IACUC GUIDELINE: Guideline for the Detection and Handling of Solid Tumors in Rodents

SOP # 409 | IACUC Approval Date: July 13, 2016

Purpose:

This policy applies to investigators and staff working with Rodents in the Animal Care Facility (ACF) of the Texas A&M University - Commerce (TAMUC).

Definitions:

When used in this document with initial capital letter(s), the following word(s)/phrase(s) have the meaning(s) set forth below unless a different meaning is required by context.

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1. Policy

The Texas A&M University - Commerce requires animal research studies that include tumor (cancer) implants limit pain, distress and discomfort in research animals.

2. Procedure

In the following a general overview over the nature of cancer research studies including tumors will be provided and detailed information will be given as to how to assess tumor burden in research animals and when to seek veterinary assistance.

2.1. Background

2.1.1. Tumor (cancer) implantation in research animals is a critically important experimental activity which also requires consideration of the effect of the tumor on the animal. The importance of limiting the discomfort, pain and distress animals may experience during the conduct of biomedical research is well recognized and the primary force behind the animal welfare regulations governing the use of animals in research.

Outcomes of tumor studies, including death as an endpoint, vary depending on the species and strain of animals, the route of injection for transplantable tumors and the subsequent chemotherapy or other modality in cancer treatment studies. It is up to the investigator, who should be the most knowledgeable of the available models, to decide which alternatives to using live animals are necessary for a study and present these to IACUC for approval. Death as an endpoint may be allowed by the IACUC only after full consideration of alternatives and a subsequent finding that none are scientifically acceptable for the proposed outcome. At all times during this process, the wellbeing of the research animals must be balanced against requirements of the study.

2.1.2. Cancer studies can broadly be divided into two categories, biology and treatment:
2.1.2.1. **Cancer biology** is the study of how tumors grow and behave. This policy is intended to limit the tumor burden an animal experiences to that which does not cause excessive pain or distress, but achieves the research goal.

2.1.2.2. **Cancer treatment** is the study of the response of tumors to chemical, radiologic or immunologic therapy. In this class of study, not only must the tumor burden be considered, but the effect of the treatment modality must also be evaluated. The purpose of all cancer treatments, whether radiologic, immunologic or chemical, is to destroy or disable the cancer cells while minimizing damage and reduction of side effects. Examples of Endpoints and Assessment Tools, see Step 10, may be used to assist with determining endpoints for hard tumor related activities.

2.2. Roles

2.2.1. Research and TAMUC staff abides by the guidelines below unless there is documented prior approval for an exemption by the IACUC.

2.2.2. Medical concerns or emergencies, as determined by the TAMUC veterinary staff, may exempt an animal from these guidelines.

2.2.3. All exemptions must be reported to the IACUC at the earliest opportunity.

2.2.4. Animals required living in individual cages or in other non-routine conditions require an amendment to the protocol for housing.

2.3. Guidelines

2.3.1. These are guidelines for cumulative tumor burden per animal. If multiple tumors occur (an unusual situation), the total tumor burden cannot exceed the parameters referred to under 2.3.2.1.

2.3.2. Euthanize animals showing any of the signs below, unless an exemption is provided by the TAMUC Attending Veterinarian or the IACUC.

2.3.2.1. Overall tumors volume exceeding

- **2.3.2.1.1. Mice:** 2000 mm$^3$ in size (which is roughly 10% baseline body weight), or
- **2.3.2.1.2. Rats:** 5000 mm$^3$ in size.

**NOTE:** For the basis of this policy, measure tumors using the following formula:

$$TV = \frac{[(Width)^2 \times Length]}{2}$$
2.3.2.2. Tumors that are ulcerated. If an exemption is provided for this condition, then the affected animals are required to be single housed (may require protocol amendment and/or alternate environmental enrichment or medical treatment).

2.3.2.3. Tumors where the animals chew on the lesion or pay undue attention to the ulcer.

2.3.2.4. Tumors that interfere with 'normal' mouse/rat functions (e.g. eat, drink, or ambulate).

2.3.2.5. Tumor burden is greater than 10% of the baseline body weight (mice) or 5% of the baseline body weight (rats).

2.3.3. Other clinical signs that require veterinary intervention and are suggestive of tumor related disease such as metastases or ascites are extant:

   2.3.3.1. Weight loss greater than 15%
   2.3.3.2. Significant abdominal distension especially when it begins to compromise the respiratory ability of the animal.
   2.3.3.3. Hunched posture with easily visible vertebral bodies
   2.3.3.4. Failure to eat or drink
   2.3.3.5. Absence (or abnormal) of fecal or urine output
   2.3.3.6. Rough hair coat
   2.3.3.7. Reluctance to move or abnormal gait
   2.3.3.8. Discharges or hemorrhage
   2.3.3.9. Abnormal behavior or vocalization

2.3.4. Examples of endpoints and assessment tools

   In the following a brief overview over possible endpoints will be given along with a choice of examples for the respective endpoints.

   In the last column of Table 1 (Clinical Assessment) approaches for assessment of afore listed endpoints are mentioned.

NOTE:

For detailed information on the specific endpoints in each individual study please consult The Principal Investigator (PI) or see the study program for details.

When in doubt about endpoint assessment or specific clinical signs please consult the TAMUC Attending Veterinarian.
<table>
<thead>
<tr>
<th>Experimental Endpoint</th>
<th>Example</th>
<th>Clinical Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor size</td>
<td>Estimated tumor mass greater than 10% of body weight</td>
<td>Frequent measuring of solitary tumor $1 \text{ cm}^3 =1 \text{ gm}$ (explanation of gm?)</td>
</tr>
<tr>
<td>Evidence of necrosis</td>
<td>Tissue degeneration</td>
<td>Physical examination for/of scabbing, ulceration, exudates, anorexia, hypothermia, etc.</td>
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<tr>
<td>Evidence of sepsis</td>
<td>Pyrexia, depression</td>
<td>Observation of restricted ambulation, inability to access/ingest food and/or water</td>
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<tr>
<td>Evidence of metastases</td>
<td>Multiple tumor development</td>
<td></td>
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<tr>
<td>Evidence of local invasiveness</td>
<td>Multisystemic involvement</td>
<td></td>
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<tr>
<td>Physical characteristics of (internal) tumor(s), tumor location</td>
<td>Neurologic impairment (esp. head/neck and extremities)</td>
<td>Clinical evidence of blindness, dementia, convulsions</td>
</tr>
<tr>
<td>Moribund or pre-moribund state</td>
<td>Define with specific clinical tests or signs</td>
<td>Evidence of dehydration (prolonged persistence of skin fold)</td>
</tr>
<tr>
<td>Cachexia, chronic wasting</td>
<td>Weight loss &gt; 15% of normal body weight</td>
<td>Frequent weighing (3-5 times/wk)</td>
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<tr>
<td>Respiratory distress</td>
<td></td>
<td>Dyspnea, rapid or labored breathing, coughing, rales</td>
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<tr>
<td>- cardiovascular</td>
<td></td>
<td>Shock, hemorrhage, anaphylaxis, diarrhea (2 days duration), vomiting</td>
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<tr>
<td>- gastrointestinal</td>
<td></td>
<td></td>
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<tr>
<td>CNS</td>
<td></td>
<td>Clinical evidence of blindness, dementia, convulsions</td>
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</table>
Lack of responsiveness
Circling
Head tilt

| Signs of organ or system failure | Impaired integrity of integument | Extensive hair loss, inflammation, self-trauma |

**History:**
Version 00 - Petra Collyer
Initial Approval: