STUDIES INVOLVING DEATH AS AN ENDPOINT POLICY

Background:

The University of Missouri – Kansas City (UMKC) Institutional Animal Care and Use (IACUC) is obligated to provide policies that notify and train personnel concerning the appropriate techniques, equipment, and agents for performing appropriate procedures to ensure humane care and use of laboratory animals.

Policy:

This policy applies to studies that use animals and that require death, other than by euthanasia, as a necessary endpoint for the hypothesis being tested. To comply with guidelines governing the use of animals in experimentation, the use of death as an endpoint to experimental manipulation, rather than performing euthanasia to humanely terminate an animal, is **strongly discouraged**. Investigators must perform euthanasia on all moribund experimental animals unless there is scientific justification that euthanasia would invalidate experimental data collection.

Moribund is defined as "a severely debilitated state that precedes imminent death." (Toth, LA 2000)

Cardinal signs of moribundity: (in no particular order any one of these = moribund)

1. Non-responsive to normal arousal physical stimuli
2. Agonal breathing – slow, open-mouth breathing
3. Inability to remain upright
4. Loss of consciousness
5. Drop in body temperature below 28º C (82.4ºF)
6. Prolonged (>48 hours) physical inability to obtain food and/or water.

There are many combinations of morbid conditions that, if taken together, would equal a moribund animal. These instances will be assessed on an individual basis.

Information required to be provided in the protocol form by the Principal Investigator (PI) for IACUC review:

- A written justification for death as an experimental endpoint that includes a description of alternative, non-lethal endpoints considered and why they cannot be used.
- A written justification for the number of animals exposed to the probability of death as an experimental endpoint that includes a clear explanation that the number is the minimum necessary to accomplish the experimental goals.
- Define opportunities to administer drugs to animals that may be subject to death as an endpoint to relieve pain or distress. If such drugs may not be used, a written explanatory justification for withholding them must be provided.

- The intervals and frequency at which the animals are subject to death as an endpoint will be observed by personnel skilled in recognizing signs of illness or injury, and behavioral abnormalities. At a minimum, animals must be observed at least twice daily, in the early morning and late afternoon, including weekends and holidays.
- A detailed description of clinical signs that are anticipated to occur prior to death.
- Actions that will be taken to minimize pain or distress other than drugs, such as removal from group housing or providing special feed and watering methods to facilitate access to food and water.
- A description of the records that will be maintained of observations of rodents that may be subject to death as an experimental endpoint.

Additional requirements:

- LARC staff must be notified of experiments in progress that may result in deaths. The cages of the specific animals that are subject to death as an experimental endpoint must be clearly labeled to indicate that death of the animal is expected, and the approximate time frame in which death is expected.
- Dead animals must be removed from cages as soon as possible.
- If euthanizing a moribund animal would invalidate the study, the 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 prior to initiating this procedure. Investigators who receive approval from the IACUC to use death as an experimental endpoint must also agree to the following:
    - To use the minimum number of animals necessary to achieve statistical significance and to use alternative endpoints other than death whenever possible.
    - Animals must be monitored at least twice daily (in the early morning and late afternoon including weekends and holidays) and any animals evidencing clinically abnormal behavior must be removed from group housing situations and housed individually with easy access to food and water.
    - Written records of all monitoring sessions, indicating the time of the observations, the person observing the animals, and any observations such as the number of animals evidencing clinically abnormal behavior and the number of animals found dead, must be maintained and made available to the IACUC on request.
    - Investigators should note that any approved use of death as an experimental endpoint will be noted on all protocol forms and regulatory papers as being in the highest USDA pain level category "E" unless analgesics or anesthetics are provided to alleviate pain or distress in the experimental animals.

Revisions to the Policy:

This policy is intended to be flexible and readily adaptable to changes in regulatory requirements. It will be changed as experience shows that a certain approach is not effective or suggests a better alternative. The UMKC IACUC has the authority to amend this policy.

Policy Approval:

The UMKC IACUC has reviewed and approved this policy as documented in the meeting minutes.

Created: January 2015
Revised: January 2018
Revised: January 2021
Revised January 2024