UACC Procedures on Submission of a Modification to an Existing Animal Use Protocol

INTRODUCTION

As per the Canadian Council of Animal Care (CCAC) Policy Statement on the *Terms of Reference for Animal Care Committees* (ACC; 2006): ***It is the responsibility of the ACC to ensure that animal users update their protocols with any modifications they intend to make, and approve any modifications to a protocol before they are implemented.***

Approved Animal Use Protocols (AUPs) require submission of a modification when changes in personnel, animal numbers or strains, or in animal procedures occur. The Animal Research Ethics Board (AREB) must approve these modifications prior to their implementation. Depending on the magnitude of the modification and the implications for animal welfare, the Principal Investigator (PI) may submit an AUP Modification Form or may be required to submit a new AUP Form.

PURPOSE

1. To provide guidance to PI and the AREB with respect to how to proceed with a protocol modification.
2. To provide more clarity to the statement found on the AUP Modification Form: **Use this form to request changes to an active Animal Use Protocol (AUP) e.g., different species or strain, change in numbers of animals, change in procedure(s), addition of personnel.**

PROCEDURE

The AREB delegates responsibility to the University Veterinarian and the AREB Chair to determine whether a new AUP or a modification of an existing AUP is sufficient to address the proposed change in an existing approved AUP. Changes that negatively impact animal welfare or multiple changes in a number of AUP elements are normally referred to the full AREB. Changes that deviate substantially from the existing protocol are more likely to require completion of a new AUP. The number of changes throughout the history of the protocol is also considered.

Proposed changes to protocols are classified as either minor or major, as defined below. Any changes not conforming to these classifications may require submission of a new AUP. Contact uacc.office@usask.ca if assistance with modification submission is needed or to help determine whether specific changes constitute a modification or a new AUP submission.

Note: As per the OVPR Procedures for Obtaining Assessment of Scientific Merit of Projects Relating to Animal Use Protocols by the OVPR Scientific Merit Review Committee for Animal-

Based Research (SMRCABR), the AREB has the option to request additional peer review on any submitted AUP, regardless of the agency funding and the status of peer review. This option is only used if there is a serious concern by the majority of the AREB members regarding the particulars of the animal model or experimental design not related directly to the merit of the general scientific content. If the changes requested in the modification deviate significantly from the peer-reviewed approved AUP, the AREB may request peer review by the SMRCABR on the requested modification.

I. MINOR MODIFICATIONS:

Minor modifications are uncomplicated changes to the AUP that are not expected to significantly affect animal use or welfare.

A. Some minor modifications to AUPs are reviewed/approved by Animal Care and Research Support (ACRS) staff, with consultation of the AREB Chair, as required. These modifications are usually assessed within a week of receipt of the modification form by ACRS.

Examples:

a. Change in personnel (removal or addition of personnel) involved in animal procedures.
   - Education and training information is required for new personnel as well as the identification of what procedures these individuals will perform on the AUP. Furthermore, new personnel must complete the online UACC Animal Care Course and be listed as an authorized worker on the associated biosafety permit before the new personnel are added to the AUP. UACC practical skills courses (e.g., rodent handling, rodent anesthesia, surgery, or aquatics) are also required, if applicable.

b. Change in strain of animal without changes in the total number of animals per year according to the *UACC Procedures for Categorizing Animal Strains and Allowing for Exchange of Strains on Animal Use Protocols.*

c. Change in supplier of animals.

B. The AREB Subcommittee (AREB Chair, University Veterinarian or delegate, and a community member representative) reviews minor modifications to an AUP. Minor modifications will be assessed by the AREB Subcommittee following the AREB submission deadlines and meeting dates. At the discretion of the AREB Subcommittee, a minor modification may be approved by the AREB Subcommittee or referred to the full AREB for review. A modification tabled until the next meeting of the full AREB meeting adds further time to the review process.

Examples:

a. Addition of animal strains that are not known to have specific housing or care requirements (e.g., isolator housing), or health problems (e.g., immuno-compromised).

Any new strains added must not have phenotypes that are expected to negatively impact on animal health or welfare.

b. Increase in animal numbers by less than 20% of total approved for that particular species or strain.
c. Decrease in animal numbers by less than 20% of total approved for that particular species or strain, where the decrease impacts the experimental design of the study such that the AREB (and potentially SMRCABR) must ensure the resulting group size is still adequate for statistical significance.
d. Change in drug(s) used, where the effects on the animal are equivalent.
e. Change in a procedure in a live animal, where the effects on the animal are expected to be equivalent (e.g., changes in dosing of experimental compounds, addition of similarly-acting compounds or antagonists, alterations to time points).
f. Procedural changes that are recommended by a UACC Veterinarian or that do not impact animal welfare.
g. Change in the anesthetic agent or in the use of analgesic agents. The degree of difference in efficacy, titration and difficulty in administration of the agent will be considered.
h. Changes in the use of hazardous agents. These changes must be cleared through the Animal Facility Manager and Safety Resources before being implemented. Submission of a modification form does not constitute such clearance.
i. Small pilot studies that complement the existing research.
j. Change in experimental compound(s) used, where the effects on the animal are expected to be equivalent.

II. MAJOR MODIFICATIONS:

Major modifications are changes to the AUP that may affect animal use or welfare. Major modifications require full AREB review. In all cases a thorough scientific justification for the modification needs to be provided. If procedures are added or changed, the animal strain(s) involved, if applicable, must be indicated as well as the cohorts of animals that will be affected by the change(s).

<u>Examples:</u>

a. Increase in animal numbers by 20% or more of total approved for that particular species or strain.
b. Decrease in animal numbers by 20% or more of total approved for that particular species or strain, where the decrease impacts the experimental design of the study such that the AREB (and potentially SMRCABR) must ensure the resulting group size is still adequate for statistical significance.
c. Change in sex/breed/strain/age/genetic manipulation
    - Assessment depends on the degree to which the proposed changes alter animal manipulations and procedures, introduce earlier endpoints, or have a negative impact on the animal well-being.

d. Addition of animal strain(s) that are known to have specific housing/care requirements (e.g., isolator housing) or health problems (e.g., immuno-compromised) or phenotype(s) with impact on health/welfare but do not represent an increase in the Category of Invasiveness (CI).
e. Change of animal species. (e.g., dogs to cats, zebrafish to rainbow trout)
f. Change in procedure or addition of new procedure in a live animal, where the effects on the animal are judged to result in increased potential for pain and distress (including changes to study endpoints) but do not represent a change in CI (e.g., addition of a novel route of administration, behavioural test, blood sampling, urine collection or fasting).
g. Change in endpoints likely to produce an alteration in animal welfare.
h. Change in method of euthanasia
    - A change from a non-physical to a physical method will generally require review by the full AREB.
    - A change from a recognized to a new or not normally recommended method will usually require review by the full AREB.
i. Changes in the use of hazardous chemicals, radiation or biological agents (this may require additional training).
j. A change from non-survival to survival surgery.
k. A change in the degree of invasiveness of a procedure or discomfort to an animal
    - B→D; C→D or E
    - Withholding, or reducing substantially, the use of analgesics or other drugs or procedures that provide comfort or safety for an animal or handler.

III. NEW ANIMAL USE PROTOCOL REQUIRED:

At the discretion of the AREB Chair and University Veterinarian, a modification may result in a request to submit a completely new AUP form (e.g., change in species that requires significantly different care and housing requirements). Also, if more than three major modifications are submitted within a calendar year, the AREB Chair and University Veterinarian may determine that a new AUP is required.

Additionally, certain modifications <u>may</u> necessitate submission of a new AUP rather than a modification form.

<u>Examples:</u>

a. A change in main objective of the study or a change in the direction of the research (hypotheses and objectives) from those described in the grant and/or in the existing AUP.
b. Major changes to the approved experimental protocol (e.g., addition of novel or invasive surgeries or procedures that significantly extend the scope of animal use and/or increase the CI).

IV. EMERGENCY/PROVISIONAL MODIFICATION APPROVAL UNDER EXTRAORDINARY CONDITIONS:

The AREB recognizes that unforeseen circumstances may arise in a research environment. The AREB Chair or University Veterinarian may provide emergency approval following contact (phone or email) by the PI. A modification form must be subsequently submitted to ACRS for review by the AREB within one month of the emergency approval.

Wildlife studies performed in the field may fall into this category. Refer to the UACC Procedures for Fish & Wildlife Reporting of Over-Catch, By-Catch and Mortality, Morbidity and Incidents (MMIs) for further information and guidance.

For all research studies, failure to contact ACRS and/or submit a modification form represents non-compliance in animal use, which may result in:

- Post Approval Review
- Review by the UACC Executive Committee
- Suspension of the AUP
- Inability to use data collected
- Retraction of publication

V. RETROACTIVE APPROVALS

Only under extenuating circumstances will retroactive approvals be granted. It is the PI's responsibility to report to the AREB any changes in animal use and clear justification must be provided for the UACC to consider retroactive approval. Failure to provide animal use information and justification will result in non-compliance and actions taken as listed above (See Section IV). Refer to the *UACC Procedures on Animal Use Non-Compliance*.

VI. CHANGES WHICH CAN BE MADE ON THE AUP ANNUAL REVIEW FORM AND DO NOT REQUIRE SUBMISSION OF AN AUP MODIFICATION FORM MID-YEAR:

- Title change or change in source of funding
- Procedures at the higher CI are completed and only lower level of invasiveness procedures are being performed; note this may result in a decrease CI placement (from Level C to Level B for instance)
- Information on changes in animal tissue use post euthanasia.

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Procedure Review and Revision History		
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1	23 December 2010	UCACS
2	8 May 2012	UCACS
3	19 November 2012	UACC
4	22 June 2020	UACC
5	29 September 2020	UACC
6	25 November 2021	UACC
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