UH IACUC Policy for Tumor Burden Studies in Mice and Rats

10/18/16 Michael Wong

IACUC Approved: 12/8/16	Other Approvals:
Revised and Approved:	

Tumors in research animals, whether protocol approved cancer study or spontaneous, can cause unnecessary pain and distress, and should be appropriately monitored with research animals being removed from a project when specific research end points are met, tumor size exceeds IACUC accepted level, or clinical signs and animal health dictate euthanasia.

All cells/tumors implanted or injected into rodents should be tested for infectious agents and determined to be pathogen free. Please contact AVS for assistance with determining pathogen free status of tumors.

Please use the following guidelines when writing your IACUC protocol:[1]

- Tumor size
    - Either a primary tumor size (e.g., for subcutaneous tumors the maximum size is 20 mm in diameter for a mouse and 40 mm in diameter for a rat; 5 mm in diameter for an intramuscular tumor in a mouse) or weight (4000 mg maximum for a mouse and 8000 mg maximum for a rat).
    - Please note that the total tumor mass burden (one or multiple tumors) cannot exceed this size restriction. Justification to exceed this restriction must be approved by the UH IACUC in advance.
    - The tumor size endpoint is recommended for spherical tumors while the tumor weight endpoint should be applied to oblong tumors. Tumor weight can be calculated by using the following formula (length and width in mm):

      (tumor length x tumor width x tumor width)/2 = weight in mg (or mm^3)

- Tumor Location
    - The site for injection of solid tumors should be carefully chosen to permit room for tumor growth and to avoid unnecessary distress whenever possible (e.g., subcutaneous flank or back are considered to cause the least distress).
    - As tumors located within the cranium, thoracic cavity, mouth, or behind the eyes may interfere with vital functions and result in morbidity or mortality, the maximum tumor size should be considerably smaller with assessment of overall health status taking priority. As the use of imaging or biomarkers may detect tumors before they are visible or can be palpated, consideration should also be given to the use of imaging in studies where the tumors are located at sites not readily observable.
- Humane Endpoints in tumor studies:
    - Tumor interferes with the animal's ability to eat and/or drink, or walk

    - 20% weight loss (emaciated appearance; rapid weight loss over two to four days; or progressive weight loss over a few weeks)
    - Tumor becomes ulcerated, infected, or necrotic with break of overlying skin (ulcerated and necrotic tumors can have an IACUC approval if in a regression study)
    - Palpation of tumor elicits a pain response
    - Animals become moribund, weak, comatose, unresponsive, or death appears imminent
    - Animal showing signs of respiratory difficulty
    - Animal showing signs of hypothermia (i.e., cold to the touch, pale extremities)
- If the protocol is Category E, define why analgesics cannot be used
- Monitoring procedures must be closely adhered to. The technical staff must be aware of the parameters of the study, such as tumor growth potential and whether a tumor is likely to become ulcerated. The Investigator must clearly define study parameters and endpoints in their Protocol and must provide guidance to the technical staff on all study matters.
- Requirement for monitoring will be dependent on tumor burden and study parameters.
    - In most cases, daily observation is acceptable, however, in situations where tumors may be affecting animal health and well-being, twice daily or more observations may be necessary.
- **For tumor regression studies**, careful attention should be paid to any animal exhibiting an ulcerated and/or necrotic tumor. To deter cannibalization, any animal exhibiting an ulcerated or necrotic tumor should be separated immediately and singly housed until tumor regression is complete. A watch card should be placed on each individual cage containing a mouse with an open tumor, recording the date of the tumor opening on the card. Personnel are responsible for ensuring adherence to (a)protocol approved regression timelines; (b) endpoints as described in the animal study proposal; (c) euthanasia if deemed necessary by the veterinarian after discussion with the PI due to the poor health and well-being of the animal.

References:

1. Guidelines Involving Experimental Neoplasia Proposals in Mice and Rats. https://ncifrederick.cancer.gov/lasp/acuc/frederick/Media/Documents/ACUC14.pdf