



IACUC Policy 600 : Experimental and Humane Endpoints Policy

1. Definitions of Key Terms Specific to this Policy

A. Experimental endpoint: terminal point of study that occurs when the scientific aims and objectives have been reached (Guide 2011)

B. Humane end point: the point at which pain or distress in an experimental animal is prevented, terminated, or relieved (Guide 2011)

2. Policy of endpoints

A. Developing Humane Endpoints

Humane endpoints should be selected based on their ability to accurately and reproducibly predict or indicate pain and/or distress, imminent deterioration, or death. It is required that specific humane endpoints be clearly defined in all animal protocols, and particularly for all Pain Category C D and E procedures. Humane endpoints should be determined in consultation with LAC-TU veterinarians.

Studies that commonly require special consideration for endpoints may include:

- Tumor development
- Infectious disease
- Vaccine challenge
- Pain and trauma modeling
- Monoclonal antibodies production
- Assessment of toxicological effects
- Models of cardiovascular shock
- Generation of animals with abnormal phenotypes
- Etc.

To develop a humane endpoint, the researchers should describe the clinical progression that a particular animal or group of animals is likely to experience as a result of experimental manipulation or spontaneously occurring disease during the animals' lifetime.

Research staff must be adequately trained in recognition of species-specific behaviors and, in particular, species-specific signs of pain, distress, and morbidity.

The selection of appropriate humane endpoints requires a detailed knowledge of the impact of the procedure on the animal to allow for intervention before unpredicted distress or pain develops. When novel studies are proposed or information for an alternative endpoint is lacking in the submitted protocol. Researcher need to conduct pilot studies to identify and define humane endpoints. The result should send to IACUC, and the veterinarian for reviewing.

B. Criteria of Humane Experimental Endpoints

Criteria used to end experiments on individual animals in order to avoid or terminate unrelieved pain and/or distress. Once a humane endpoint is reached, the animal should be immediately euthanized or treated as described in the approved protocol. The presence of one or more of the following criteria below may be indications for euthanasia. The professional judgment and decision of the Consulting Veterinarian will be final. The clinical signs, depending on severity and duration, that may constitute an endpoint include, but are not limited to: *this list is not exhaustive*

- **Hunched posture, lethargy, persistent decumbency** – This condition would indicate that an animal would not be able to reach for food/water. Animals should be euthanized within 24 hours of not being able to rise.

- **Rough or unthrifty hair coat** – healthy rodents fastidiously groom their hair coats.

- **Dyspnea** – labored breathing. A humane endpoint may be reached when animals show an altered respiratory rate and/or effort. Labored breathing is often accompanied by a strong abdominal component to breathing.

- **Dehydration** – as evaluated by skin turgor. Severe dehydration is manifested when an animal's skin loses elasticity. Skin pinched over the back that does not return to normal is called "tenting" and if this is excessive, it is considered a humane endpoint.

- **Anorexia/Weight loss** – A 20% weight loss over a few days would be considered rapid. This requires frequent monitoring. A gradual weight loss over an extended period of time (weeks to months), which leads to emaciation, would also be grounds for euthanasia. Degree of weight loss and monitoring frequency should be defined and described in the IACUC approved protocol.

- **Tumor size** – Tumor burden should not exceed 10% body weight in an adult rodent and/or 1.5 cm diameter in adult mouse or 3 cm in an adult rat. Tumor endpoints should also take into account the location of the tumor and the ability of the animal to ambulate. In addition, an endpoint is reached if the tumor ulcerates or is necrotic.

- **Abdominal Distension** – Animals will have enlarged abdomens and may have a difficult time breathing and/or ambulating.

- **Other clinical signs that may lead to a humane endpoint, depending on severity and duration** – Diarrhea, progressive dermatitis, jaundice and/or anemia, neurologic signs, bleeding from any orifice, self-trauma, circling or head tilt, limb paralysis, any condition interfering with eating or drinking, excessive or prolonged hyperthermia or hypothermia, prolapse of genitals or anus, malocclusion, and not response to external stimuli.

C. Other considerations for Establishing a Humane Endpoint

- **Surgery and post-procedural recovery**

Animals recovering from surgery or other stressful procedures usually lose body weight for a shorter or longer period of time. The IACUC will review any procedures or recoveries that would hinder that animal's ability to reach food and/or water. However, animals which are able to reach food and water may still lose weight due to loss of well-being and accompanying inappetence or due to pain. The investigators will need to address monitoring frequency for post-procedural recovery for potential pain and/or distress increase in animals in animal care and use protocol.

- **Pilot Study**

The selection of appropriate humane endpoints requires a detailed knowledge of the impact of the procedures on the animal. The IACUC reserves the right to request a pilot study if these factors are unknown.

- **Moribund Condition and Death as an Endpoint**

Moribund is defined as the condition that occurs immediately prior to death. The moribund state is preferred to death as an endpoint because it is assumed that euthanizing a moribund animal will help reduce terminal pain and/or distress; however defining moribundity is usually subjective. The continuation of a study until an animal dies is almost never acceptable. Strong scientific justification is required for such a study.