

**UIC** UNIVERSITY OF ILLINOIS  
AT CHICAGO  
**GUIDELINES – Tumor  
Growth and Cancer  
Research**

Version 2.1

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## I. Introduction

The UIC Animal Care Committee (ACC) is charged with evaluating and ensuring that research projects are conducted in accordance with the Animal Welfare Act and the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals. These regulations and policies require that any research, testing and teaching that uses animals be performed in such a way as to minimize discomfort, distress and pain consistent with sound research design.

The UIC-ACC has adopted the position that animals with local or disseminated tumors are likely to experience pain and/or distress. The UIC-ACC also recognizes that many questions in oncology research can only be addressed using in vivo models. Therefore, the ACC has developed the following guidelines to assist investigators with the process of completing the UIC Protocol for Animal Use and to assure animal welfare issues are appropriately addressed. The ACC recognizes that tumor biology, tumor inoculation sites, mode of growth and associated treatments preclude the establishment of a rigid set of guidelines for studies involving tumor models. Therefore, the ACC reserves the right to evaluate each protocol using tumors on an individual basis.

## II. Institutional Guidelines

The following guidelines should be considered and incorporated in the development of a protocol using tumors in vivo.

- 1. Tumor Kinetics** - The selection of appropriate humane endpoints requires a detailed knowledge of the biology of the proposed tumor model, including an understanding of the growth characteristics of the tumor, the onset and nature of any adverse effects on the animals, and the patterns of local invasiveness and/or metastasis. If these factors are not known, a pilot experiment may be required by the ACC to establish these criteria.
- 2. Viral Status** - Cell lines or tumor tissues may be contaminated with viruses that can serve as a source of infection for animals in a colony or may confound experimental results. Therefore, they should be tested for the presence of contaminating viruses (i.e., ectromelia, Sendai virus, mouse hepatitis virus, lactic dehydrogenase virus) prior to being introduced into an animal. All cost associated with testing is the responsibility of the investigator. Animals inoculated with cell lines known to contain virus must be isolated from the rest of the colony.
- 3. Solid Tumor Inoculation** - In order to minimize trauma to the animal, solid tumors should be dispersed or minced into fine pieces prior to transplant. For mice, the transplantation of tumor fragments < 1mm is preferred and transplantation of larger fragments (up to 3 mm) may require anesthesia and/or surgical incision.
- 4. Transplantation Site** - Careful consideration should be given to selecting a transplant/inoculation site. Whenever possible, the tumor should be placed into a site where it can grow with minimal impact on the animal's ability to ambulate and perform normal bodily functions. Moreover, the site should allow for ready assessment of the tumor. The caudal flank is one recommended site. Whenever possible the use of muscle as an inoculation site should be avoided as distension of muscle is considered painful.
- 5. Monitoring Criteria** - The ACC recommends that experiments should be terminated at the earliest time

point possible. For example, if the experimental goal is to induce a tumor, the experiment should be ended as soon as a tumor is detected. Alternatively, if the experimental goal is to analyze a treatment procedure, then evidence of tumor growth in the face of treatment should serve as an endpoint. For any protocol, the experiment should be terminated prior to the animal becoming debilitated.

- a. Animals should be observed with a frequency that allows for euthanasia to occur prior to the tumor ulcerating or achieving a size that interferes with normal activity. The ACC may require a pilot study to develop an appropriate monitoring schedule if the growth characteristics and sequela of the tumor of interest are not known.
- b. Experiments should be terminated before a tumor reaches a predetermined size. In general, the tumor size should not exceed 15% of the body weight. For a mouse the approximate maximal diameter is 2 cm.
- c. The tumor should not invade surrounding tissue to the extent that the tumor mass interferes with normal bodily functions, causes pain or distress due to its location or provokes persistent self-trauma.
- d. Experiments should be completed before any ulceration occurs. Ulceration is most likely to occur when a tumor develops in the subcutaneous or dermal tissue of the host or from abrasion caused by a large tumor on the ventral surface. The ACC recognizes that certain tumor types and cell lines are predisposed to ulceration and it may be necessary to maintain an animal with an ulcerated tumor. In this case, the status of the ulcerated tissue and the animal's condition must be assessed daily.
- e. Mature animals should be euthanatized prior to losing 20% of their body weight. The weight loss should take into account the tumor mass. In some cases, such as with young growing animals, a change in body-condition score rather than weight loss may more accurately reflect the animal's general condition (see UIC ACC Guidelines for Humane Experimental Endpoints). In certain cases the development of a generalized diseased or debilitated state may be anticipated. For such cases, the UIC ACC Guidelines for Humane Experimental Endpoints should be consulted.
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### III. Protocol for Animal Use

The following items should be addressed on the UIC Protocol for Animal Use:

1. Form A, complete item 7b if murine tumor lines will be used. If human tumor lines will be used, complete item 7a.
2. Form A, item 8g, include a description of the experiment in its entirety from inoculation until the endpoint, including tumor kinetics.
3. Form A, mark item 12a "Yes". A response of "Yes" requires that Form A, item 13 as well as Form B be completed.
4. Form A, item 13 should include a justification for the procedure and a description of the resources used to determine that an alternative for the potentially painful or distressful procedure, including the use of an in vitro system, computer model or less sentient animal, is not available.
5. Form B, complete item 9, and include a description of the duration of the study, the monitoring frequency, the endpoint of the study and a justification for the model.
6. Form B, complete item 11 if death or a diseased/debilitated state is the endpoint.

**Additional Reading:**

- *Workman P., Twentyman P., Balkwill F., Balmain A., Chaplin D., Double J. Embleton J., Newell D., Raymond R., Stables J., Stephens T. Wallace J. (1998). United Kingdom Coordinating Committee on Cancer Research (UKCCCR Guidelines for the welfare of animals in experimental neoplasia (2nd ed,). Br J Cancer 77:1-10.*
- *Canadian Council on Animal Care (1998). Guidelines on choosing an appropriate endpoint in experiments using animals for research, teaching and testing. Ottawa Ontario Canada: CCAC*
- *National Research Council (2000). Humane endpoints for animals used in biomedical research and testing. Institute for Laboratory Animal Research Journal 1(2)*
- *Tomasavic S.P., Coghlan L.G., Gray K.N., Mastromarino A.J., and Travis E.L., (1988). IACUC Evaluation of Experiments Requiring Death as an End Point: A Cancer Center's Recommendations. Lab Animal (Jan. - Feb.) 31-34.*