IACUC Policy on Humane Endpoints in Animal Use Proposals

Definitions:

moribund \textit{\textbackslash MOR-uh-bund\}, adjective: In a dying state; dying; at the point of death.
morbid\textit{\textbackslash MOR-bid\}, adjective: pertaining to, affected with, or inducing disease; diseased.

Policy:

Experimental studies may involve procedures that cause clinical symptoms or morbidity in animals. Ideally, studies should be terminated when the animals begin to exhibit clinical signs of disease (morbidity) if these endpoints are compatible with meeting the research objectives. Such endpoints minimize pain or distress and are preferable to death or moribundity as endpoints which can involve considerably more pain or distress.

Although infrequent, allowing animals to become moribund or die as endpoints may be necessary for some research projects. The moribund condition is defined as a clinically irreversible condition leading inevitably to death. In these studies, animals are permitted to die or become moribund as a result of experimental procedures, in some cases without the use of pain relieving measures, because such measures may compromise the integrity of the study.

It is the policy of the Institutional Animal Care and Use Committee (IACUC) that studies requiring moribundity or death as the endpoint will not be approved without specific written scientific justification. Animals that become moribund will be humanely killed by approved methods.

In those cases where death is the only acceptable endpoint, the investigator must provide an explicit explanation for this endpoint. Particular attention should be paid to providing the rationale for not humanely killing moribund animals, e.g., what additional scientific information will be gained.

In cases involving tumor growths, the maximum size tumor allowed is 10% of the body size. When there is impaired mobility or of homeostatic mechanisms (i.e., eating, drinking, etc.), less tumor growth is tolerated.

When an infectious agent is administered, the investigator must monitor the animal for the following signs of acute or chronic pain:

1. guarding - attempts to protect, move away, or bite;
2. crying, flinching on movement, or palpation;
3. mutilation - excessive licking, biting, scratching, or shaking;
4. restlessness - pacing, lying down and getting up, shifting weight;
5. recumbency - reluctance to move or rise for an unusual length of time.

Animal Study Proposals utilizing death or moribund condition as an endpoint should contain the following information:

1. The scientific rationale for death or moribund condition as an endpoint, including:
   a. What alternatives were considered, why morbidity as an endpoint cannot be used, and how alternatives will be used whenever possible.
   b. Why pain relieving measures cannot be utilized.
   c. Number of animals to be used and why this is the minimal number of animals required.
   d. Whether animals will be euthanized when moribund and if not, what information is to be gained in the interval between moribundity and death.

2. A plan for the following animal care and monitoring procedures:
   a. Animals involved in experiments that may lead to a moribund condition or death will be monitored daily (including weekends and holidays) by personnel experienced in recognizing signs of morbidity (illness, injury, or abnormal behavior) for at least the following: abnormal posture, rough hair coat, head tucked into abdomen, exudate around eyes and/or nose, skin lesions, or abnormal breathing, difficulty with ambulation, decreased food or water intake, or self mutilation.
   b. The frequency of observation will be increased (including on weekends and holidays) when animals exhibit the above or other signs of moribundity. Designated personnel, including a veterinarian, should be notified as soon as animals show signs of disease. An assessment of the animals' condition should be made as soon as possible and a plan of action established.
   c. Consideration will be given to moving animals to individual cages when their condition deteriorates to the point that injury from other animals is likely. Dead animals must be promptly removed.
   d. Written records will be kept of monitoring.

**Recognizing Signs of Morbidity and Moribundity**

The following are signs for judging morbidity (disease/illness) and moribund condition (state of dying) in animals:

**Morbidity**

- Rapid breathing rate
- Breathing rate very slow, shallow, and labored (preceded by rapid breathing)
- Rapid weight loss
- Ruffled fur (rough hair coat)
Hunched posture
Body temperature less than 30°C (hypothermia)
Hyperthermia
Ulcerative dermatitis or infected tumors
Anorexia (loss of appetite)
Diarrhea or constipation

**Moribund Condition:**  Signs and symptoms for morbidity plus:

- Impaired ambulation (unable to reach food or water easily)
- Evidence of muscle atrophy or other signs of emaciation (body weight is not always appropriate)
- Any obvious severe illness including such signs as lethargy (drowsiness, aversion to activity, lack of physical or mental alertness), anorexia (loss of appetite, especially when prolonged), bleeding, difficulty breathing, CNS disturbance, or chronic diarrhea
- Inability to remain upright
- Loss of consciousness
- Drop in body temperature for a prolonged period (six hours)
Addendum
IACUC Policy on Humane Endpoints
Regarding HIV-Transgenic Rats

Background

HIV transgenic (tg) rats carry seven of the nine HIV genes and display alterations in neurological function. As they age the HIV-tg rats develop immunodeficiency, inflammation and AIDS-associated conditions. They are noninfectious due to the functional deletion of Gag and Pol within the HIV-1 provirus.

Purpose

This policy provides consistent and appropriate endpoints for all studies utilizing HIV-tg rats. The endpoints take into account the adverse clinical outcomes that are known to develop in these animals.

Policy

If it is judged by the Attending Veterinarian (AV) that an animal has met ANY of the established criteria, the animal will be removed from the study and euthanized. The AV or his/her designee will take reasonable steps to contact and consult with the principal investigator prior to removing and euthanizing an animal.

If there is a reasonable expectation that during the course of a research study, that the animals will reach any of the described endpoints, they must be placed in USDA Pain and Distress Category E. Exceptions to these endpoints may be granted by the IACUC; however, any exceptions will constitute departures from university policy and will be reported to OLAW annually.

Clinical Endpoints

1. Weight loss exceeding 20%.
2. Conjunctivitis or other ocular problems that do not respond to prescribed veterinary treatment within 7 days or that the Attending Veterinarian determines to be painful.
3. Recurrent vocalization when handled.
4. Dermatitis affecting greater than 10% of the body that does not respond to prescribed veterinary treatment within 7 days as determined by the Attending Veterinarian.
5. Inability to ambulate normally.
6. Hunched posture for greater than 48 hours
7. Labored breathing.
8. Bloodstained or mucopurulent discharge from any orifice.
9. Clinical signs consistent with organ failure (icterus, generalized or systemic edema, anemia, etc.)
10. Self-mutilation.
11. Presence of a tumor with any of the following: exceeding 40 mm in any direction, exceeding 10% of the non-tumor body weight, ulceration, interference with normal body movements or posture, necrosis.
12. Central nervous system disorder (e.g., seizures, tremors, paresis).
13. Reaching 20 months of age.