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POLICY ON USE OF DEATH AS AN ENDPOINT IN ANIMAL EXPERIMENTS

1. Policy statements

This policy outlines the standards and expectations for researchers using death as an experimental endpoint in animal studies. In accordance with the NACLAR guidelines, unless there is strong scientific justification for death as an endpoint, death as an endpoint must be avoided. PIs must not allow the experiments to proceed to a painful, distressful or lingering death of animals unless no other experimental endpoint is feasible, and has been approved by the IACUC.

Increased public interest, regulation and revisions in publication requirements have led to a reevaluation of using death as an endpoint in cancer, infectious disease, drug safety and other animal studies. Regulatory testing requirements for acute toxicity now allow for animals that are exhibiting clinical signs of severe pain and distress to be euthanised humanely. Prompt intervention points are also crucial to protect animal welfare and promote quality research outcomes.

If death as an endpoint must be used, and is approved by the IACUC, the PI must ensure that the animal's distress or pain is minimised, including the appropriate use of sedation, analgesia, anaesthesia or other interventions.

For any study that defines death of the experimental animal as the endpoint, the PI must ensure, and the IACUC must be convinced, that there is no earlier point when the necessary data can be obtained and the animal could be euthanised. The study must be fully justified and approved before being executed.

2 Definitions

Death as an experimental endpoint	When death of an animal is the deliberate measure to evaluate biological and chemical processes, responses or effects
Pain and distress	An awareness of acute or chronic discomfort resulting from intense or damaging stimuli, which manifests as observable, abnormal physiological or behavioural responses.

3 Scope

This policy applies to all species used for research, testing and teaching in NUS.

4 Guidelines

4.1 IACUC protocol requirements and scientific justifications

The use of death as an experimental endpoint is mostly ethically unacceptable, and if required by the study, must be included in the IACUC protocol, scientifically justified and approved before being implemented.

Protocols involving the use of death as an endpoint must include the following information,

1. A clear description of the study including:
    a. justification/s for selecting death as an experimental endpoint

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b. consideration/s of alternative or earlier endpoints,
c. reason/s why alternative(s) or earlier endpoints cannot be used
d. any loss of scientific information if animals are euthanised at earlier endpoints
e. the use of pain-relieving and/or supportive measures or reasons why they cannot be used
f. the number of animals to be used and why this is the minimum number
g. criteria and frequency of monitoring

* A CM veterinarian should be consulted on the alternative and/or humane endpoints for studies with potential lethality.

4.2 Considerations

The use of death as an endpoint on research animals requires special IACUC consideration due to its impact on animal well-being.

Endpoints other than death must be considered and should be used whenever the research objective can be attained with non-lethal endpoints.

Euthanasia also provides tissues more appropriate for subsequent study and alleviate potential suffering by the animal. Hence euthanasia must be considered, rather than death, for both scientific and ethical reasons.

When death as an endpoint cannot be avoided, the experiments must be designed to result in the deaths of as few animals as possible

4.3 **Animal monitoring**

The CM operations team should be informed prior to starting the experiment/s and markings on the cage card, indicating the use of death as an endpoint, must be placed on every cage throughout the study.

Animals included in the study using death as an endpoint must be monitored as defined in the protocol. This monitoring must be documented.

Researchers must adhere to the monitoring criteria and frequency defined in the protocol. Should the animal/s exhibit abnormal behaviour or symptoms not indicated in the protocol, researchers should consult the CM veterinarians for advice.

Consider moving ill animals, when their condition affects their access to food and water or exposes them to injury from their cage mates, to individual cages. Dead animals must be removed promptly.

The researchers must keep a written record for animals in the study. The records must be maintained, made available to the IACUC, PAM officers and/or CM staff, and should include at least the following, or as required by the study:

1. date and time of the observation
2. personnel who had made the observation
3. animals displaying abnormal behaviour, signs of pain and distress
4. number of animals found dead

5. References

1. Guidelines on the Care and Use of Animals for Scientific Purposes. National Advisory Committee for Laboratory Animal Research. 2022

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2. Guide for the Care and Use of Laboratory Animals. National Research Council, 2011.

6 Related documents/SOPs

1. CM SOP 407: Humane intervention points

Revision	Author	IACUC approval date
Last revised	Dr Lee Liying Corinne	19 November 2018
P209.01. Reviewed to: 1. ensure policies are in compliance with the NACLAR Guidelines 2022 and the updated Animals and Birds (Care and Use of Animals for Scientific Purposes) Rules 2004; and 2. up-to-date with current practices Changes made to: 1. section 1. "Position statements" to update to "unless there is strong scientific justification for death as an endpoint……unless no other experimental endpoint is feasible, and has been approved by the IACUC."; and add "If death as an endpoint must be used, and is approved by the IACUC…….PI must ensure, and the IACUC must be convinced, that there is no earlier point when the necessary data can be obtained and the animal could be euthanised."; and 2. section 4.2 to add "Hence euthanasia must be considered, rather than death, for both scientific and ethical reasons."; and 3. under section 5, updated to "Guidelines on the Care and Use of Animals for Scientific Purposes. National Advisory Committee for Laboratory Animal Research. 2022"	Dr Chew Li Li IACUC	3 January 2023

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