

**UNIVERSITY OF CALIFORNIA SAN DIEGO
INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE**

Policy on Experimental Neoplasia in Rodents

Purpose

The purpose of this document is to provide guidelines for the UCSD research community on experimentally induced neoplasia in rodents. Investigators producing tumors in rodents should use this document as a reference in preparing their Animal Care and Use Protocols. These guidelines may be reviewed and followed as written, or exceptions may be requested.

Policy

Legal, regulatory, and moral guidelines require that animal pain, distress, and suffering be minimized in any experiment. In order to minimize pain and distress in studies on experimental neoplasia in rodents, investigators must address issues concerning tumor burden, the status of the tumor (e.g. ulceration), and criteria for euthanasia. The following guidelines are intended to provide investigators with an indication of the standards and criteria for euthanasia that have been considered acceptable by the IACUC. The IACUC will evaluate an investigator's request for an exception to these policies. The scientific rationale for the exception must be clearly stated.

Tumor burden

In general, tumor burdens should not be so large as to interfere with ambulation, eating, drinking, defecating, and urination. Subcutaneous tumor burdens in rodents should not exceed 20% of the animal's body weight. In the case of a 25 gram mouse, this would represent a single subcutaneous nodule of approximately 2.5 cm diameter. Without a specific exception justified in the animal protocol, animals should be euthanized before tumors reach this size.

Tumor Status

Ulceration is often an inevitable complication of subcutaneous tumors. Animals with ulcerations or necrotic tumors must be sacrificed unless an exception has been approved.

Animals with skin ulcerations, particularly if immunocompromised, may have subclinical infections which can influence the tumor biology and confound experiments. The investigator must monitor animals with ulcerations at least daily. Animals must be sacrificed if the ulcerated tumor is painful (animal reacts to probing of the tumor) or if there is evidence of significant infection.

Monitoring of animals with tumors

In addition to the daily health checks performed by the animal care staff, documented daily health checks should be initiated by the investigator before the tumor begins to interfere with the physiological function of the animals.

It is a violation of federal guidelines if, on daily health checks by the animal care staff or the PI, the condition of the animal is found not to be in accordance with the approved protocol.

Criteria for Euthanasia

Investigators must administer euthanasia in moribund animals. The IACUC requires that an investigator judge when euthanasia is appropriate for moribund rodents based on objective signs. Some of the known signs of illness or dying which may be applied are shown below.

Examples of Clinical Signs for Judging Moribundity

- 1) inability to remain upright.
- 2) impaired ambulation (unable to reach food or water)
- 3) breathing rate very slow, shallow, and labored
- 4) any obvious prolonged illness including such signs as lethargy (drowsiness, aversion to activity, lack of physical or mental alertness), prolonged inappetence, bleeding, difficulty breathing, central nervous system disturbances, or chronic diarrhea or constipation
- 5) evidence of muscle atrophy or other signs of emaciation (body weight is not always proportionate)

Survival Duration

Death as an endpoint studies are generally not approved by the Institutional Animal Care and Use Committee. Investigators are expected to justify the use of death as an endpoint in the animal use protocol application and the written justification will be reviewed by the IACUC. If approved, investigators are expected to monitor animals at least daily in these studies including weekends and holidays.

The scientific justification for use of death as an endpoint must include:

1. what alternatives were considered and why moribundity can't be used in place of death
2. what additional information is gained in the interval between moribund condition and death
3. the number of animals in survival duration protocols should be clearly stated, as well as the statistical techniques used to estimate the numbers in the study groups.

The IACUC recognizes that unexpected results may occur and the Principal Investigator may need to apply for exceptions to these guidelines at a critical time period in an approved protocol. When an immediate change is scientifically justified, the PI needs to submit a protocol amendment.