

TITLE:	Death as an Endpoint
Policy Number:	2014-032
Responsible Department:	Institutional Animal Care and Use Committee
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Purpose of Policy: To ensure that research animals are not subjected to unnecessary pain and suffering.

Policy Information: The [Guide for the Care and Use of Laboratory Animals](#) states that “The humane endpoint is the point at which pain or distress in an experimental animal is prevented, terminated or relieved” and that the use of humane endpoints contributes to the [3Rs](#) “by providing an alternative to experimental endpoints that result in unrelieved or severe animal pain and distress, including death.”

Death as an endpoint refers to observing or studying an animal until death occurs from some form of experimental treatment as occurs in LD₅₀ studies or certain studies involving deprivation of food, water or sleep. There are moral as well as legal guidelines that require that unnecessary pain and suffering in animals used in scientific experiments be avoided. Therefore, such studies will generally not be approved by the IACUC without extraordinary scientific justification that must include the following:

- A discussion of
 - alternatives that were considered,
 - why morbidity cannot be used instead of death as an endpoint, and
 - what additional information will be gained by using death instead of moribund condition as an endpoint.
- A clear statement of the number of animals needed and the statistical methods used to estimate the numbers of animals in each study group.

In the absence of clear, scientific justification for the use of death as an endpoint, investigators must euthanize animals prior to actual death. If the IACUC approves death as an endpoint, animals must be monitored at least daily, including weekends and holidays, by personnel trained in recognizing

signs of morbidity (see below). Specific indicators for the use of euthanasia must be included in the experimental design and must be clearly stated in the animal use protocol.

Common Signs of Illness, Injury, Pain or Disease

- Respiration very slow, very rapid, shallow or labored
- Rapid weight loss (such as 10% in 48 hours)
- A decrease in **body condition score** to <2
- Ruffled fur, hunched posture
- Hypothermia or hyperthermia based on measured body temperature
- Severe ulcerative dermatitis or infected/ulcerated tumors
- Diarrhea
- Impaired ambulation
- Lethargy/inactivity/decreased normal activity
- Neurologic signs e.g. seizures, ataxia, head tilt, circling
- Dehydration
- Ocular infections/discharge, persistent squinting

LD₅₀ studies, in which the dose of a drug or other toxic substance required to kill 50% of the animals in a group is determined, are considered cruel and wasteful of animals and are no longer considered acceptable by federal regulatory agencies. There are now statistical methods available that can reduce the number of animals required in an experiment without compromising experimental reliability.

The up-and-down procedure is an alternative to the traditional dose-response method that uses much fewer animals to determine an LD₅₀. In this procedure, animals are dosed one at a time. If an animal survives, the dose for the next animal is increased; if it dies, the dose is decreased. Computer programs are available to calculate the LD₅₀. Investigators are encouraged to discuss this alternative with the Attending Veterinarian when designing their experiments.