	UCSD INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE POLICY MANUAL	POLICY 9.04 Originally Issued: 7.17.02 Revised: 11.17.04 Revised: 2.15.12 Revised 8.19.15
	Policy on Experimental Neoplasia	

I. Background and Purpose

Research animals are used to study cancer biology, to develop new therapeutic approaches, or to evaluate potential carcinogens. Many tumors grow rapidly and can compromise the health and well-being of the research animals. The IACUC emphasizes the need for frequent monitoring during neoplasia development to allow for appropriate intervention before significant deterioration of animal health or death occurs.

The purpose of this document is to provide general end points for experimentally induced neoplasia. Investigators should use this document as a reference in preparing their Animal Protocols. The standards described in this policy may not be applicable in all cases. Alternate standards should be clearly described and justified by the Principal Investigator in the protocol, and must be approved by the IACUC prior to start of study.

II. Who Should Read This Policy

Personnel who use neoplasia animal models

Personnel working in all animal activity areas

III. Definitions

Term	Definition
Neoplasia	The excessive proliferation of cells to form an abnormal mass of tissue or hematological malignancy
Experimental Neoplasia	Defined at UCSD as neoplasia which is induced through genetic manipulation, application of mutagens, injections of tumor cells, or surgical implantation of tumor cells. Excludes spontaneous, non-expected tumors of old age or those not related to the animal research * See section VI.
Ulceration	Lesion of the skin or of a mucous membrane that is accompanied by formation of pus and necrosis of surrounding tissue, usually resulting from inflammation or ischemia
Morbidity	A diseased state
Moribund	In a dying state; near death

IV. Policy

1) **Requirements for using tumor cells or cancer-causing agents:** Every tumor cell line, tumor source, or implantable material used for establishing tumors in animals must be:
   - Included on an approved IACUC protocol
   - Tested to ensure that they are free from pathogens, according to IACUC Policy 17.01 Use of Biologicals in Rodents (Biosecurity).
   - Approved for use on an appropriate hazard use authorization

- If primary human cells or material, approved for use by the Institutional Review Board of the Human Research Protections Program

2) **Cage labeling:** Cages must be labeled in such a way as to describe the experimental tumor model employed (genetically engineered mutation, exposure to carcinogen, cell injection). If applicable, the date the tumor was initiated and the expected latency period must also be indicated.

3) **Observation requirements:** The investigators must assess the overall condition of the animal including appearance, posture, and behavior. For solid tumors, inspection and palpation to locate the sites of tumor growth, distension, ulceration, and compromised mobility must be performed and documented.

4) **Frequency of monitoring:** The required frequency of monitoring increases as the animal begins to show evidence of tumor burden, as described below:

	Observations	**Monitoring**
Stage 1	No visible, palpable, clinical, or behavioral signs of tumor burden	WEEKLY
Stage 2	Visible or palpable tumors; Changes in appearance or behavior	2X/WEEK
Stage 3	Any signs of morbidity or mortality; Subcutaneous tumor diameter in excess of 1.5 cm (for mice) or 3.0 cm (for rats) as determined by the largest diameter	DAILY

5) **Record keeping:** Tumor monitoring data sheets must be kept within the housing room until the death of the animal. Records must contain all pertinent information, including the protocol number, the name of the person monitoring the animals, identification of the animals, date of monitoring sessions, and any treatments given to the animals. Baseline and weekly weights must be recorded; more frequent weighing may be indicated with some models.

6) **Allowable tumor burden and criteria for euthanasia:** The overriding consideration for humane endpoints must be the overall health of the animal. According to Policy 14.02, death-as-an-endpoint studies may only be performed after rigorous scientific justification and IACUC approval. Each of the below conditions requires euthanasia of the animal unless the investigator receives prior approval from the IACUC.

Immediate euthanasia is required:

- If an animal is unable to ambulate in order to obtain food and water
- If an animal displays unrelieved clinical signs of pain or distress
- If an animal reaches the moribund state
- If an animal has lost more than 20% of its pre-procedure body weight
- By order of the UCSD Attending Veterinarian
- For subcutaneous tumors:
    a. If a tumor becomes ulcerated or necrotic
    b. If a single subcutaneous tumor exceeds 2cm in diameter (for mice) or 4cm (for rats)
    c. If the combined Volume of multiple subcutaneous tumors exceeds $4cm^3$ (for mice) or $32cm^3$ (for rats), where Volume = ½ ($Width^2$ x Length)

V. Related Documents and References

UCSD Documents
Policy 14 Death as an Endpoint Studies Policy 26 Minimizing Pain and Distress in Animals Policy 17 Use of Biologicals in Rodents (Biosecurity)
Other Documents and References
James Wallace, 2000. Humane Endpoints and Cancer Research 2000, *ILAR*Journal, 41(2) http://dels.nas.edu/ilar_n/ilarjournal/41_2/CancerResearch.shtml NCI Frederick ACUC Guidelines Involving Experimental Neoplasia Proposals in Mice and Rats, 2006. Carstens E, Moberg GP. Recognizing pain and distress in laboratory animals. ILAR J 41:6271,2000. Dennis M. Humane endpoints for genetically engineered animal models. ILAR J 41:9498, 2000.

VI. Helpful Information

***Spontaneous, naturally occurring tumors**

Naturally occurring tumors or masses are also found in laboratory rodents, as well as in other animals including humans. These may include benign masses such as lipomas (usually benign unless interfering with a physiologic function), but can also be cysts, hematomas, abscesses or masses of various etiology. Animals being diagnosed with a non-experimental tumor or mass must be evaluated as soon as possible. Depending on the findings and the condition of the animal, the PI (in conjunction with the ACP veterinarian) may decide to euthanize the animal.

Rats and mice sometimes develop tumors as part of their genetic predisposition. Examples of these are mammary tumors in both rats and mice, pituitary tumors in aging Sprague-Dawley rats and interstitial cell tumors in male Fisher-344 rats. There are many others, most frequently seen as the animal gets older. Depending on the findings and the condition of the animal, the PI (in conjunction with the ACP veterinarian) may decide to euthanize the animal.

Training of Personnel and Research Staff

Scientific staff responsible for monitoring the animal on a neoplasia study should not only be familiar with normal animal health and behavior, but must also be able to observe adverse changes in health, behavior, or tumor burden. Specifically, since there are differences in normal behavior between different mouse and rat strains, the responsible research staff must be familiar with the animal(s) on study before the experiment begins.

Husbandry

Once animals show signs of tumor burden, it may be necessary to separate them and allow them more space to avoid disturbance from cage mates. They may require supportive care such as food on the cage floor. Nursing care may be given as indicated by the animal's condition and consistent with the research goals.