GUIDELINES FOR SOLID TUMOR STUDIES IN RODENTS

These guidelines are intended for investigators whose studies involve the induction of solid tumors in rodents. As a general rule, tumor studies in rodents should incorporate the earliest endpoints compatible with the scientific requirements of the study. Protocols that require morbidity or death as an endpoint are *strongly discouraged* and are unlikely to be approved without very strong and compelling scientific justification.

Tumor Inoculations:

- In order to minimize trauma to the animal, solid tumors should be dispersed or minced into fine pieces prior to transplant. For mice, transplantation of tumor fragments < 1mm is preferred. Transplantation of larger fragments (up to 3 mm) may require anesthesia and/or surgical incision and will require strong scientific justification for approval.
- Careful consideration should be given to selecting a transplant/inoculation site on the animal. Whenever possible, the tumor should be placed into a site where it can grow with minimal impact on the animal's ability to ambulate, feed and perform normal bodily functions. Moreover, the site should allow for ready assessment of the tumor. The caudal flank is one recommended site. The use of muscle as an inoculation site should be avoided when possible since distension of muscle is painful.
- Cell lines or tumor tissues may be contaminated with viruses that can serve as a source of infection for animals in a colony or that may confound experimental results. Therefore, they should be tested for the presence of contaminating viruses (i.e., ectromelia, Sendai virus, mouse hepatitis virus) prior to being introduced into an animal. The IACUC will require that cell lines be tested for contamination prior to approval.

Endpoints for Tumor Studies:

As a general rule, animals should be euthanized before their tumor burden becomes excessive and before they become debilitated or moribund. The IACUC Guidelines on Humane Endpoints should be consulted for additional information. The following are endpoint criteria specific to tumor load studies:

- The maximal tumor size should be limited to 10% of body weight.
- Animals which have subcutaneous or skin tumors should be humanely euthanized when the tumor reaches 1.5 centimeters in diameter for mice or 4 centimeters in diameter for rats.
- Animals with a tumor where the overlying skin has ulcerated, or where the tumor or surrounding area has become necrotic or infected should be euthanized.
- Animals whose tumor interferes with the function of vital organs, such as the lungs or digestive tract should be euthanized, regardless of the size of the tumor.
- Animals unable to obtain food or water because the tumor interferes with locomotion, chewing or swallowing should be euthanized.
- Animals in which either the tumor, or anti-tumor therapies that may be part of the experiment, cause the animal to lose 20% of their original body weight should be euthanized. If tumor induction is done in young animals, animals that fail to attain a weight of at least 80% of untreated controls should be euthanized.
- Animals exhibiting signs of pain or distress, or animals that engage in self-trauma (cannibalizing tumor or surrounding tissue) should be euthanized.

Experimental and scientific demands may require exceptions to these guidelines but such deviations must be clearly described and scientifically justified in the protocol.

Monitoring:

Animals in which tumors have been induced should be checked at least three times weekly - either by the PI or by his/her designee. Animals that fall into any of the categories listed above should be reported to the PI who must take appropriate steps within 24 hours of receiving such a report.

In the case of very rapidly growing tumors or other situations in which the progression of clinical signs is likely to be rapid, animals should be examined daily.

The IACUC recommends that a dedicated record be kept in the animal housing room when tumor studies are in progress. This document should record date of transplant, monitoring frequency, tumor size, body weight, and animal condition. The BRF staff should also be informed prior to the initiation of such experiments.

The veterinarian, by law, has final authority in animal care and use and can make a decision to euthanize any animal. Of course the BRF veterinary and animal care staff will make an effort to work with the PI in difficult cases to balance animal welfare with the scientific objectives of the study. Emergency contact information for the PI should be provided on the animal protocol as well as to the BRF staff.