

1. PURPOSE

This Standard Operating Procedure (SOP) describes the guidelines for the use of cumulative endpoints.

2. CONSIDERATIONS

Research animals are vital for the advancement of science; however, consideration of their long-term welfare is a continuing concern.

Not all scientific endpoints in animal-based research require euthanasia and thus many animal ethics committees have adopted an alternative term to describe animal disposition when the scientific endpoint is reached, the experimental endpoint. An experimental endpoint in this context may include euthanasia but could also include repurposing the animal. However, repurposing of animals in multiple studies or procedures may result in cumulative suffering due to subsequent procedures or purpose. that may cause pain, discomfort, or stress. Along a similar line of reasoning, cumulative endpoints and overall lifetime use should be considered for animals used in one or more protocols for an extended period (i.e., duration of use) or in individual protocols that involve multiple procedures conducted over an extended period of time (i.e., multiplicity of procedures, frequency of use, and intensity of use) when euthanasia is not required at study end.

The establishment of the cumulative endpoints is done in accordance to the CCAC guidelines: Identification of scientific endpoints, humane intervention points, and cumulative endpoints.

3. RESPONSIBILITY

Veterinarian, veterinary care staff, animal care staff, Principal investigator (PI) and their research staff.

4. MATERIALS

- 4.1 Humane intervention points monitoring logs for rodents such as the one available on the [McGill University Animal Ethics and Compliance website](#):
- 4.1. Procedure summary sheets for large animals

5. PROCEDURES

- 5.1. Prior requirements:
 - 5.1.1. Specific evaluation of the scientific and humane intervention points and associated interventions by the Facility Animal Care Committee (FACC) prior to protocol approval.
 - 5.1.2. Development of an animal monitoring regime according to the procedures performed on an animal. Reference to pre-existing experimental guidelines is useful with any modifications needed to further encompass all aspects of the scientific research proposed. See Experimental Guidelines SOPs on the McGill University Animal Ethics and Compliance site..
 - 5.1.3. The number, duration, frequency, and severity of procedures performed to date, and the time an animal has spent on a holding protocol, must be considered when assessing the animal's welfare according to the Animal Welfare Assessment SOP.
- 5.2. During the scientific activity:
 - 5.2.1. Monitor animals as they progress through the scientific activity.
 - 5.2.2. Ensure consistency in the application of any scoring sheets or checklists used.
 - 5.2.3. Apply interventions as required and previously approved on the Animal Use Protocol.
 - 5.2.4. Adapt scientific endpoints and humane intervention endpoints as required in the event of unexpected outcomes. In any such event occurs, the PI must provide an amendment to their animal use protocol for approval from the FACC.

- 5.2.5. Keep records of all monitoring and intervention activities both in the animal room and electronic archives.
 - 5.2.6. Animals should be subjected to only one severe or high welfare impact experience in their lifetime (a category of welfare impact level D or E; see the CCAC guidelines on categories of welfare impact).
 - 5.2.7. For large animals with cumulative endpoints, animal welfare will be assessed by a committee composed of a veterinarian, a member of the research staff, the principal investigator, and a representative of animal welfare (e.g., animal health technician, animal welfare coordinator) to assess the quality of life of each animal and determine if cumulative endpoints have been reached. Meetings will be held annually, and the decisions will be based on the veterinarian's annual exam, the welfare assessment, observations of the animal behaviors, and the number of surgeries/anesthesia events performed on the animal.
- 5.3. After the scientific activity is complete: retrospective analysis
- 5.3.1. Evaluate the effectiveness of the scientific endpoints and humane intervention points.
 - 5.3.2. Incorporate the accumulated experience and evaluations to further improve the animal monitoring regime, endpoints, and welfare assessment to improve the animal's welfare.

6. EXAMPLES OF 'LONG-TERM' STUDIES

- 6.1. Animals in breeding colonies
- 6.2. Animals used for teaching and training
- 6.3. Aging and longevity studies
- 6.4. Large animals with long lifespan (i.e., non-human primates)

7. REFERENCES

- 7.1. Russell, W.M.S.; Burch, R.L. *The Principles of Humane Experimental Technique*; Methuen: London, UK; UFAW: Potters Bar, UK; Herts, UK, 1959; p. 239.
- 7.2. Canadian Council on Animal Care (CCAC). [Guide to the Care and Use of Experimental Animals Volume 1, 2nd ed.](#); Canadian Council on Animal Care (CCAC): Ottawa, ON, Canada, 1993; Available online (accessed on 5 March 2021).
- 7.3. Canadian Council on Animal Care (CCAC). [Identification Of Scientific Endpoints, Humane Intervention Points, And Cumulative Endpoints](#). March 2022; Available online:
- 7.4. Developing Recommendations for Cumulative Endpoints and Lifetime Use for Research Animals by Elizabeth A. Nunamaker, Shawn Davis, Carly I. O'Malley and Patricia V. Turner; *Animals* 2021, 11(7), 2021; <https://doi.org/10.3390/ani11072031>