



Animal Care Committee Guideline

Number: 24

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Date Revised: N/A

Cumulative Endpoints

Background

To prevent suffering of animals involved in multiple procedures or studies, their overall lifetime use must be considered. *Cumulative endpoints*, as defined by the CCAC ([CCAC, 2022](#)), are the threshold values for when individual animals have reached their lifetime maximum involvement in scientific activities and must be retired to prevent unexpected welfare impacts; they differ from scientific endpoints. Cumulative endpoints must be considered for all animals used in research or teaching. The assessment of an animal's cumulative lifetime experience includes both measures of physical impact (e.g., invasive procedures, disease, trauma) and affective states (e.g., fear, distress, anxiety, anhedonia).

Choosing and monitoring cumulative endpoints follows this process:

1. *Before starting the scientific activity* – Cumulative endpoint criteria must be defined and included in the Animal Utilization Protocol (AUP).
 - a. Consider if animals have been previously used and the impact of that use.
 - b. Consider the lifetime experience of an animal within your study.
2. *During the scientific activity* – Monitor the animals, use scoring sheets or checklists, apply interventions as required, and keep records.
3. *After the scientific activity* – Evaluate your criteria and make a retrospective analysis of the animal welfare impacts.
 - a. This information will be requested as part of your annual renewal and regular review is encouraged.

This guideline will be implemented over the lifetime of existing AUPs at yearly renewals.

Responsibility

The Animal Care Committee (ACC), including the veterinary reviewer, are responsible for ensuring endpoints balance humane interventions that safeguard animal welfare and scientific outcomes. The ACC reviews and

approves the endpoints described in the AUP and has final authority over deciding if an animal has reached their cumulative endpoint while on study (CCAC, 2022).

The development of cumulative endpoints is a collaborative process involving the scientific team, veterinary and animal care personnel, and members of the Post-Approval Review (PAR) team. The Principal Investigator/Instructor (PI) is responsible for considering how to minimize negative welfare impacts and, wherever possible, proposing ways to balance these impacts with measures that positively influence welfare (e.g., social housing, enrichment, longer rest periods). During AUP review, ACC members are responsible for ensuring endpoints balance humane interventions that safeguard animal welfare and the scientific outcome. The PAR program will also work with the research team to refine endpoints when new information arises and as the project progresses.

Expectations

1. Animals should only be subjected to one high welfare impact experience in their lifetime (a category of welfare impact D or E per the CCAC guidelines on categories of welfare impact) unless sufficient scientific justification is provided for additional high welfare impact experiences and approved by the ACC ([CCAC, 2022](#)).
2. Animals being transferred between AUPs, internally or between institutions, should have a cumulative endpoint assessment performed at the time of the transfer. This information must be included with the transfer documents to allow the receiver to consider the animals lifetime experiences.
3. All proposed cumulative endpoints should consider the following criteria:
 - a. Species
 - b. Early life experiences (e.g., rearing environment, weaning age, maternal involvement)
 - c. Invasive procedures (number, duration of impact, frequency, and severity), including all aversive components of a procedure (e.g., handling, restraint, administered compounds)
 - d. Clinical condition (e.g., body condition, coat condition, activity level, disease status, medical history)
 - e. Negative or positive associations with humans or procedures based on past experiences.
 - f. Housing environment (social, physical, enrichment)
 - g. Behavioural and physiological indicators of negative welfare states– see the [CCAC guidelines: Animal welfare assessment, 2021](#)
4. There are additional cumulative endpoint considerations for animals in the categories below. SOPs will be developed for each category to provide further instructions.
 - a. **Teaching and training** animals are generally held for longer periods (relevant to the species lifespan), used intermittently throughout their lifetime, and are exposed to students who may have less experience and skill.
 - b. **Breeding** animals are impacted by mating, gestation, parturition, and associated routine husbandry procedures. Their welfare also influences the welfare of their offspring. Age should not be used as the sole determinant for when animals are retired from a breeding program, and the experiences of male and female breeders should be evaluated separately.
 - c. **Aging and longevity studies** animals are at a higher risk of developing behavioural and physical signs of negative welfare due to their advanced age and cage mate attrition. They may have also had a lifetime spent in a research environment that may restrict their behavioural needs.

- Because it can be hard to distinguish between lifetime cumulative experiences that affect general welfare and the biological effects of aging, key points in the animal's experience when increased monitoring or interventions may be required must be included.
- d. **Production** animals also present a challenge as individual animals can be difficult to assess when in a large group and/or when not habituated to human handling. The development of endpoints should consider how welfare will be practically assessed at the individual level.
 - e. **Aquatic species** may not be afforded the same level of welfare protection as other laboratory animals due to a lack of research into practical, validated signs of negative and positive welfare. They also are often held in large groups and visually distinguishing individuals may be challenging.

Terms

- Cumulative endpoint: the threshold values for when individual animals have reached their lifetime maximum involvement in scientific activities and must be retired to prevent unexpected welfare impacts.
- Humane endpoint: the point at which an experimental animal's pain and/or distress is terminated, minimized, or reduced, by taking actions such as killing the animal humanely or terminating a painful procedure.
- Humane intervention point: pre-established criteria that indicates when an intervention should occur to reduce negative welfare impacts.
- Scientific endpoint: the earliest point at which the approved objectives of the scientific activity can be achieved.
- Scientific activity: Includes all activities related to research, teaching, and training that involve live animal use.

References

- CCAC. (2022, March). [*CCAC Guidelines: Identification of scientific endpoints, humane intervention points, and cumulative endpoints*](#)
- CCAC. (2021, April). [*CCAC Guidelines: Animal welfare assessment*](#).

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