



## A. PURPOSE

To standardize the procedures for studies where death or moribundity is an experimental endpoint.

## B. GUIDELINES

Regulatory guidelines and humane considerations require that animal pain, distress and suffering be minimized in any experiment. Optimally, studies are terminated when animals begin to exhibit clinical signs related to the study procedures, if this endpoint is compatible with research objectives. Such endpoints are preferable to death or moribundity, as they minimize pain, distress and suffering.

The use of death or moribundity as an experimental endpoint in studies is strongly discouraged. The IACUC recommends the use of alternative endpoints where possible. Protocols incorporating the use of death or moribundity as an endpoint will receive additional review and approval may be granted on a case-by-case basis.

Note that at any time, University Animal Care veterinarians are authorized to provide necessary medical treatments or prevent pain and distress by humane euthanasia. University Animal Care veterinarians will attempt to notify the appropriate protocol personnel using the emergency contact information provided but note that such contact may not always be possible prior to providing medical treatments or performing euthanasia.

**If death or moribundity is necessary as an experimental endpoint, the PI must include the following information as part of the protocol:**

- A strong scientific justification for the necessity of death or moribundity as an experimental endpoint. This must also include details on the methods used to determine the absolute minimum number of animals required for statistical significance.
- A description of alternative, non-lethal endpoints that were considered and why they cannot be used. This includes, but is not limited to, diagnostic tests, physical appearance, specific clinical signs (e.g., bleeding, diarrhea, lethargy, neurological signs, persistent recumbency, prolonged hypothermia or hyperthermia, weight loss), and/or specific tumor burden (e.g., >20mm in any one dimension).
- A description of palliative therapies, including non-drug therapies (e.g., soft bedding, heating pads, easier access to food or water, alternate food types) provided or a justification as to why they must be withheld.
- In the case of death as an endpoint, what specific information will be gained in the period between moribundity and death?
- A detailed description and timeline of clinical signs and/or behavioral abnormalities that are anticipated to occur prior to death.
- The frequency and intervals at which the animals will be monitored by personnel skilled in recognizing these clinical signs and/or behavioral abnormalities.
- A description of the records that will be maintained of animal observations and the personnel responsible for the observation, including the name(s) of the individual(s) who will be responsible for the monitoring.

**Once the study is underway, the following must be performed:**

- The cages of the specific animals that are subject to death or moribundity as an experimental endpoint must be labeled to indicate that death or moribundity of the animal is expected, and the approximate time



frame in which this will occur.

- Animals must be monitored at least daily (including weekends and holidays). Animals may need to be monitored more frequently depending on the type of study.
- Records documenting the monitoring of these animals must be maintained and be available for review during IACUC inspections.
- Consideration should be given to moving animals to individual cages when their condition deteriorates to the point that injury from cage mates is possible.
- Dead animals must be removed from cages as soon as possible.

#### **Suggested signs and symptoms for judging morbidity (disease/illness) in rodents**

- Rapid weight loss (>20% in 1 week)
- Extended period of weight loss progressing to emaciation
- Diarrhea or vomiting if debilitating or prolonged (more than 3 days)
- Rough hair coat, hunched posture, distended abdomen, or lethargy if debilitating or prolonged (more than 3 days)
- Respiratory distress (dyspnea) or cyanosis
- Persistent cough, rales, wheezing, or nasal discharge
- Persistent bleeding from any orifice
- Persistent anemia leading to debilitation
- Distinct icterus (jaundice; yellow color to skin)
- Markedly discolored urine, polyuria, or anuria if prolonged (more than 3 days)
- Severe pain and/or distress
- 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
- Paralysis
- Persistent lateral recumbency
- Impaired mobility or lesions interfering with eating, drinking, or ambulation
- Tumors:
  - That are >10% of the animal's original body weight
  - With a mean tumor diameter >2 cm in mice
  - With a mean tumor diameter >4 cm in rats
  - That are ulcerated >1 cm diameter
- Extensive necrotic tissue or skin ulceration (10% body surface affected)
- Excessive or prolonged hyperthermia or hypothermia (more than 3 days)
- Persistent self-induced trauma
- Clinical signs of suspected infectious disease requiring a necropsy for diagnosis
- 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

### **C. REFERENCES, MATERIALS, AND/OR ADDITIONAL INFORMATION**

- [Guide for the Care and Use of Laboratory Animals pp 27-28](#)



**D. HISTORY (History page to be removed prior to publishing on website.)**

Effective Date	Version #	Authors	Description
04/08/2013	000	IACUC	New document
05/09/2016	001	IACUC	Revisions
03/11/2019	002	IACUC	New format