

## **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 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. Effective monitoring systems and endpoints should include limits on the tumor burden and severity of tumor-associated disease. This policy limits the tumor burden an animal experiences to that which does not cause excessive pain or distress, and are for cumulative tumor burden per animal. At all times, the well-being of the research animals must be balanced against requirements of the study.

## **POLICY AND PROCEDURE**

- **Tumor Type** - Because transplantable tumors, hybridomas, cell lines, and other biologic materials can be sources of murine viruses that can contaminate rodents, all transplantable murine tumors, must be assayed for contamination with adventitious murine viruses to prevent possible spread of pathogens into our rodent colonies. For more information, contact the Attending Veterinarian. All transplantable human tumor lines require Institutional Biosafety Committee (IBC) review and approval.
- **Tumor Location** – The site of the tumor implantation should be chosen to minimize damage to adjacent normal structures. The IACUC recommends implanting tumors on the dorsum or flank of an animal as these areas will likely have minimal or no site-related morbidity.
- **Tumor Size** - The visible size of the tumor is only one of the criteria used for determination of humane endpoint. The overriding consideration for humane endpoints of oncological experiments as well as spontaneous tumors must be the overall health of the animal. For subcutaneous tumors the maximum allowable size is 20 mm in diameter for a mouse or 40 mm diameter for a rat. If the animal is host to more than one tumor, this size is the maximum allowable size for all tumors combined.
- **Monitoring** - Animals that are on a tumor production study must be monitored by the investigators at least once a week during the time when the tumor is not yet detectable, to observe when tumor growth has begun. After a visual or palpable tumor is evident, the animals must be monitored by the investigator at least twice weekly. More frequent observations may be necessary based on tumor growth rate, study parameters, and general condition of the animal. Monitoring should include the overall condition of the animal including appearance, posture, behavior and physiological responses. Food and water intake must be recorded daily.

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- **Humane Endpoints** - Experiments should be completed before tumor development or tumor-associated disease causes death or a significant deterioration in the host. The overall well-being of the animal takes priority over precise tumor measurements in decisions regarding euthanasia or other interventions. In circumstances involving declining health status, morbidity, or unrelieved pain and discomfort, every attempt will be made contact the PI and to reach consensus with the PI bearing experimental endpoints in mind. However, the final analysis of when and if euthanasia is required is the responsibility of the Attending Veterinarian. The following clinical signs are indications of morbidity. The presence of one or more of the criteria below is indication for euthanasia:
  - Impaired mobility (the inability to reach food and water)
  - Inability to remain upright
  - Interference with a vital physiological function: This includes respiration, mastication, swallowing, urination, defecation or locomotion
  - Location of the tumor on the animal's ventral abdomen causing the tumor to be abraded or medial thigh interfering with locomotion
  - Hunched abnormal posture for > 48 hours
  - Labored breathing and cyanosis [bluish pinnae (ears), foot pads or mucous membranes]
  - Clinical dehydration ( $\geq 5\%$ ) and/or prolonged ( $\geq 24$  hours) decreased food intake
  - Muscle atrophy, signs of lethargy and lack of physical activity
  - Weight loss/Body condition score <2
  - Diarrhea or constipation for more than 48 hours
  - Hematological or biochemical values that indicate organ failure
  - Severe anemia [pale pinnae (ears), foot pads or mucous membranes]
  - Bloodstained or mucopurulent discharge from any orifice
  - Self-mutilation, lack of grooming behavior, or rough/unkept hair coat for >48 hours
  - Enlarged lymph nodes or spleen
  - Abdominal distension, ascites, or pleural effusion
  - Cranial deformity
  - Neurological signs (circling, seizures, weakness, restless/uncomfortable, altered level of consciousness)
  - Exophthalmos (bulging eye)
  - Skin pathology including ulceration or necrosis of tumor for  $\geq 48$  hours.

## **TRAINING**

Scientific staff responsible for monitoring the animal on tumor study should not only be familiar with normal animal health and behavior, but must also be able to observe adverse changes in

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**IACUC POLICY  
TUMOR PRODUCTION IN MICE AND RATS**

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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.

**EXCEPTIONS**

If there is a strong scientific justification for maintaining tumors exceeding any of the guidelines described above, then the investigator must specifically request an exemption from the policy and receive approval from the IACUC.

**REFERENCES**

Boston University IACUC Tumor Policy for Mice and Rats

<http://www.bu.edu/orccommittees/iacuc/policies-and-guidelines/tumor-policy-for-mice-and-rats/>

Duke University and Duke University Medical Center Animal Care and Use Program Policy on Tumor Burden in Rodents

[http://vetmed.duhs.duke.edu/PDF/Policies/Animal%20Use%20Policies/policy\\_on\\_tumor\\_burden\\_in\\_rodents.pdf](http://vetmed.duhs.duke.edu/PDF/Policies/Animal%20Use%20Policies/policy_on_tumor_burden_in_rodents.pdf)

Guide for the Care and Use of Laboratory Animals, 8<sup>th</sup> Edition (2011)

<http://grants.nih.gov/grants/olaw/Guide-for-the-Care-and-Use-of-Laboratory-Animals.pdf>

University of Pennsylvania IACUC Guideline on Rodent Tumor Production

<http://www.upenn.edu/regulatoryaffairs/Documents/iacuc/guidelines/iacucguideline-rodenttumorproduction.pdf>

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