

Version: 3.4 Effective Date: July 1, 2021	POLICY ON PROTOCOL REVIEW	Supercedes Document Dated: <i>November 1, 2020</i>
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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. In addition, ACUC annually reviews all AUPs that use USDA regulated animals. If changes are proposed to an ongoing approved activity, principal investigators must submit a 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; or, OACU staff review with OLAC VVC for significant changes; or OACU staff review as specified in Appendix A.
- B. Annual review – The yearly review of an existing protocol during which the ACUC assesses the status of the research or course.
- C. *De novo* 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 a protocol following 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 of the ACUC members meets as a committee to review a protocol.

- G. AUP – Animal Use Protocols describe projects that contain a limited group of study aims, species, related procedures; a single AUP may not encompass all of the animal work done by any one PI and his/her 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 DMR, FCR, or DMR post FCR review process; or administratively processed with or without OLAC VVC depending on the nature of the proposed revision.

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), Designated Member Review (DMR) or Administrative Review method. Using the criteria described below, protocols or amendments are initially triaged by the Director of the Office for Animal Care and Use (OACU) or his/her designee as to the ACUC review path required.

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 full committee review of any AUP.

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. In the situation in which the protocol PI is an OLAC Veterinarian, the OACU Director will arrange for an appropriately credentialed and experienced Veterinarian employed by the UC System 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 A are assigned to be individually discussed and voted upon by ACUC members at a convened meeting of the committee. The ACUC Chair or his/her 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 no less than five calendar

days before the meeting. 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 A 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 protocols that contain procedures assigned to pain categories B or C will undergo the DMR call to FCR process. In addition, *de novo* protocols can undergo DMR call to FCR if they use mice and/or rats, do not include procedures assigned to pain category E, and all category D procedures used are pre-filled procedures approved by the ACUC or are pre-approved procedures posted on the OLAC website. If there is no call to FCR, these protocols will be reviewed by DMR procedures.

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. Annual Review

1. Only protocols that involve USDA regulated must undergo an annual review. PIs whose protocols meet these criteria must submit an Annual Renewal Form verifying among other things, that there are no changes in:
 - a) animal species;
 - b) animal numbers or procedures proposed for the coming year; and
 - c) additionally that there were no unanticipated outcomes to the procedures performed during the past year
2. The ACUC Chair and/or Vice Chair will generally perform these annual reviews if there is no call to bring the protocol to FCR review (per DMR call to FCR procedures). If there are no questions or concerns, the research will continue until the next annual or *de novo* review.

F. Administrative Review

1. Administrative Review with Verification of Veterinary Consultation (VVC)

Some significant changes to an AUP may be handled administratively by OACU staff in consultation with an OLAC veterinarian if the changes meet the criteria described below. OACU staff will document the nature of the changes and the consultation with the OLAC veterinarian; through his/her review, the OLAC veterinarian verifies that the changes proposed meet the criteria set forth in this policy.

The OLAC veterinarian has the authority to request ACUC review of the proposed changes for any reason and must request such ACUC review for any changes which do not meet the parameters of this policy. The OLAC veterinarian is the expert who determines that the proposed significant change meets the ACUC policy for Administrative Review with VVC and does not require committee review. Significant changes eligible for administrative review with VVC are described in Appendix A.

2. Administrative Review of minor changes

Changes (amendments) may qualify for administrative review and approval by OACU staff as described in Appendix A.

- G. 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 A (for Administrative review, 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.

- H. In summary, as a result 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* review).

V. 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 with or without VVC.

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.

VI. 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.

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- C. NIH Guidance on Significant Changes to Animal Activities, NOT-OD-14-126
- D. https://grants.nih.gov/grants/olaw/140821_seminar_transcript.pdf

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Appendix A – ACUC 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)
<ol style="list-style-type: none">1. Substituting or adding a qualified person, other than the PI (student/staff/faculty)2. Change in protocol title without any other changes3. Addition of new funding sources with no change in procedures4. Less than 10% total increase in total animal number of the originally approved protocol5. Correction of typographical errors, grammar and contact information updates6. Change in ACUC-approved animal housing/procedure room in consultation with OLAC7. 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.	<ol style="list-style-type: none">1. Changes in euthanasia methods consistent with current AVMA Guidelines2. Changes in anesthesia, analgesia or sedation) (e.g. dose, route, timing) - consistent with ACUC Policy & Guidelines3. Change in experimental substances and fundamentally similar compounds that are documented in the literature regarding safety and toxicity in the same species - consistent with ACUC Policy & Guidelines4. Greater than 10% increase in animal numbers of any one species5. Change in stock, strain, or genetic modification, unless the new stock, strain, or modification results in abnormalities that require special support.6. Change to previously approved procedures involving duration, frequency, type, or number of procedures performed on an animal - consistent with ACUC Guidelines (e.g. Blood Collection, Dosing Techniques, Compound Administration)	<ol style="list-style-type: none">1. De novo protocols involving procedures with only pain and distress categories B & C2. 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 D3. Change in PI4. Addition of a minor surgery5. Change in survival time (only if already chronic) or change from chronic to acute6. 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 personnel8. Change that impacts personnel safety9. Change in objectives, purpose or aim of study10. Change to or an addition of a species	<ol style="list-style-type: none">1. All new protocols2. 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 surgery4. Changes that result in greater pain, distress or invasiveness (e.g. severe post procedural handicap, tumor growth exceeding 10% of animal body weight)6. Change from acute to chronic procedure5. Change in housing and/or use of animals in a location that is not part of the animal program overseen by the ACUC