POLICY ON TUMOR BURDEN IN RODENTS

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

BACKGROUND/PURPOSE: 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 is the primary force behind the animal welfare regulations that govern the use of animals in research. Outcomes of tumor studies vary depending on the species and strain of animals, the route of injection for transplantable tumors, and the subsequent cancer treatment. Death as an endpoint may be allowed by the IACUC only after full consideration of alternatives, if the IACUC finds that none are scientifically acceptable for the proposed outcome. At all times, 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:
1. 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.
2. 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 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 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 allow exceptions from these guidelines for specific animals.
3. All exceptions shall be reported to the IACUC at the earliest opportunity.
4. Animals required to live in individual cages or under other non-routine conditions will require an IACUC-approve exemption from animal welfare standards for those conditions.
POLICY OUTLINE: This policy is for cumulative tumor burden per animal. If multiple tumors occur, the total tumor burden cannot exceed the parameters noted below:

1. Animals showing any of the signs below will be euthanized, unless an exception is provided by the Duke Attending Veterinarian or an exemption is approved by the IACUC:
   a. Overall tumors volume exceeding:
      i. Mice
         1. Total: 2000 mm$^3$ in size
         -- OR --
         2. Spherical tumors: >15 mm in diameter
      ii. Rats
         1. Total: 5000 mm$^3$ in size
         -- OR --
         2. Spherical tumors: > 21 mm in diameter
   b. Tumors that are ulcerated. If an exemption is provided for this condition, then the affected animals are required to be single-housed. This may require protocol amendment and / or alternate environmental enrichment or medical treatment.
   c. Tumors where the animals pay undue attention to or chew on the lesion.
   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). Body condition of the animal should be considered when using this parameter; tumor burden will be greater in animals with a lower body condition score.

2. Other clinical signs that require veterinary intervention and are suggestive of tumor-related disease such as metastases or ascites are present:
   a. Weight loss greater than 15%; Body condition of the animal should be considered when using this parameter; tumor burden will be greater in animals with a lower body condition score.
   b. Significant abdominal distension, especially if it begins to compromise respiratory ability of animal.
   c. Hunched posture
   d. Body condition score ≤ 2 (see Appendix A: Body Condition Chart).
   e. Failure to eat or drink.
   f. Absence of (or abnormal) feces or urine output.
   g. Rough hair coat,
h. Reluctance to move or abnormal gait,
i. Discharges or hemorrhage,
j. Abnormal behavior or vocalizations.

REFERENCES:

Appendix A: Body Condition Score Chart

BC 1
Mouse is emaciated.
- *Skeletal structure extremely prominent; little or no flesh cover.*
- *Vertebrae distinctly segmented.*

BC 2
Mouse is underconditioned.
- *Segmentation of vertebral column evident.*
- *Dorsal pelvic bones are readily palpable.*

BC 3
Mouse is well-conditioned.
- *Vertebrae and dorsal pelvis not prominent; palpable with slight pressure.*

BC 4
Mouse is overconditioned.
- *Spine is a continuous column.*
- *Vertebrae palpable only with firm pressure.*

BC 5
Mouse is obese.
- *Mouse is smooth and bulky.*
- *Bone structure disappears under flesh and subcutaneous fat.*

A "+" or a "-" can be added to the body condition score if additional increments are necessary (i.e. ...2+, 2, 2-...)