

Brigham Young University IACUC Guidelines

Date: August 17, 2016

University Veterinarian

Guideline XII: Policy on Tumor Production

1.0 Introduction

1.1 The purpose of this document is to provide general end points for experimentally induced neoplasia(tumors) in rodents. Investigators producing tumors in rodents should use this document as a reference in preparing their IACUC protocol form.

2.0 Background

2.1 Many tumors grow rapidly and can compromise the health and well-being of the research animals. If the tumor is subcutaneous or on the skin's surface, it can become large enough to interfere with the animal's locomotion, grooming, and ability to access food and water. In addition, these tumors can ulcerate and result in secondary bacterial infections. If the tumor is growing in the animal's abdominal or chest cavity, it can compromise respiration, food intake, and in some cases, locomotion.

3.0 Policy

3.1 It is the policy of the BYU IACUC to require that each project involving tumor production in rodents define a set of conditions under which the affected animals will be euthanized. Use of survival time as an end point is rarely justifiable and should be avoided. Animals should be euthanized before their tumor burden becomes excessive and before the animals become debilitated. Four general criteria for euthanasia are given:

- 3.1.1 Maximal tumor size should be limited to 10% of body weight. Mice which have subcutaneous or skin tumors should be humanely euthanized when the tumor reaches 2.0 cm in diameter. Rats should be euthanized if the tumor size exceeds 4.0 cm in diameter. If the animal is host to more than one tumor, this size is the maximum allowable size for all tumors combined. All animals should also be euthanized if a tumor ulcerates prior to reaching this size.
- 3.1.2 In some studies, either the tumor itself or anti-tumor therapies may cause the animal to lose condition. In these studies, adult animals should normally be euthanized if adult animals lose 20% of their original body weight, or if growing animals attain a weight less than 80% of untreated controls.

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- 3.1.3 Some tumors, depending on type and location, may interfere with the function of vital organs, such as the lungs or digestive tract. If animals are seen to be in distress (e.g. labored breathing) due to an experimentally induced tumor, they should be euthanized regardless of the size of the tumor or the weight of the animal.
- 3.1.4 In addition, some tumors may interfere with locomotion, making it difficult for the animal to reach food or water. If the animal is unable to eat or drink, it should be euthanized.

3.2 Monitoring Frequency

- 3.2.1 Animals in which tumors have been induced should be checked at least three times a week and weighed twice a week. -either by the principal investigator or his/her designee, Animals that fall into any of the four categories listed above should be reported to the principal investigator. The principal investigator will examine the animal and take appropriate steps within 24 hours of receiving such a report.
- 3.2.2 In the case of very rapidly growing tumors or other situations in which the progression of clinical signs is likely to be rapid or a tumor has reached 50% of the maximum allowable size or 1 cm in any dimension in mice and 2 cm in any dimension in rats, the principal investigator or his/her staff must examine the animal daily, including weekends and holidays and all findings documented. Animals in the terminal stages of tumor-associated disease or drug toxicity may require monitoring several times a day.

3.3 Training of Personnel and Research Staff

- 3.3.1 Scientific staff responsible for monitoring animals on the tumor study should not only be familiar with normal animal health and behavior, but must also be able to observe adverse changes in health, behavior, or tumor burden. Specifically, since there are differences in normal behavior between different mouse and rat strains, the responsible research staff must be familiar with the animals on study BEFORE the experiment begins.

3.4 The presence of one or more of the criteria below is indication for euthanasia:

- Impaired mobility (the inability to reach food and water)
- Inability to remain upright
- Interference with a vital physiological function: This includes respiration, mastication, swallowing, urination, defecation or locomotion
- Location of the tumor on the animal's belly or its inner leg causing the tumor to be abraded or interfering with locomotion
- Hunched abnormal posture for > 48 hours

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- Labored breathing and cyanosis [bluish pinnae (ears) or feet or mucous membranes]
- Clinical dehydration and/or prolonged decreased food intake
- Muscle atrophy and signs of lethargy and lack of physical activity
- Weight loss/Body condition score <2
- Chronic diarrhea or constipation for more than 48 hours
- Hematological or biochemical values that indicate organ failure
- Severe anemia [pale pinnae (ears) or feet or mucous membranes]
- Bloodstained or mucopurulent discharge from any orifice
- Self-mutilation; Lack of grooming behavior/Rough/Unkempt hair coat for >48 hours
- Enlarged lymph nodes or spleen
- Significant abdominal distension
- Cranial deformity/Neurological signs
- Exophthalmos (bulging eye)
- Skin pathology including ulceration or necrosis of tumor for > 72 hours.
Ulcerated or necrotic tissue may result in a continuous loss of body fluid and/or infection.
- Restlessness/Unable to get comfortable
- Unconsciousness with no response to external stimuli