

**SEATTLE CHILDREN'S RESEARCH INSTITUTE
OPERATING POLICIES / PROCEDURES**

DEPARTMENT: Institutional Animal Care and Use
Committee
POLICY NUMBER: IACUC-027
REPLACES:
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POSTED FROM:

TITLE: Criteria For Review Of Protocols Involving Humane Endpoints

SUMMARY:

Federal regulations require that the IACUC determines that discomfort to animals will be limited to that which is unavoidable for the conduct of scientifically valuable research, and that unrelieved pain and distress will only continue for the duration necessary to accomplish scientific objectives. Public Health Service Policy on Humane Care (PHS) and Use of Laboratory Animals, and Animal Welfare Regulations (AWRs) further state that animals, that would otherwise suffer severe chronic pain and distress that cannot be alleviated, should be humanely euthanized at the end of the procedure or, if necessary, during the procedure.

DEFINITIONS:

1. Humane Endpoint: Criteria used to end experimental studies earlier in order to avoid or terminate unrelieved pain and/or distress.
2. Moribund: In the state of dying; at the point of death.

POLICY/PROCEDURE:

027-1 Developing Humane Endpoints

- 027-1.1 Humane endpoints must be listed in the protocol. They should be developed such that they ensure the objectives of the study are met.
- 027-1.2 Humane endpoints should be used to end studies before the onset of pain and distress.

Criteria For Review Of Protocols Involving Humane Endpoints

027-1.3 Regardless of whether pain and distress are anticipated in a study, a detailed plan for when and how it is alleviated should be provided in the protocol. This plan should consist of detailed, specific and objective parameters that will be used to determine when animals should be removed from the study. The plan should also include contingency procedures for situations which may arise on weekends, holidays, or in the absence of the responsible investigator.

027-2 Moribund Condition as an Endpoint

027-2.1 A moribund condition is an appropriate humane endpoint for studies involving the induction of severe disease states and high rates of mortality.

027-2.2 These studies should establish well defined, specific and objective criteria to detect and humanely euthanize moribund or pre-moribund animals. Incorporation of such criteria contributes to reduce the number of animals which die spontaneously. Criteria should also address the frequency at which animals are monitored. This will help detect suffering so they can be euthanized in a timely manner.

027-2.3 Clinical signs of moribund animals may include, but are not limited to, one or more of the following:

027-2.3.1 Impaired ambulation or inability to remain upright (prevents access to food and water);

027.2.3.1.1 Excessive weight loss and emaciation (equal to, but not greater than, 15% body weight);

027.2.3.1.2 Lack of physical or mental alertness;

027.2.3.1.3 Dyspnea (*difficult or labored respiration*), and/or;

027.2.3.1.4 Severe dehydration.

027-3 Death as an Endpoint

Because it provides an objective and unequivocal data point, spontaneous death has historically been used as an endpoint in cancer, infectious disease and other animal studies, especially for regulatory purposes. However, current

regulatory testing requirements allow for euthanasia of moribund animals, or animals experiencing clinical signs of severe pain and distress.

027-4 Toxicity Testing

Toxicity testing regulations currently allow treatment of pain and distress in animals only if there is no interference with the study objectives. If the use of such pharmacologic intervention produces such confounding effects, management of pain and distress should be accomplished by humane euthanasia of animals experiencing significant pain and distress.

027-5 Other Humane Endpoints

027-5.1 Assessing tumor burdens

027-5.1.1 Effective monitoring systems and endpoints should include limits on tumor size and severity of tumor-associated disease (e.g., tumor burden in excess of 10% of normal body weight; necrosis, infection, ulceration, interference with ambulation);

027-5.1.2 Frequent and appropriate monitoring of animals during tumor development is required to allow for timely intervention before significant deterioration or death.

027-5.2 Transgenic animals

027-5.2.1 Genetically altered animals are sometimes accompanied by unintended or unpredictable alterations that adversely affect the well being of the animal;

027-5.2.2 Such protocols should establish a plan for addressing unanticipated adverse outcomes and systematic characterization of phenotypes to facilitate assessment of their possible utility and timely decisions on disposition or retention.

REFERENCES

National Research Council, *"The Guide for the Care and Use of Laboratory Animals"*. National Academy Press; Washington, DC. 1996.

"Public Health Service Policy on Humane Care and Use of Laboratory Animals", amended August 2002.

Submitting Office: Office of Animal Care

Approved by:

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