Help with Pain, Distress and impairment and Endpoints

Your protocol must describe what will be done with animals that experience pain, distress or impairment, whatever the cause. Routine handling, and procedures that may result in momentary pain or stress (*e.g.,* routine injections) when done properly need not be discussed. These are procedures for which you would not routinely provide anesthesia. However, you must discuss all procedures for which you anesthetize animals because you are using the anesthesia to minimize pain and distress.

In many cases, the investigator does not **expect** the procedures to cause more than momentary pain or distress, but there is the possibility that animals might become ill (e.g. injection of substances for which effects are not know, production of small tumors, irradiation, surgery). UCAR policy requires that any animal exhibiting significant weight loss (e.g. 10%), inability to ambulate, inability to maintain food or water intake, and clinical signs of pain, including ruffled fur, hunched posture, vocalization, and guarding behavior, be removed from the study, euthanized or provided with supportive care. Therefore, you must describe in your protocol symptoms that your animals might develop based on the treatments they will receive, and state what will be done with animals that meet UCAR clinical endpoints. If such animals must be maintained without intervention, you must provide a scientific justification for doing so.

Experimental pain, distress or impairment may include any physical, physiological or pathological damage (temporary or permanent) resulting from treatment of animals with

a hazardous agent,

radiation,

physical or chemical restraint longer than a few minutes duration to facilitate either substance administration or specimen collection,

aversive conditioning (*e.g.*, food/water scheduling or sensory deprivation),

use of adjuvants;

chronic insertion or attachment of a foreign object (*e.g.*, osmotic pump or electrodes), or

recovery surgery.

For transgenic, knockout, or mutant animals, there may be known or predicted phenotypic consequences of the genetic manipulations to the animals that impair normal physiological functions.

Examples of procedures that result in pain distress or impairment include:

Muscle Paralysants (paralytic agents): See instructions in the Procedure Checklist, and discuss the use of paralytic agents with a DLAM veterinarian before submitting your protocol.

Aversive Conditioning, Food or Water Scheduling: If any form of aversive conditioning (*e.g.*, footshock) is proposed, describe the aversive condition qualitatively and quantitatively. If access to food or water is restricted in any manner, scientific justification is required. Describe in detail the criteria you propose to use to determine that each animal, so restricted, receives adequate dietary and fluid intake. DLAM veterinarians have developed an acceptable record-keeping procedure that places the responsibility on the PI or on Vivarium animal care technicians. A daily feeding or watering log for each individually housed animal must be kept. All water restricted animals must be weighed at least once a week and weight records must be maintained by the PI. A statement indicating that these procedures will be followed must appear in the protocol. Consultation with a DLAM clinical veterinarian or Vivarium Supervisory personnel in developing and implementing any restricted or scheduled food or water regimen

is highly recommended. If the creation of caloric or other specific nutritional deficiency is an intrinsic part of the proposed study, you must provide a rationale and description for it in the protocol.

Sensory deprivation: If any form of sensory deprivation is proposed, scientifically justify and describe in detail the duration, extent and known or anticipated effect of the sensory deprivation.

Harmful physical agents: Harmful or potentially harmful physical agents include irradiation, microwaves, radio frequency waves, thermal injury, physical injury, environmental injury, such as high levels of sound or ultrasound, high or low temperature, high or low barometric pressure, ultrasound, high intensity light or exposure to potentially damaging wavelengths of light. Please scientifically justify the use of such physical agents and describe the conditions of exposure, the amount (in units appropriate to the agent), duration and frequency of exposure, and the expected effects of such exposure.

Experimental endpoint studies: Such endpoints may include tumor size, percentage body weight gain or loss, inability to eat or drink, behavioral abnormalities, clinical symptomatology, or signs of toxicity.

Death-as-an-endpoint studies

are discouraged and must always be scientifically justified. This justification must include a discussion stating why endpoints short of death cannot be used.

Help with Procedures to minimize pain, distress or impairment:

For transgenic, knockout or mutant animals, describe any special care or monitoring that the animals will receive. Examples include increasing the frequency of monitoring, euthanasia of animals expressing premature lethality, providing supportive care such as soft food to toothless mice, delaying weaning time for pups with stunted growth, or providing foster moms to replace dams with abnormal mammary gland development.

Procedures to minimize pain/distress may include; analgesics or other drugs to prevent or reduce perception of painful stimuli, physical or environmental changes to reduce discomfort or injury, and general anesthesia. If general anesthesia is used, describe the methods used to assess a surgical plane of anesthesia.