IDENTIFICATION OF SCIENTIFIC ENDPOINTS, HUMANE INTERVENTION POINTS, AND CUMULATIVE ENDPOINTS

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These frequently asked questions (FAQs) are intended to assist investigators, instructors, and members of animal care committees in the implementation of the *CCAC guidelines: Identification of scientific endpoints, humane intervention points, and cumulative endpoints* (CCAC, 2022). FAQs provide general responses to comments and questions received by the Canadian Council on Animal Care (CCAC) during the external reviews of this guidelines document.

If you do not find the answer to your question here, do not hesitate to contact the CCAC and we will be pleased to provide assistance.

1. Do protocol authors conducting off-site observational studies have to intervene if animals are found to have compromised welfare?

If the animals are owned by a third party (e.g., pets, commercial farm animals), the protocol author should notify the animal owner of the issue but is not responsible for correcting the problem themselves. For wildlife, there is no obligation to intervene. However, if the protocol author interacts with the animals, they become responsible for the welfare of those animals for the duration of the scientific activity.

2. When working with third-party-owned animals, what are the monitoring expectations?

The institution has a responsibility to ensure that the effects of any scientific procedures are monitored. If the activity is observation only, there is generally no need to monitor the animals. Each animal care committee should decide on the level of monitoring required, based on risk to animal welfare.

3. Do 'scientific endpoints' fall under 'scientific merit review'?

No. It is within the animal care committee's purview to question whether earlier or surrogate endpoints can be used to determine that the scientific goal has been achieved (though it is not up to the animal care committee to challenge the scientific goal itself). If an animal care committee is not comfortable with the proposed scientific endpoints and they cannot be refined, the animal care committee can refuse to approve the protocol. If an animal care committee lacks the expertise to evaluate the scientific endpoints, they may seek independent advice or discuss the issue directly with the protocol author to better inform their decision.

4. Where can one find information about implementing earlier scientific endpoints?

Protocol authors are expected to keep up to date with best practices in their field of study. This can be done through literature reviews, consultation with peers, attending conferences, using resources provided by various Three Rs organizations (e.g., NC3Rs), etc.

5. When considering cumulative endpoints, what action should be taken in the case of surgical complications, particularly those requiring re-anesthesia (e.g., wound dehiscence)?

Occasionally, animals are approved to undergo a single recovery surgery, yet unexpectedly, may require subsequent anesthesia to perform a corrective action. In such cases, the protocol author and veterinarian must work together to assess the individual and determine the best course of action. Animal welfare should be the top priority, and the veterinarian is ultimately responsible for decision-making.

6. How should experiences be summed over an animal's lifetime to track cumulative endpoints?

There is no clear answer to this question at this time. This is a new and evolving area of scientific inquiry, and the CCAC recognizes that it may be challenging to implement. However, tracking cumulative endpoints is ethically important, and it is better to start doing so imperfectly, than not doing it at all. The expectation is

that institutions will improve over time; this will be sped up by institutions sharing ideas and best practices with each other. For now, each institution should tailor its cumulative endpoints policy to suit its needs and update it over time (see Section 3, "Cumulative Endpoints", of the *CCAC guidelines: Identification of scientific endpoints, humane intervention points, and cumulative endpoints*). There are too many variables for the CCAC to standardize an approach that will work for everyone.

7. How should cumulative endpoints be tracked in third-party-owned animals?

Evaluating cumulative endpoints in third-party-owned animals can be difficult because individual lifetime experience records may not exist. However, an animal's previous experiences must be considered as much as possible before its involvement in a scientific activity. If lifetime records are not available, other options which demonstrate due diligence may include performing a site audit to ensure initial conditions are acceptable, consulting with the animal's veterinarian, and conducting a welfare assessment or physical exam on the animals. All available information about the history of the animals should be incorporated into the protocol and approved by the animal care committee.

Any animals that exceed a pre-determined threshold for prior welfare impacts should not be included in the scientific activity unless approved by the animal care committee for scientific reasons (e.g., in cases where the effects of different practices are being compared, in epidemiological surveys).

Once the scientific activity is complete, cumulative endpoints do not have to be tracked into the future.