



THE UNIVERSITY OF TOLEDO
INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE

SUBJECT: Tumor Monitoring

DATE: April 6, 2020

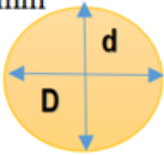
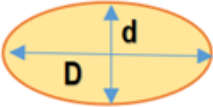
Rodent Tumor Monitoring Guideline

The *Guide for the Care and Use of Laboratory Animals* states that tumor models require special consideration of humane endpoints. Tumor induction in research animals is a critically important experimental activity which requires consideration of the effect of the tumor(s) on the animal. Effective monitoring systems and endpoints should include limits on the tumor burden and severity of tumor-associated disease. The use of altered physiological, biochemical, and other biomarkers is suggested as potentially more objective and reproducible endpoints than clinical signs. These guidelines limit the tumor burden an animal experiences to that which does not cause excessive pain or distress, and apply to spontaneous as well as experimentally induced tumors.

1. For all studies in which rodents have experimentally induced or implanted tumors, the expected size, clinical complications (e.g., ulceration or necrosis), experimental endpoints, and criteria for intervention or early termination of an animal from the study must be specified in the protocol for review by the IACUC.
2. Rodents used in tumor production studies must be observed and measurements recorded by laboratory personnel at least once a week from the time of cell/tissue inoculation until a visible or palpable tumor is observed.
 - a. Animals must be observed and measurements recorded by laboratory personnel at least twice weekly following observation of a visible or palpable tumor.
 - b. More frequent observations and measurements may be necessary based on tumor growth, study parameters, and general health of the animal. If environmental changes, diet restriction, or sleep deprivation are parts of the study design, more frequent monitoring may also be required following cell/tissue inoculation.
 - c. Observations must be spread out in equal intervals within the week.
3. Observations and measurements must include tumor size (mm or cm) and should include one or more of the following: body condition score, body weight, presence of tumor ulceration, presence of movement, moribund condition, relative tumor to body weight ratio.
4. Tumor monitoring records must be available to veterinary staff at all times.
5. Tumor size must not exceed 20mm (2.0cm) in any direction in an adult mouse and 40 mm (4.0cm) in adult rats (Figure 1)

- a. If multiple tumors are present, the combination of the two largest diameters may not exceed 2.0cm for mice and 4.0cm for rats.
6. The overall health and well-being of the animal take priority over precise tumor measurements in decisions regarding euthanasia or other interventions. General euthanasia criteria include:
 - a. Body condition score <2, see below
 - b. Weight loss > 20%
 - c. Tumor size equal to 15% of body weight (Figure 1)
 - i. The weight reference is the weight of the animal on the day of tumor implantation
 - ii. The mass of the tumor is calculated from the following formula:
 - iii. Mass (mg) = Tumor volume (mm³) = $d^2 \times D/2$ where d and D are the shortest and longest diameter in mm, respectively.
 - iv. Mass of tumor (g)/ Weight of the animal (g) x 100= % of body weight
 - d. Tumor ulceration
 - e. Discharge or hemorrhage from tumor
 - f. Tumor interferes with normal body functions, including but not limited to ambulation, eating, drinking, defecation, or urination; tumor negatively affects animal's gait or posture independent of tumor size
 - g. Labored breathing
 - h. Lack of movement
 - i. Hypothermia
 - j. Self-mutilation
 - k. Animals that in the opinion of the University Attending Veterinarian require euthanasia for humane reasons.

Figure 1: Mouse Tumors (25g animal)

Tumor examples	Mass of Tumor (mg) Tumor volume= $d^2 \times D/2$	Meets Criteria for end point?
d=20mm D=20mm 	$20^2 \times 20/2 = 4000\text{mm}^3$ or 4g Mean tumor size=20mm Tumor burden=4g/25g=16%	Yes-exceeds 15% body weight and mean tumor size 20mm
d=15mm D=25 mm 	$15^2 \times 25/2 = 2812\text{mm}^3$ or 2.8g Mean tumor size=20mm Tumor burden=2.8g/25g=11%	Yes-mean tumor size 20mm

References

1. *The Guide for the Care and Use of Laboratory Animals*, 8th Edition. National Research Council Committee for the Update of the Guide for the Care and Use of Laboratory Animals. Washington (DC): National Academies Press (US).
2. Ullman-Cullere, M. H. and C. J.Foltz. 1999. Body Condition Scoring: a rapid and accurate method for assessing health status in mice. *Lab Animl Sci* 49(3): 319-323.
3. Wallace, J. Humane Endpoints in cancer research. *ILAR Journal* 41: 87-93 2000

Body Condition Scoring



BC 1

Animal is emaciated

- Skeletal structure extremely prominent
- Little or no flesh cover
- Vertebrae, ribs, and pelvic bones distinctly segmented



BC 2

Animal is under-conditioned

- Segmentation of vertebral column evident
- Dorsal pelvic bones are readily palpable or observable



BC 3

Animal is well-conditioned

- Vertebrae and pelvis not prominent
- Ribs palpable under slight pressure



BC 4

Animal is over-conditioned

- Vertebrae palpable only under firm pressure
- Noticeable fat deposits over spine



BC 5

Animal is obese

- Animal is smooth and bulky, abdomen is distended
- Bone structure disappears under flesh and subcutaneous fat