

WVU IACUC Policy: Tumor Development Endpoints for Euthanasia in Rodents

Purpose and Background

This policy describes the expectations of the WVU Animal Care and Use Committee (IACUC) for monitoring tumor development and establishing humane endpoints for euthanasia in rodents with experimentally induced or spontaneously occurring tumors. “The identification of humane endpoints is often challenging, however, because multiple factors *must* be weighed, including the model, species (and sometimes strain or stock), animal health status, study objectives, institutional policy, regulatory requirements, and occasionally conflicting scientific literature.” (Guide, page 27).

The *Guide for the Care and Use of Laboratory Animals*, 8th ed (2011, *Guide*) states (p27): “While all studies should employ endpoints that are humane, studies that commonly require special consideration include those that involve tumor models, ...” The *Guide* also states (p123): “Criteria for euthanasia include protocol-specific endpoints (such as degree of a physical or behavioral deficit or tumor size) that will enable a prompt decision by the veterinarian and the investigator to ensure that the endpoint is humane and, whenever possible, the scientific objective of the protocol is achieved.”

The goal of this policy is to ensure that scientific objectives are achieved while adhering to humane endpoints for euthanasia, which generally require coordination and communication between research, husbandry, and veterinary staff. This policy provides standard euthanasia criteria which apply to all rodent protocols with tumors unless exceptions have been scientifically justified and approved by the IACUC.

Definitions

Experimental Endpoints: Endpoint of a study which occurs when the scientific aims and objectives have been reached (Guide p. 27)

Humane Endpoints: The point at which pain and distress in an experimental animal is prevented, terminated, or relieved.

Tumor Ulceration: A break in the skin overlying a tumor (open lesion or scabbed area).

Policy

1. Communication
 - a. Communication between laboratory faculty/staff and animal care/veterinary staff regarding tumor induction and anticipated outcomes are important to maintain animal welfare.
 - b. Tumor communication form (*see Appendix A*):
 - i. When a tumor study is initiated (induced or spontaneous) a colored dot sticker *must* be placed on the cage cards of all animals in that cohort/experiment.

- ii. A colored sticker **must** be placed onto the corresponding Tumor Communication Sheet maintained within the animal room. This sheet will outline site of cell injection, expected location of tumor growth, and humane endpoints for the study.
 - The sheet should be initiated at the time of tumor induction or weaning/arrival of strains with spontaneous tumors.
- iii. If hazardous agents are administered during a tumor study, the animals **must** be placed into designated hazard housing locations and cages appropriately marked with the compound they are receiving.
- c. Animals **must** be monitored at the frequency indicated in their approved IACUC protocol.
- d. Tumor burden records **must** be maintained and available upon request by the IACUC and vet staff for all tumor animals.
- e. OLAR husbandry and veterinary staff will monitor rodents for clinical condition using typical veterinary care standards.
 - i. Parameters include activity level, attitude, mobility, respiratory rate, hydration, body condition score, and ability to obtain food and water. Records will be maintained on Clinical Care cage cards.
 - ii. OLAR husbandry staff will assist with monitoring tumor burden during cage change and contact laboratories if tumor burden endpoints are reached.

2. Tumor Burden Endpoint

- a. Once humane endpoints for a tumor study are reached, the laboratory will have 24 hours to euthanize the animals if they remain in a stable condition.
- b. Subcutaneous Tumors (spontaneous or induced)
 - i. It is the laboratory's responsibility to monitor and adhere to the tumor burden endpoints described in this policy and their approved IACUC protocol.
 - ii. Tumors should be monitored frequently enough to ensure animals are not maintained beyond the described tumor burden endpoints.
- iii. Any one of the criteria below *could* lead to clinical intervention and/or euthanasia:
 - Tumor burden (single tumor)
 - The size of any single tumor should not exceed 10% BW (~20 mm diameter in mice or ~40 mm diameter in rats).
 - $\text{Volume (mg)} = (\text{Length(mm)} \times \text{width}^2(\text{mm}))/2$
 - Tumor burden (multiple tumors)
 - Multiple small tumors may not have the same impact on welfare as a single large tumor. The total volume of multiple tumors cannot exceed 15% BW or ~3000 mm³. All tumors **must** remain smaller than the tumor limit described for a single tumor (10% BW).
- iv. Body Condition Score <2/5 or body weight loss >20%.
- v. Tumor interferes with normal ambulation, ability to reach food/water, ability to eat/drink.
- vi. Tumor ulceration/infection/necrosis: If tumor ulceration occurs, veterinarians **must** be contacted and provide treatment recommendations to maintain animal welfare. Animals with ulcerated tumors **must** be euthanized when deemed necessary by veterinary staff. Euthanasia will be recommended if signs of infection are present, tumor size exceeds 5% BW, pain

- cannot be effectively managed, or treatment is deemed inappropriate/ineffective. If ulcerations are anticipated, this should be described and justified in the IACUC protocol.
- c. Metastatic/liquid/orthotopic tumors
 - i. Monitor frequently enough to ensure animals are not maintained beyond the described endpoints and are euthanized before a moribund state is reached.
 - Type and location of tumor will determine endpoints which are described in the animal use protocol.
 - ii. Criteria to consider when developing humane endpoints (may vary by tumor):
 - Lethargy
 - Difficulty ambulating/eating/drinking
 - Respiratory distress
 - Neurological signs
 - Body Condition Score <2/5
 - Body weight loss > 20%
 - Signs of anemia (pale, jaundice)
 - Ascites

References

[Guide for the Care and Use of Laboratory Animals](#), National Research Council, 2011.

Appendix A:

Tumor Communication Form

PI: _____

Protocol Number: _____

Sticker	Date	Number of Cages	Site of Cell Injection (write spontaneous if not induced)	Location of Tumor Growth	Humane Endpoints