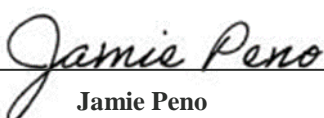
 <div> <div>DIVISION OF RESEARCH & INNOVATION</div> <div>Research Integrity & Compliance</div> </div>		Institutional Animal Care and Use Committee Standard Operating Procedures	
Title: Tumor Burden Guidelines			
Effective Date:	December 22, 2020	Document Number:	IACUC-SOP-02-14.00
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REVISION HISTORY			
Date	Section	Author	

PURPOSE

These guidelines are written to ensure that rodents with spontaneous and induced tumors are assessed frequently and managed to minimize pain and distress while at the same time accomplishing the research objectives; as tumor studies often rely upon the ability of the investigators and all parties involved being able to judge the signs of morbidity (disease/illness) in which the animal could recover from signs of moribund condition (state of dying).

SCOPE

It is the responsibility of the Principal Investigator and research personnel to follow these guidelines when conducting research with spontaneous and induced tumors of laboratory animals. In situations where the welfare of the animal is an issue and there is no clear agreement, the decision of the Attending Veterinarian concerning the treatment of the animal will be final, as designated by the federal Animal Welfare Act.

DEFINITIONS AND ABBREVIATIONS

UNT- University of North Texas, Denton

IACUC- Institutional Animal Care and Use Committee

SOP/SOP's- Standard Operating Procedure(s)

PI- Principal Investigator

LAF- Laboratory Animal Facility

AV- Attending Veterinarian

USDA- United States Department of Agriculture

PROCEDURES

- I. Animals should be monitored and tumors assessed at least three times per week until the tumor is palpable as a part of a monitoring plan. Once palpable, the animal and tumor should be observed at least once daily. Measuring the tumor dimensions with calipers is a reliable method of monitoring tumor growth. Body weight should be recorded at least twice per week.
 - A. In order to maximize study data acquisition and minimize animal pain and distress, the general health and welfare of test subjects will need to be continually and comprehensively assessed and documented as tumors and associated disease progresses. With these health assessments, veterinary staff in conjunction with research personnel can determine when euthanasia is appropriate for the animal. In the absence of responsible lab personnel, euthanasia will be performed at the discretion of the Attending Veterinarian or their designees.
 1. Animals should be euthanized if:
 - a) The mass severely restricts the animal's ability to eat, drink, eliminate wastes, breathe or move
 - b) The mass becomes necrotic or ruptures
 - c) Body fluid is excessive
 - d) The tumor weight vs. body weight exceeds 15%
 - e) Animal is becoming emaciated and/or loses more than 20% of their prestudy weight
 - f) There is a large mass around the head.
 - B. All induced tumor studies are recommended to be at least Category D due to the ulceration of tumors and the undetectable presence of metastatic cells.
 1. Pathogen free animals and tumor lines free of rodent viruses should be used.
 2. To address biosafety guidelines, all tumor cell lines must be MAP (Mouse Antibody Production) tested prior to injection into animals. All UNT safety and health guidelines will be followed in testing, handling, deriving and injecting all tumor cell lines.
 3. Tumor cells or promoters should be injected in such areas as subcutaneous sites on the back or flank where growth is not restricted.
 4. Animals should be isolated if tumors are found to be ulcerated, abraded and/or bleeding and the veterinarian and investigator contacted. Since superficial tumors can open, drain and even regress in size, there may be a significant individual variation in the response an animal has to a tumor burden; it is necessary to rely on experience and clinical judgment in assessing the need for euthanasia. If the tumor is excised, the animals must be able to ambulate and access food/water following the surgical procedure.
 5. For subcutaneous tumors, the maximum size allowed for a mouse is 20 mm in diameter and 40 mm diameter in a rat. If an animal has more than one tumor, these sizes are the maximum allowable sizes for all tumors combined.
 - a) If a tumor is required for study reasons to grow larger than these recommendations, scientific justification must be included in the animal use protocol.
 6. If death is to be used as an endpoint, the animals fall under USDA Category E and full scientific justification and documentation must be provided by the Principal Investigator and must be reviewed and approved by all voting members of the IACUC.
 7. When extended survival data are needed from a tumor model it becomes necessary to try to determine a specific point or parameter at which to record the animal as 'moribund' or as 'dead' without causing the animal needless distress or suffering.
 - a) Alternatives to painful procedures should be researched thoroughly before using death as an endpoint. Alternatives to death-as-endpoint studies can be determined

several ways.

- i. Determine a specific tumor size to designate as ‘moribund’ or ‘dead’
- ii. Determine a measurable concentration of a tumor marker associated with the model.
- iii. Use a scientific approach involving termination after a fixed period of time.
- b) Investigators using a tumor model to gather survival data should investigate a relevant parameter that will yield a statistically significant efficacy without jeopardizing the humane treatment of the animals, and will not necessitate the use of death as an endpoint.
- c) When assessing the health of animals utilized for cancer studies, the following clinical presentations warrant special attention as they indicate diminished health status that may result from increasing tumor burden and metastasis:
 - i. Weight loss and decreasing body condition
 - ii. Severe diarrhea
 - iii. Progressive dermatitis
 - iv. Rough hair coat, hunched posture, lethargic and/or recumbent
 - v. Respiratory-associated symptoms such as labored breathing, coughing and nasal discharge
 - vi. Icterus/Jaundice
 - vii. Hemorrhage from any orifice
 - viii. Neurological signs such as circling or ataxia
 - ix. Self-inflicted Trauma
 - x. Impairment of ambulation likely to interfere with access to food and water
 - xi. Ulceration and necrosis of visible tumors
- C. When assessing tumors in rodents, see the charts attached to this procedure and follow recommendations on vet care and/or euthanasia.

REFERENCES

- 1. The Guide for the Care and Use of Laboratory Animals.
- 2. Animal Welfare Act
- 3. Wallace, J. Humane Endpoints and Cancer Research

APPENDICES

IACUC Standard Operating Procedures

Mouse Tumor Scoring Chart

Rat Tumor Scoring Chart