Humane Endpoints

Animal studies may involve procedures that cause pain or distress to the animals, which cannot be alleviated with analgesia, anesthesia, sedation, or palliative care. In these cases, the application of a humane experimental endpoint is required. The phrase humane endpoint\(^1\) refers to the termination of an experiment, and humane euthanasia of the animal, in order to minimize the pain, distress, or suffering experienced by the animal, while still achieving the scientific goal.

Any animal experiment with the potential for pain or distress (e.g. administration of tumor cells, infectious agents, or toxic chemicals; induced or spontaneous mutations causing pain or distress) should have a humane experimental endpoint, which requires:

1. A review of as much information as possible about the substance to be tested, or the gene of interest in the case of genetic mutations, or the disease process being modeled, in order to prospectively identify any expected and possible adverse effects the research animals may experience.

2. Determination of the most accurate signs of a painful or distressful state, which should involve consultation with the veterinarian.

- Accurate clinical signs are often based on measurable parameters (e.g. body temperature, and body weight), and subjective criteria (e.g. physical appearance, unprovoked behavior, and response to external stimuli).\(^2-4\)

- Changes in physical appearance or behavior, which generally constitute a humane endpoint and would require that the animal be euthanized in order to avoid any further pain, distress or suffering include, but are not limited to:
  
  - Inability to eat or drink, or prolonged (>48 hours) inappetance or dehydration.
  
  - Impaired mobility, inability to maintain a normal postural position (i.e. hunched posture), or loss of righting reflex.
  
  - Prolonged inactivity, or unresponsive to external stimulus such as gentle prodding.
• Signs indicating organ failure or shock such as respiratory distress (e.g. agonal breathing), pale or cyanotic skin or mucus membranes, bleeding from any orifice, or seizures.

3. Appropriate training of the personnel responsible for the animal evaluation/monitoring, record keeping, and notification of the investigator and/or veterinarian.
   • Checklists or score sheets may be helpful in ensuring appropriate observations are made, consistently interpreted, and properly documented. Written records should be kept of all monitoring and treatment activities.
   • The frequency of the animal monitoring, including weekends and holidays, should be described in the protocol. The frequency of observation of the experimental cohort (i.e. group of similarly treated animals) should be increased when any animal in the cohort begins to exhibit abnormal clinical signs (see above).

4. Consideration should be given to moving animals to individual cages when their condition deteriorates to the point that injury from other animals is likely.

**Death or Moribundity as the Endpoint**

There may on occasion be an animal study in which the endpoint that is compatible with the scientific requirements of the study requires moribundity or mortality. The moribund condition is defined as a clinically irreversible condition leading inevitably to death. In these types of studies (e.g. sepsis studies), animals are permitted to die or become moribund out of scientific necessity (e.g. the need to study late-stage disease process or determine survival rates). In most cases, pain-relieving measures are not used because such measures would compromise the experimental integrity of the study. However, these studies must demonstrate that the benefits of the research are greater than the harm done to the animal, and that the earliest scientifically valid humane endpoint will be used. Specifically, these protocols must include a scientifically justified experimental design that addresses the following animal welfare concerns:

1. Are any scientifically valid alternatives available? If available, why are they not being utilized?
2. Are pain-relieving measures available? If available, why are they not being utilized?
3. How many animals will be used for experiments in which pain or distress will be unrelieved, and how was it determined that this is the minimum number of animals required?
4. Will animals be euthanized when moribund, and if not, what scientific information (i.e. data) is gained or lost in the interval between moribundity and death?

**References:**


**Additional Reference Material:**


