



POLICY: Amendment Classifications and IACUC Review Processes

Objective:	To provide guidance on classifications and IACUC review processes of amendments to IACUC-approved protocols.
Author:	Office of Research Protections and Integrity (ORPI)
Date:	July 24, 2023

The IACUC is required by federal regulations¹ to review proposed significant changes to a previously approved application. IACUC approval for all proposed changes to an approved application is required prior to:

- 1) procurement of animals,
- 2) commencement of activities, and
- 3) the implementation of proposed changes to the approved protocol.

I. **AV CONSULTATION**

Prior to submitting an amendment to the IACUC, the principal investigator must consult with the Attending Veterinarian regarding the category of the proposed change. If the proposed change is not in either of the categories below, the Attending Veterinarian will make the determination regarding the category on a case-by-case basis. The principal investigator must consult with the Attending Veterinarian regarding potential painful procedures as well as changes in anesthesia, analgesia and euthanasia.

II. **AMENDMENT CLASSIFICATIONS**

A. *Minor Amendment* – A minor amendment is a change that is unlikely to reduce animal welfare or may decrease the potential for pain/distress (i.e., a refinement). Examples of minor amendments include (but are not limited to):

- addition or substitution of qualified personnel,
- title change,
- change in funding source,
- small increase in animal numbers $\leq 10\%$,
- addition of another strain of same species,
- change in sex of animal used,
- addition of collaborator(s)

NOTE: Changes in personnel (other than the Principal Investigator) are considered minor and may be processed by the Office of Research Protections and Integrity IF it can be documented that all such personnel are appropriately identified, adequately trained and qualified, enrolled in applicable occupational health and safety programs, and meet other criteria as required by the IACUC.

¹ Regulations include: PHS Policy, the Animal Welfare Act regulations, and the *Guide for the Care and Use of Laboratory Animals*.

NOTE: Congruency reviews and the post-award addition of funding information (grants, award funds, etc.) by amendment may be processed by the Office of Research Protections and Integrity as a minor amendment with administrative review. “It is not a required IACUC function and may be performed by other qualified institutional personnel...” per guidance from OLAW (NOT-OD22-005, 10/18/2021).

Research Strategy, Vertebrate Animals Section, and Methods from the grant or research funding application are recommended attachments with the post-award amendment to the IACUC protocol.

If there is any question regarding the scope, methods, or justification for the research protocol, the IACUC Chair will be consulted.

B. Significant Amendment – Examples of changes that could qualify for review as a significant amendment and therefore may require Full Committee Review include:

- changes in purpose or specific aim of study,
- changes in principal investigator,
- changes in the species or approximate number of animals to be used,
- large increase in animal numbers >10%,
- changes resulting in greater discomfort, pain, or in a greater degree of invasiveness,
- changes in the duration, frequency, or number of procedures performed on an animal,
- changes from non-survival to survival surgery,
- addition of survival surgery,
- changes in method of anesthesia (either the use of or withholding of),
- changes in post-operative care,
- changes in method of euthanasia, or
- addition of embryonated egg studies where embryos are >80% incubation, use of hatchlings, and/or any use of embryonated eggs that will subsequently be allowed to hatch.

III. **AMENDMENT REVIEW PROCEDURES**

- A. Only personnel changes (except for PI) and funding/award amendments (noted above) are considered *Minor Amendments* and may be reviewed and approved by the IACUC administration.
- B. Other *Minor Amendments* (as defined above) may be reviewed by the Committee Chair and/or the Attending Veterinarian, do not require full committee review (FCR), and are considered administrative unless the Committee Chair, The AV, or the PI request FCR.
- C. All *Significant Amendments* are subject to IACUC review (full committee review (FCR) or designated member review (DMR). The IACUC Coordinator will distribute a copy of the amendment to the IACUC. The Committee will perform an initial review to determine whether a significant amendment can be further reviewed using the DMR process or FCR at the next convened meeting.

NOTE: A maximum of three (3) significant amendments can be approved by the IACUC without requiring submission of a new protocol. More than three significant amendments require submission of new protocol.

IV. **AMENDMENTS ELIGIBLE FOR ADMINISTRATIVE HANDLING BY VETERINARY VERIFICATION AND CONSULTATION (VVC)**

Specific Significant Amendments that do not unduly impact animal welfare or alter study objectives may be eligible for administrative approval through the Veterinary Verification and Consultation (VVC)

process. VVC enables the administrative approval of eligible changes to an IACUC protocol without full committee or designated member review. If VVC is implemented, the veterinarian is not conducting designated member review, but is serving as a subject matter expert to verify that compliance with IACUC-reviewed and -approved reference documents is appropriate for the animals in this circumstance. The veterinarian may refer any request to the IACUC for review for any reason and must refer any request that does not meet the parameters of this policy.

Per guidance from OLAW ([NOT-OD-14-126](#); 08/26/2014), if an institution has defined IACUC-reviewed and -approved policies, guidelines, and/or SOPs for the conduct of animal activities, such reference documents may be used in conjunction with consultation by the Attending Veterinarian to administratively handle the following categories of significant changes to a protocol:

- **Anesthesia, analgesia, sedation, or experimental substances:** The veterinarian may verify acceptable changes to the dose, route, concentration, volume, and/or duration of an experimental substance that has already been approved for use in the protocol. The veterinarian may verify a change from one analgesic, anesthetic, or sedative agent to another provided that animal welfare is not compromised.
- **Euthanasia to any method approved by the current version of the AVMA Guidelines for the Euthanasia of Animals:** The veterinarian may verify the appropriateness of changes to the method of euthanasia, provided that the proposed changes are consistent with the current edition of the AVMA Euthanasia Guidelines.
- **Duration, frequency, type, or number of procedures performed on an animal:** The veterinarian may verify acceptable procedural changes to the duration, frequency, type or number of approved experimental procedures, as long as the change does not unduly impact animal welfare (i.e., lessens or involves equivalent pain, acute or chronic stress, distress or invasiveness), does not change study objectives, and is related to a procedure already in the protocol and approved by the IACUC.

Note: Addition of a new procedure is not eligible for VVC and requires full IACUC review.

Per the OLAW guidance, the above categories of significant changes may be reviewed administratively as long as AV consultation has occurred AND that consultation is documented. Consultation with the veterinarian is documented via an email notification to the IACUC Coordinator approving the change. A list of IACUC protocols amended by VVC is provided to the IACUC at the next scheduled IACUC meeting.

Reference documents to be used for *Veterinary Verification and Consultation* of eligible changes include (but are not limited to):

Anesthesia, analgesia, sedation, or experimental substances

- ACLAM e-Formulary App
- *American College of Laboratory Animal Medicine Series* (2015)
- *Formulary for Laboratory Animals* (Hawk & Leary)
- *Plumb's Veterinary Drug Handbook* (Plumb, 9th edition)
- *Anesthesia and Analgesia in Laboratory Animals* (Fish et al)
- *Laboratory Xenopus Sp.* (Green, 1st edition)
- *Lab Animal and Exotic Pet Medicine* (Sirois, 2nd edition)
- *Mader's Reptile and Amphibian Medicine and Surgery* (Divers & Stahl, 3rd edition)

- IACUC SOP: [Analgesics Recommended to Reduce Pain & Distress](#)

Euthanasia to any method approved by the current AVMA Guidelines for the Euthanasia of Animals

- [AVMA Guidelines for the Euthanasia of Animals](#)
- IACUC Guidelines: [Euthanasia of Mice and Rats](#)

Duration, frequency, type, or number of procedures

- IACUC Policy: [Policy for Transfer of Animals Between Protocols](#)
- IACUC Policy: [Cage Compliance](#)
- IACUC Policy: [Food or Water Restriction](#)
- IACUC Policy: [Housing of Rodents](#)
- IACUC Policy: [Social Housing of Multiple Species of Rodents in One Room](#)
- IACUC Policy: [Use of Non-Pharmaceutical Grade and Expired Materials in Animals](#)
- IACUC Policy: [Physical Restraint of Animals](#)
- IACUC Policy: [Rodent Surgery](#)
- IACUC Guideline: [In vivo Optical Imaging of Mice and Rats](#)
- IACUC Guideline: [Use of Nanoparticles](#)
- IACUC Guideline: [Rodent Genotyping](#)
- IACUC Guideline: [Guidelines for Tumor Production in Rats & Mice](#)
- IACUC SOP: [Rodent Blood Collection](#)

References

National Research Council. *Guide for the Care and Use of Laboratory Animals: Eighth Edition*. Washington, DC: The National Academies Press, 2011.

Animal Welfare Act (P.L. 89-544 -1966; amended 1970 [P.L. 91-579], 1976 [P.L. 94-279], 1985 [P.L. 99-198], 1990 [P.L. 101-624]).

Office of Laboratory Animal Welfare, Public Health Service. Public Health Service Policy on Humane Care and Use of Laboratory Animals. Washington, D.C.: Department of Health and Human Services. Revised August 2002.

Office of Laboratory Animal Welfare, Public Health Service. *“Guidance on Significant Changes to Animal Activities”* (NOT-OD-14-126). Released on August 26, 2014.

Revision History

Approved April 23, 2012

Revised November 24, 2014; February 27, 2017

Re-approved March 23, 2020

Revised February 22, 2021

Administrative changes September 18, 2022

Revised July 24, 2023

Administrative changes October 17, 2023