



**Duke University & Duke University Medical Center
Animal Care & Use Program
Policy**



**TUMOR POLICY
(Solid Tumors in Rodents)**

PERFORMANCE STANDARD: To prevent under distress or suffering of research animals while providing physiologically stable biologic models for cancer research.

BACKGROUND: Tumor (Cancer) implantation in research animals is a critically important experimental activity which also requires consideration of the effect of the tumor on the animal. The importance of limiting the discomfort, pain and distress animals may experience during the conduct of biomedical research is well recognized and the primary force behind the animal welfare regulations governing the use of animals in research. Outcomes of tumor studies, including death as an endpoint, vary depending on the species and strain of animals, the route of injection for transplantable tumors and the subsequent chemotherapy or other modality in cancer treatment studies. It is up to the investigator, who should be the most knowledgeable of the available models, to decide which alternatives to using live animals are necessary for a study and present these to IACUC for approval. Death as an endpoint may be allowed by the IACUC only after full consideration of alternatives and a subsequent finding that none are scientifically acceptable for the proposed outcome. At all times during this process, the well being of the research animals must be balanced against requirements of the study. Cancer studies can broadly be divided into two categories, biology and treatment:

- Cancer biology is the study of how tumors grow and behave. This policy is intended to limit the tumor burden an animal experiences to that which does not cause excessive pain or distress, but achieves the research goal.
- Cancer treatment is the study of the response of tumors to chemical, radiologic or immunologic therapy. In this class of study, not only must the tumor burden be considered, but the effect of the treatment modality must also be evaluated. The purpose of all cancer treatments, whether radiologic, immunologic or chemical is to destroy or disable the cancer cells while minimizing damage to healthy tissues. The success of a treatment becomes a balance between cancer destruction and reduction of side effects. Examples of Endpoints and Assessment Tools (end of this policy) may be used to assist with determining endpoints for hard tumor related activities.

ROLES:

1. Research and DLAR staff will abide by the position statement below unless there is documented PRIOR approval for an exemption by the IACUC.
2. Medical concerns or emergencies, as determined by the DLAR veterinary staff, may exempt an animal from these guidelines.
3. All exemptions shall be reported to the IACUC at the earliest opportunity.
4. Animals required to live in individual cages or in other non-routine conditions will require an amendment to the protocol for housing.

PROTECTIVE POSTURES REQUIRED: Personnel PPE will be worn as prescribed by the specific care facility management.

OUTLINE OF POLICY: This policy is for cumulative tumor burden per animal. If multiple tumors occur (an unusual situation), the total tumor burden cannot exceed the parameters noted below:

1. Animals showing any of the signs below will be euthanized, unless an exemption is provided by the Duke Attending Veterinarian or the IACUC:
 - a. Overall tumors volume exceeding:
 - i. Mice: 2000 mm³ in size (which is roughly 10% baseline body weight), or
 - ii. Rats: 5000 mm³ in size,
For the basis of this policy, tumors may be measured using the following formula:
$$TV = [(Width)^2 \times Length] / 2$$
 - b. Tumors that are ulcerated. If an exemption is provided for this condition, then the affected animals are required to be single housed (may require protocol amendment and / or alternate environmental enrichment or medical treatment),
 - c. Tumors where the animals chew on the lesion or pay undue attention to the ulcer,
 - d. Tumors that interfere with 'normal' mouse functions (e.g. eat, drink, or ambulate),
 - e. Tumor burden is greater than 10% of the baseline body weight (mice) or 5% of the baseline body weight (rats).
2. Other clinical signs that require veterinary intervention and are suggestive of tumor related disease such as metastases or ascites are extant:
 - a. Weight loss greater than 15%,
 - b. Significant abdominal distension, especially when it begins to compromise respiratory ability of animal,
 - c. Hunched posture with easily visible vertebral bodies,
 - d. Failure to eat or drink,
 - e. Absence (or abnormal) of fecal or urine output,
 - f. Rough hair coat,
 - g. Reluctance to move or abnormal gait,
 - h. Discharges or hemorrhage,
 - i. Abnormal behavior or vocalizations.

REFERENCES:

- Office for Protection from Research Risks (NIH) and Applied Research Ethics National Association. 1992. Institutional Animal Care and Use Committee Guidebook. NIH Publication No. 92-3415. B15-B17.
- Tomasovic SP, LG Coghlan, KN Gray et al. 1988. IACUC Evaluation of Experiments Requiring Death as an End Point: A Cancer Center's Recommendations. Lab Animal 17(1) : 31-34.
- Workman P, A Balmain, JA Hickman et al. 1988. UKCCCR guidelines for the welfare of animals in experimental neoplasia. Laboratory Animals 22:195-201. Montgomery CA. 1990.
- Oncologic and Toxicologic Research: Alleviation and Control of Pain and Distress in Laboratory Animals. The Cancer Bulletin 42(4):230-237.
- Browder EJ. 1995. Death as an Endpoint. In Current Issues and New Frontiers in Animal research. Greenbelt, MD: Scientists Center for Animal Welfare. pp 25-29.
- Olfert ED. 1995. Defining and Acceptable Endpoint in Invasive Experiments. AWIC Newsletter 6 (1) :3-7.
- Rygaard J. 1994 Animal Models in Cancer Research. In Handbook of Laboratory Animal Science, Vol. II. Boca Raton, FL: CRC Press, Inc. pp 199-205.

Examples of Endpoints and Assessment Tools

Experimental Endpoint	Example	Clinical Assessment
Tumor Size	Estimated tumor mass not to exceed 10% of body weight	Frequent measurements of solitary tumor (1 cm ³ = 1 gm)
Evidence of necrosis		Physical examination: scabbing, ulceration, exudate, anorexia, hypothermia, etc.
Evidence of sepsis		Restricted ambulation, inability to access food or water
Evidence of metastasis		Circling, blindness, dementia, convulsions
Evidence of local invasiveness		Inability to access or ingest food and water, inability to ambulate and keep clean
Physical Characteristics of Tumor(s)	Neurologic impairment	Evidence of dehydration
Tumor Location	Head/neck and extremities	
Moribund or Pre-moribund State	Define with specific clinical tests or signs	
Cachexia, Chronic Wasting	Weight loss >15% of normal body weight	Frequent weighing (3-5 times/week)
Respiratory		Dyspnea, rapid or labored breathing, coughing, rales
Cardiovascular		Shock, hemorrhage, anaphylaxis
Gastrointestinal		Diarrhea (>2 days' duration), vomiting
CNS		Circling, blindness, dementia, convulsions, unresponsiveness
Signs of Organ or System Failure	Integument	Extensive hair loss, inflammation, self-trauma