

Institutional Animal Care and Use Committee		UNTHSC
Title: Scoring Endpoints in Tumor Studies in Rats and Mice		
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A. BACKGROUND INFORMATION

- a. Tumor (cancer) research in animals is an important experimental activity which also requires consideration of the effect of the tumor on the animal.
- b. This policy is designed to insure that rodents with induced tumors are assessed frequently and managed to minimize pain and distress while at the same time accomplishing the research objectives. The Principal Investigator will be consulted concerning the termination of any animal for humane reasons. 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.
- c. Tumor studies as well as all other studies should be done with minimal pain, distress, or suffering to the animals. Most tumor studies 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).

B. RESPONSIBILITIES

- a. Research staff and the Department of Laboratory Animal Medicine (DLAM) staff shall follow the procedures outlined below.

C. PROCEDURES

- a. Animals will be monitored and tumors assessed on 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.
- 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.
- c. Animals will 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.

- d. 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. If a tumor is required for study reasons to grow larger than these recommendations, scientific justification must be included in the animal use protocol.
- e. If death is to be used as an endpoint, full scientific justification and documentation must be provided by the principal investigator and must be reviewed and approved by all voting members of the UNTHSC IACUC.
- f. To address biosafety guidelines, all tumor cell lines must be MAP (Mouse Antibody Production) tested prior to injection into animals. All UNTHSC safety and health guidelines will be followed in testing, handling, deriving and injecting all tumor cell lines.
- g. 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. Alternatives to painful procedures should be researched thoroughly before using death as an endpoint.
- h. 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.
- i. 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.
- j. 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, the DLAM 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 facility veterinarian or their designees.
- k. The animals should be euthanized if:
 - i. The mass severely restricts the animal's ability to eat, drink, eliminate wastes, breathe or move,
 - ii. The mass becomes necrotic or ruptures,
 - iii. Body fluid is excessive,

- iv. The tumor weight vs. body weight exceeds 15%,
 - v. Animal is becoming emaciated and/or loses more than 20% of their pre-study weight,
 - vi. There is a large mass around the head.
- l. 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
- m. When assessing tumors in rodents, see the charts, attached below, and follow recommendations on vet care and/or euthanasia.

D. REFERENCES

- a. Wallace, J. Humane Endpoints and Cancer Research. ILAR 41(2), 2000

E. ATTACHMENTS

- a. Mouse Tumor Scoring
- b. Rat Tumor Scoring

Mouse Tumor Scoring

1. Appearance and Body Condition Score (BCS):

- BCS of 3: Normal; Score=0.
- BCS of 3: poor hair coat, decreased activity, normal posture and mobility; Score=2.
- BCS of 2: poor hair coat, decreased activity or hunched posture; Score=3.
- BCS of 1: poor hair coat, severe lethargy; Score=6.
- Moribund and/or severe cachexia; Score=19.

2. Tumor & degree of necrosis or ulceration (degree of ulceration to be determined by DLAM staff):

- Tumor \leq 7mm in any dimension; Score=0.
- Tumor \leq 7mm in any dimension with minor ulceration; Score=4.
- Tumor 7-17mm in any dimension; Score=9.
- Tumor \geq 18mm in any dimension, or abdominal distention; Score=12.
- Tumor \geq 20mm in any dimension; Score=14.

3. Bodyweight Change (for growing animals subtract percent deviation from normal growth pattern).

- No change from pre-tumor weight; Score=0.
- Weight loss of 5-10%, or gain of 5%; Score=9.
- Weight loss of 10-15%, or gain of 6-9%; Score=12.
- Weight loss of $>$ 15%, or gain of $>$ 10%; Score=15.
- Weight loss of $>$ 25%; Score=18.

BC1

Mouse is emaciated



- Segmentation of vertebral column prominent if not visible.
- Little or no flesh cover over dorsal pelvis. Pins prominent if not visible.
- Segmentation of caudal vertebrae prominent.

BC2

Mouse is under conditioned



- Segmentation of vertebral column prominent.
- Thin flesh cover over dorsal pelvis, little subcutaneous fat. Pins easily palpable.
- Thin flesh cover over caudal vertebrae, segmentation palpable with slight pressure.

BC3

Mouse is well conditioned



- Segmentation of vertebral column easily palpable.
- Moderate subcutaneous fat store over pelvic region. Pins easily palpable with slight pressure.
- Moderate fat store around tail base, caudal vertebrae may be palpable but not segmented.

<u>Cumulative Score</u>	<u>Recommended Action</u>
0-7	Routine monitoring adequate.
8-13	Routine monitoring adequate. Consider supportive therapy such as fluid administration and easy access to food.
14-17	Contact lab animal personnel to discuss action plan. Euthanasia is likely and should be considered.
$>$ 17	Contact lab animal personnel to discuss action plan. Euthanasia is warranted.

Rat Tumor Scoring

1. Appearance and Body Condition Score (BCS):
 - a. BCS of 3: Normal; Score=0.
 - b. BCS of 3: poor hair coat, decreased activity, normal posture and mobility; Score=2.
 - c. BCS of 2: poor hair coat, decreased activity or hunched posture; Score=3.
 - d. BCS of 1: poor hair coat, severe lethargy; Score=6.
 - e. Moribund and/or severe cachexia; Score=19.
2. Tumor & degree of necrosis or ulceration (degree of ulceration to be determined by DLAM staff):
 - a. Tumor \leq 20mm in any dimension; Score=0.
 - b. Tumor \leq 20mm in any dimension with minor ulceration; Score=4.
 - c. Tumor 20-34mm in any dimension; Score=9.
 - d. Tumor \geq 35mm in any dimension, or abdominal distention; Score=12.
 - e. Tumor \geq 40mm in any dimension; Score=14.
3. Bodyweight Change (for growing animals subtract percent deviation from normal growth pattern).
 - a. No change from pre-tumor weight; Score=0.
 - b. Weight loss of 5-10%, or gain of 5%; Score=9.
 - c. Weight loss of 10-15%, or gain of 6-9%; Score=12.
 - d. Weight loss of > 15%, or gain of > 10%; Score=15.
 - e. Weight loss of > 25%; Score=18.



- BC 1**
Rat is **emaciated**
- Segmentation of vertebral column prominent if not visible.
 - Little or no flesh cover over dorsal pelvis. Pins prominent if not visible.
 - Segmentation of caudal vertebrae prominent.



- BC 2**
Rat is **under conditioned**
- Segmentation of vertebral column prominent.
 - Thin flesh cover over dorsal pelvis, little subcutaneous fat. Pins easily palpable.
 - Thin flesh cover over caudal vertebrae, segmentation palpable with slight pressure.



- BC 3**
Rat is **well-conditioned**
- Segmentation of vertebral column easily palpable.
 - Moderate subcutaneous fat store over pelvis. Pins easily palpable with slight pressure.
 - Moderate fat store around tail base, caudal vertebrae may be palpable but not segmented.

<u>Cumulative Score</u>	<u>Recommended Action</u>
0-7	Routine monitoring adequate.
8-13	Routine monitoring adequate. Consider supportive therapy such as fluid administration and easy access to food.
14-17	Contact lab animal personnel to discuss action plan. Euthanasia is likely and should be considered.
>17	Contact lab animal personnel to discuss action plan. Euthanasia is warranted.