Effective Date: 2/1/2025	POLICY ON PROTOCOL REVIEW	Supercedes Document Dated: 7/1/2024

I. Background

The Public Health Service (PHS) Policy as well as the US Department of Agriculture (USDA)'s Animal Welfare Act and Regulations (AWA/AWR) require that the Animal Care and Use Committee (ACUC) either approve, require modifications (to secure approval), or withhold approval of proposed research or instructional animal activities using live vertebrate animals.

II. Policy

UC Berkeley Principal Investigators (PIs) are required to submit Animal Use Protocols (AUPs) that describe proposed vertebrate animal use for a three-year period prior to obtaining or using animals in research or teaching. If changes or modifications are proposed to an ongoing approved activity, PIs must submit an amendment/revision to their AUP, which may be reviewed by the ACUC or administratively – with or without Veterinary Verification and Consultation (VVC) with an Office of Laboratory Care (OLAC) Veterinarian - depending on the nature of the revision as outlined below. Revisions to animal procedures must not be implemented until approval is granted.

III. Definitions

A. Administrative review – The OACU staff review nonsignificant or minor revisions and/or other changes as specified by ACUC in Appendix B.

B. Administrative review with Veterinarian Verification and Consultation (VVC) – A UCB employed veterinarian as an employee of the Office of Laboratory Animal Care - authorized by the ACUC - may administratively handle significant changes as specified by ACUC in Appendix B according to ACUC-reviewed and -approved policies as noted in Appendix A.

C. *De novo* (continuing) review – The triennial review of an existing protocol during which the protocol is read and reviewed "as new".

D. Designated Member Review (DMR) – At least one voting ACUC member reviews and determines if the protocol is suitable for approval.

E. Designated Member Review post Full Committee Review (DMR post FCR) – Process by which the ACUC can designate one or more members to continue to review and eventually approve on their behalf a protocol following review at a full committee meeting if the ACUC did not have sufficient information or needed clarification to reach a decision during the meeting.

F. Full Committee Review (FCR) – A quorum (one more than half) of the ACUC members meets synchronously as a committee to review a protocol.

G. AUP – Animal Use Protocols describe projects that contain a limited group of study aims, species, and related procedures; a single AUP may not encompass all the animal work done by any one PI and their lab, in which case a PI may maintain multiple AUPs.

H. Revision or Amendment – A change to the protocol (AUP) that must be reviewed and approved by the ACUC either using the administrative, DMR, FCR, or DMR post FCR review process.

IV. Types of ACUC Review

A. In accordance with PHS Policy and USDA Regulations, all protocols are reviewed by the ACUC using either the Full Committee Review (FCR) or Designated Member Review (DMR) methods. Using the criteria described below and approved by the IACUC as specified to determine potential review path (e.g., FCR, DMR, Administrative with or without VVC), protocols or amendments are initially triaged by the Director of the Office for Animal Care and Use (OACU) or their designee as to the ACUC review path required. When DMR criteria are determined to be potentially met, such that a DMR call to FCR process is initiated, IACUC members are automatically notified by email of the document's availability in the eProtocol software. For *de Novo* reviews or AUP revisions, the members are invited to request additional information or call for full committee review (FCR). If no request for FCR is made within one (1) working day of the electronic availability (distribution) of the materials, DMR will proceed as described in the procedures below.

Protocols are reviewed by the ACUC, OLAC Veterinarians, an OACU analyst, and ACUC liaisons as necessary, for compliance with all applicable laws, regulations, and guidelines. In accordance with PHS Policy and AWA/AWR, this institution provides each ACUC member with complete descriptions (the AUP) of all research and/or teaching projects that involve the care and use of animals. Any member of the ACUC may call for a full committee review of any AUP at any time.

No member may participate in the ACUC review or approval of a research project in which the member has a conflicting interest (e.g., personal involvement in the project) except to provide information as requested by the ACUC during the review of the protocol. In addition, a member who has a conflicting interest may not contribute to the constitution of a quorum during the review and vote on that protocol. For the situation in which the protocol PI is an OLAC Veterinarian, the OACU Director (or designee) will arrange for an appropriately credentialed and experienced Veterinarian employed by the UC System in laboratory animal care to serve as the consulting veterinarian for said protocol(s).

B. Full Committee Review (FCR)

All new protocols and de novo submissions seeking ACUC approval of *custom procedures* that are classified as pain categories D and/or E will be reviewed by the FCR process. All amendments containing significant changes that meet the criteria described in Appendix B are assigned to be individually discussed and voted upon by ACUC members at a convened meeting of the committee. The ACUC Chair or their designee assigns each protocol to a member of the committee for detailed review and presentation at a convened ACUC meeting. Generally, another ACUC member is assigned as a secondary reviewer. The AUPs and significant amendments to be reviewed at a convened meeting are made available electronically to all ACUC members at least three (3) working business days before the meeting on the secure, password protected eProtocol website. If there are non-protocol business items to be shared with the full committee, those are securely distributed to all members. At the meeting, the convened quorum of the committee discusses and votes on each protocol and amendment. At the meeting, the primary and secondary reviewers present the protocol, and all members present at the meeting (in person, via real-time computer connection (e.g., Zoom) or via teleconference in compliance with PHS policies) are offered an opportunity to ask questions and participate in real-time discussion of the protocol.

C. Designated Member Review (DMR)

Amendments or revisions that do not meet the criteria listed in Appendix B for FCR may be assigned to DMR. When an amendment is eligible for DMR, ACUC members are provided with the complete AUP, with changes highlighted in eProtocol. Members may request additional information as needed to aid their decision to allow DMR. If no request for FCR is made within one working day of the electronic distribution of the proposed revised AUP(s), review by DMR will proceed.

De novo (continuing) protocols that contain procedures assigned to pain categories B or C will undergo the DMR call to FCR process. In addition, de novo (continuing) protocols will undergo DMR call to FCR if they only use mice and/or rats, do not include procedures assigned to pain category E, and all category D procedures used are pre-filled procedures in eProtocol approved by the ACUC. If there is no call to FCR, these protocols will be reviewed by DMR procedures. Non-significant (minor) changes or revisions to protocols may be reviewed by DMR or administratively per ACUC policy.

In addition to review by OACU staff, an OLAC veterinarian (or other qualified veterinarian; see III.A), and ACUC Liaisons as applicable, at least one qualified member of the ACUC (as assigned by the chairperson or his/her designee) will conduct the review. The ACUC member(s) has/have the authority to approve, to require modifications (to secure approval) or to request full committee review of the AUPs. Designated ACUC reviewers do not have the authority to withhold approval.

D. DMR post FCR Protocols

In those cases where an AUP has undergone review at a convened meeting of the full committee, but the ACUC is unable to approve the protocol due to unanswered questions that must be clarified by the PI, the quorum of members present at the convened meeting may decide by unanimous vote to use DMR subsequent to FCR. Although review in these cases will proceed via the DMR post FCR process, all committee members may, through their discussion indicate what clarification and/or answers is/are needed before approval by DMR. However, if one or more DMR post FCR reviewer/s finds that answers to questions or requests for clarification are insufficient, the protocol must be called back for FCR for further discussion and review before approval.

E. By reviewing and approving this policy and in particular the DMR post FCR process, all ACUC members agree to delegate full responsibility for reviewing and approving protocols that meet the criteria listed in Appendix B (DMR or DMR post FCR) to the ACUC Reviewer(s) assigned by the Chair or to the staff and/or liaisons as assigned by the OACU Director.

F. In summary, because of each of the above processes of review, the ACUC approves, requires modification (to secure approval) or withholds approval of every AUP at least once every 3 years (de novo/continuing review).

V. Non-IACUC Review

A. Administrative Review of Significant Changes with Veterinary Verification and Consultation (VVC)

In support of the use of performance standards and professional judgment and to reduce regulatory burden, ACUC-reviewed and -approved policies (e.g., guidance documents, standard operating procedures, drug formularies) for the conduct of animal activities will be used for the administrative handling of significant changes under VVC. The ACUC will review its approved list of policies (see Appendix B for list of documents as noted above) every three years or more frequently if needed.

The specific significant changes described in a.- e., below, must be documented by OACU staff; then the VVC review/approval is handled administratively according to the ACUC-reviewed and -approved policy on Protocol Review. In this policy, under Appendix B there is a list of the references that can be used by an OLAC veterinarian as authorized by the ACUC in doing a VVC review/approval. OACU staff may informally consult with an OLAC veterinarian in deciding if an amendment fits VVC criteria

prior to triage which facilitates the formal veterinary consultation and verification of compliance with our ACUC policy for significant changes that is done after triage and assignment via our software.

The veterinarian is serving as a subject matter expert to consult and verify that compliance with the ACUC-reviewed and -approved policy on a significant change is appropriate for the animals in this circumstance.

The veterinarian may refer any request to the ACUC for review for any reason and must refer any request that does not meet the parameters of the ACUC-reviewed and -approved policies.

This includes changes in:

a. Dosage, route, frequency or duration as found in ACUC Approved references (Appendix B) for anesthesia, analgesia, sedation, or experimental substances including substituting one analgesic, anesthetic or sedative agent to another or changing the dosage, timing or route of an experimental substance if that will not increase the potential for animal pain or distress;

b. euthanasia to any method approved in the current AVMA Guidelines for the Euthanasia of Animals;

c. duration, frequency, type, or number of procedures performed on an animal;

d. change in stock, strain, or genetic modification, unless the new stock, strain or modification results in abnormalities that require special support; and,

e. greater than 10% increase in animal number of any one species.

B. Administrative Review of other changes

Minor changes (amendments) may qualify for administrative review and approval by OACU staff as described in Appendix A. The only significant change that may be handled administratively by OACU staff per ACUC Policy without additional consultation or notification of ACUC is an increase in previously approved total animal numbers per species by less than 10% during a 3-year AUP approval period, as long as there is no accompanying change to the original rationale or study objectives. (PHS Policy IV.D.1.a.).

VI. Approval and Expiration Dates

A. New protocols

1. New protocols will be assigned an approval date and become effective either when:

a) The full committee approves said AUP; or,

b) The final DMR reviewer approves the protocol in the DMR post FCR process.

2. The expiration date will be the last day of the month prior to the calendar month in which the protocol receives final approval.

B. *De novo* review

1. *De novo* reviews and approvals must be completed prior to the last day of the month in which the AUP expires and are effective on the first day of the next month.

2. If a lapse in approval occurs, all work must stop immediately, and the Attending Veterinarian becomes responsible for the animals covered by that protocol.

C. Amendments are effective immediately upon ACUC approval by DMR, FCR, or DMR post FCR and, similarly, after administrative review.

1. Researchers or instructors must not implement changes to an AUP without prior approval by ACUC or administrative review as required by the nature of the change.

Research or teaching activities with animals must not continue after the AUP expiration date. PIs are responsible for knowing the expiration date of their protocol.

References

A. Animal Plant Health Inspection Service (APHIS). United States Department of Agriculture (USDA). *Code of Federal Regulations*. Title 9, Chapter 1, Subchapter A, Part 2 – Regulations, Subpart C, §2.31 Institutional Animal Care and Use Committee.

B. Office of Laboratory Animal Welfare. (2002). Public Health Service Policy on Humane Care and Use of Laboratory Animals.

C. NIH Guidance on Significant Changes to Animal Activities, NOT-OD-14-126

D. OLAW Online Seminar: Guidance on Significant Changes to Animal Activities, August 21, 2014

E. AWA Research Facility Registration Updates, Reviews, and Reports, RIN 0579-AE54

Appendix A –Types of Review

All protocols are triaged on a case-by-case basis and may be assigned a different path, regardless of eligibility to be reviewed under alternative processes.

Administrative Review	Administrative Review with Veterinarian Verification & Consult (VVC)	Designated Member Review (DMR)	Full Committee Review (FCR)
1. Substituting or adding a qualified person, other than the PI (student/staff/faculty) 2. Change in protocol title without any other changes 3. Removal of protocol information that does not alter the overall scope of the research; does not compromise the integrity or credibility of the data; and/or does not result in any animal welfare issues e.g., increased animal pain, distress, injury. 4. Addition of new funding sources with no change in procedures 5. Less than 10% total increase per species during the ACUC 3-year approval period as long as there is not accompanying change to the original rationale or study objectives 6. Correction of typographical errors, grammar and contact information updates 7. Change in ACUC-approved animal housing/procedure room in consultation with OLAC **8.** Formatting protocol content that has been approved by ACUC but that must be updated due to software changes. Staff work with the PI to place approved information in the new correct location in the protocol	1. Changes in euthanasia methods consistent with current AVMA Guidelines for the Euthanasia of Animals 2. Changes in anesthesia, analgesia, sedation or experimental substances (e.g., dose, route, timing) – consistent with ACUC reviewed policies 3. Greater than 10% increase in animal numbers of any one species 4. Change in stock, strain, or genetic modification, unless the new stock, strain, or modification results in abnormalities that require special support 5. Change to previously approved procedures involving duration, frequency, type, or number of procedures performed on an animal – consistent with ACUC reviewed policies (e.g., Blood Collection, Dosing Techniques, Compound Administration)	1. De novo protocols involving procedures with only pain and distress categories B & C 2. De novo protocol with rodents (rats or mice bred for research) involving only pre-filled procedures with pain and distress categories B, C and/or D 3. Change in PI 4. Addition of a minor surgery 5. Change in survival time (only if already chronic) or change from chronic to acute 6. Addition of behavior studies (if no potential for pain/distress) 7. A need to repeat the experiment if due to test article failure or inadequate training/expertise of personnel 8. Change that impacts personnel safety 9. Change in objectives, purpose or aim of study 10. Change to or an addition of a species	1. All new protocols 2. De novo protocol involving procedures with pain and distress categories D & E (see rat/mice exception #2 under DMR) 3. Non-Survival to a survival surgery 4. Changes that result in greater pain, distress or invasiveness (e.g., severe post procedural handicap, tumor growth exceeding 10% of animal body weight) 5. Change from acute to chronic procedure 6. Change in housing and/or use of animals in a location that is not part of the animal program overseen by the ACUC

Appendix AB – ACUC Approved References for VVC

- Veterinary Textbooks (e.g., Carpenter's Exotic Animal Formulary, Flecknell's Laboratory Animal Anesthesia; Plumb's Veterinary Drug Handbook; Fowler's Zoo and Wildlife Medicine; Lumb and Jones Veterinary Anesthesia and Analgesia; Quesenberry's Ferrets, Rabbits and Rodents: Clinical Medicine and Surgery; Fish's Anesthesia and Analgesia of Laboratory Animals; Lumb & Jones' Veterinary Anesthesia and Analgesia, Hernandez's Medical Management of Wildlife Species)
- ACLAM Formulary
- "Nonhuman Primate Formulary", Association of Primate Veterinarians
- Peer reviewed journal publications
- Personal communications with veterinary anesthesiologist(s)
- OLAC Mouse Anesthesia-Analgesia Formulary, available through UCB sign-in, or PDF upon request
- OLAC Rat Anesthesia-Analgesia Formulary, available through UCB sign-in, or PDF upon request