mean tumor diameter >2cm in mice. |
| 7. Persistent bleeding from any orifice | c. with a mean tumor diameter >4 cm in rats. |
| 8. Persistent anemia leading to debilitation. | d. that are ulcerated >1 cm diameter |
| 9. Distinct icterus (jaundice; yellow color to skin). | 16. Extensive necrotic tissue or skin ulceration (10% body surface affected.) |
| 10. Markedly discolored urine, polyuria, or anuria if prolonged (more than 3 days) | 17. Excessive or prolonged hyperthermia or hypothermia (more than 3 days). |
| 11. Central nervous system signs such as head tilt, tremors, spasticity, seizures, circling, or paresis if associated with anorexia and if hindering animal's ability to obtain food or water. | 18. Persistent self-induced trauma |
| | 19. Clinical signs of suspected infectious disease requiring a necropsy for diagnosis. |
| | 20. Other clinical signs judged by experienced veterinary or technical staff to be indicative of a moribund condition. |



Suggested Signs and Symptoms for Judging the Moribund Condition (state of dying) in Rodents

- signs and symptoms for morbidity **plus**:
 - impaired ambulation (unable to easily reach food or water)
 - evidence of muscle atrophy or other signs of emaciation (body weight is not always appropriate, especially since tumors may artificially increase body weight)
 - any obvious illness including such signs as lethargy (drowsiness, aversion to activity, lack of physical or mental alertness), prolonged anorexia, bleeding, difficulty breathing, central nervous system disturbances, or chronic diarrhea or constipation.
 - Inability to remain upright

Example of acceptable Criteria for Moribundity statement:

“Animals will be observed on a daily basis and monitored for signs of cachexia/debilitation. Animals will be observed for signs of pain and suffering including rapid, slow, shallow or labored breathing, rapid weight loss, anorexia, hunched posture, hypo- hyperthermia, severe ulceration, dermatitis or infected tumors, diarrhea or constipation, paralysis or impaired ambulation. Lethargy, and/or nasal/ocular discharge. Animals displaying any of these signs which cannot be controlled/alleviated with pain management medications will be euthanized by study personnel.”

JUSTIFICATION:

Legal, regulatory, and moral guidelines require that animal pain, distress, and suffering be minimized in any experiment. For these reasons, investigators should be encouraged to administer euthanasia in death-end-point experiments prior to actual death of the animals -- if experimental validity will not be compromised. These objectives assume that investigators can differentiate between animals that are morbid (i.e., affected with disease or illness), and those that are moribund (i.e., in the state of dying).

The IACUC believes that an investigator can judge and should perform euthanasia on moribund rodents based on objective signs or symptoms of dying depending on experience with the animal model, professional judgment, and the experimental protocol. Some of the known signs and symptoms of such information are encouraged with the understanding that the combination of signs or symptoms indicating euthanasia may vary with experimental end point.