Subject: Defining Humane Endpoints

BACKGROUND

Animals used in biomedical research may at times display signs of pain or distress related to the experimental protocol. A balance must be achieved between minimization of pain and distress, which is mandated by moral and ethical obligation, the Animal Welfare Act, and Public Health Service Policy, and the need to obtain reliable, reproducible data. This is best achieved by the use of endpoints, or criteria used to define when an animal is to be removed from a study. Death as an endpoint is strongly discouraged and requires sound scientific justification and IACUC approval. Rather, the use of clinical, behavioral, and physiological signs which may predict death or a moribund state are encouraged whenever possible. This requires knowledge of species specific symptoms and the course of the disease condition.

IACUC Guidelines

**Examples of criteria that establish when the endpoint has been reached include:**

1. Evaluation of five aspects of an animal’s condition. These include body weight, physical appearance, measureable clinical signs, unprovoked behavior and response to external stimuli.
2. Clinical observations used in cancer research and toxicological studies. Parameters include changes in general appearance, skin, hair, eyes, nose, mouth and head, respiration, urine, feces and locomotion.
3. Body condition scoring

**Specific examples of clinical signs used as endpoint criteria in some experiments include:**

1. Weight loss (either rapid or chronic; meeting or exceeding 20% body weight of age matched controls)
2. Hypothermia: a decrease of 4 – 6 degrees C has correlated with impending death in several disease models; body temperature monitoring can be accomplished using infrared scanners or implanted microchips
3. Clinical conditions (rough hair coat, hunched posture, lethargy or recumbency, coughing, nasal/ocular discharge, labored breathing/respiratory distress) unresponsive to treatment
4. Significant self-induced trauma
5. Any condition which interferes with the ability to eat/drink or ambulate
6. Tumor which exceeds 5-10% of the animal’s body weight or is ulcerated*

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Protocols involving pain or distress that may lead to early euthanasia must clearly identify which criteria or clinical signs will be employed to ascertain that the endpoint has been reached and the animal(s) must be euthanized. Plans for monitoring and monitoring frequency must be included. Provisions for the animal's comfort and care prior to removal from study must be fully described; identify who will provide this care. These plans should be developed as a component of the veterinary consultation required during protocol preparation.

*Ulceration or necrosis of tumors may develop due to continuous abrasion of the tumor surface or if the tumor has outgrown its blood supply. However, certain tumor types (e.g. papillomas, or tumors of ductal origin) and some cell lines may be predisposed to ulceration. “When ulceration is characteristic of the tumor line, the aim should be to complete the experiment in the latent period before ulceration. As soon as a tumor has ulcerated, the growth pattern will alter, which may be sufficient grounds for terminating the experiment. Ulcerated or necrotic tissue may result in a continuous loss of body fluid and/or infection. When it is necessary to maintain an animal with an ulcerated tumor, both the status of the ulcerated tissues and the animal's overall condition must be assessed daily.”