Procedure: IACUC-07
Date: February 6, 2025
Enabled by: PHS, AWR, Guide
Supersedes: October 17, 2024

UC Davis
Institutional Animal Care and Use Committee (IACUC)

Title: Animal Care and Use Protocol/Amendment Review and Renewal Process

I. Background:

A critical component of the IACUC Charge is the review of all procedures involving animals with careful consideration of their relevance to human or animal health and the advancement of knowledge for the good of society. The following policy exists to guide IACUC staff, university faculty and their staff, and veterinary staff specializing in laboratory animal medicine of the goals, objectives, and scientific benefits of all proposed projects to verify the following: the project has appropriate merit; the proposed research complies with all federal, state, and university laws, regulations, and guidelines; humane use guidelines are followed and all animals involved are provided with the best possible treatment and professional veterinary care; a sufficient, but not excessive, number of animals being used is justified; those who will be working with the animals have received the proper training; and proper practices and procedures are in place to reduce as much discomfort, pain, and/or distress to the animals as possible.

Each member of the IACUC is provided access to all applications submitted for review. Members review the applications during a designated review period and indicate their approvals or any topics of concern before the end of the review period. Reviewer concerns are communicated to the applicant, and their response is returned to the designated reviewer for further consideration. Once all outstanding questions are resolved to the satisfaction of the reviewers, the protocol or amendment can be approved.

Scientific Merit Note:

Peer review of the scientific and technical merit of an application is considered the purview of the NIH Scientific Review Groups, which are composed of scientific experts from the extramural research community in a particular area of expertise. NIH reviewers can also raise specific animal welfare concerns that may require resolution prior to a grant award.

Although not intended to conduct peer review of research proposals, the IACUC is expected to include consideration of the U.S. Government Principles in its review of protocols. Principle II calls for an evaluation of the relevance of a procedure to human or animal health, the advancement of knowledge, or the good of society. Other Public Health Service (PHS) Policy review criteria refer to sound research design, rationale for involving animals, consideration of biological variables (e.g., inclusion of males and females unless there is a scientific rationale for only one sex), and scientifically valuable research. Presumably a study that could not meet these basic criteria is inherently unnecessary and wasteful and, therefore, not justifiable.

The primary focus of the NIH review is scientific merit and the primary focus of the IACUC is animal welfare. The two bodies have differing constitutions, mandates, and functions. However, since it is not entirely possible to separate scientific value from animal welfare some overlap is inevitable. NIH reviewers may raise concerns about animal welfare and IACUCs may question the scientific rationale or necessity for a procedure, rigor and reproducibility, particularly if the proposed project has not been peer reviewed.

II. Purpose:

To describe the UC Davis IACUC procedures for reviewing newly submitted Animal Care and Use Protocols, changes to existing protocols (amendments), and protocol annual reviews/renewals.

III. Policy:

The Animal Welfare Regulations (AWRs), the Guide for the Care and Use of Agricultural Animals in Research and Teaching (Ag Guide), and the Institute for Laboratory Animal Resources (ILAR) Guide for the Care and Use of Laboratory Animals (Guide) all require the IACUC to review and approve all proposals for animals used in research, teaching, or testing, and any change to existing approved proposals.

Principal Investigators (PIs) requesting the use of animals for research, teaching, or testing are required to submit protocols to the IACUC for approval. PIs are also required to submit amendments for approval with any proposed change(s) to approved protocols prior to implementing the change, and to provide notification of unanticipated adverse events. The IACUC will review the request to ensure that the protocol/amendment is in accordance with the PHS Policy, AWRs, US Government Principles Regarding the Care and Use of Animals, ILAR Guide, and the Ag Guide.

IV. Procedure:

A. Protocol/Amendment Pre-review
    1. Requests are submitted to the IACUC office via the online IACUC system.
    2. Requests are assigned to an IACUC Staff Specialist, a Staff Veterinarian, and applicable Safety Committee(s) for review.
    3. The veterinarian and IACUC Specialist and the applicable Safety Committee Specialist enter the pre-review questions in the online system.
    4. The assigned IACUC Specialist reviews the request to ensure the submission is complete and will communicate any questions/suggestions to the PI to finalize the request for IACUC review.
    5. If applicable, the IACUC staff will request specific portions of a newly submitted Animal Component of Research Protocol (ACORP) for Veterans Affairs (VA) funded protocols to compare to the Animal Care and Use Protocol.
    6. Funding agencies may require a grant comparison. The PI will complete the grant congruency document provided by the Office of Research, Sponsored Programs, that includes the Cayuse number provided on the Cayuse datasheet submitted to Sponsored Programs prior to submitting the grant or contract.

7. Once any necessary revisions have been made, the protocol/amendment is placed on the next IACUC agenda for review.
8. If a protocol or amendment has received no response to questions from the PI/lab within three months, it will be withdrawn. A template will be saved of the protocol and questions, and it can be re-submitted at a later date.

B. IACUC Review

The IACUC may either review the protocol/amendment by Designated Member Review (DMR) or Full Committee Review (FCR). Any IACUC member may request that a protocol or amendment identified for DMR be reviewed by FCR.

Protocols/amendments involving the following will typically be reviewed by the full committee at a convened IACUC meeting:

- Survival surgery.
- Category E procedures.
- Adverse effects reports.
- Changes from a non-survival to a survival study.
- Addition of surgical and/or invasive procedures.
- Any protocol that involved nonhuman primates.
- Nonhuman primate amendments that include additions of approximately 25% greater than the overall approved number, which is reflected cumulatively over the parent protocol and any amendments where animals may have been added.
- Any terminal surgery or invasive procedure not approved in a referenced California National Primate Research Center (CNPRC)/Center for Neuroscience (CNS) Nonhuman Primate Standing Operating Procedure (SOP).

Protocols falling into the above categories may only be assigned to DMR if an exception is approved by the IACUC Chair or designee or if the protocol/amendment has been reviewed by FCR and voted on by the Full Committee to be moved to DMR.

Members who are associated with a protocol or have a related conflict of interest must abstain from voting on the protocol or amendment and must recuse themself from any assignments as one of the two designated reviewers.

The IACUC may approve policies, guidance documents, SOPs, or drug formularies for the conduct of animal activities. These may be referenced in a protocol in lieu of the PI including a full description of the procedure(s) in the body of the protocol and must be reviewed at least every three years.

The IACUC may request an *ad hoc* outside subject matter expert be consulted if needed.

C. Full Committee Review

1. Full committee protocols will be placed on an IACUC agenda and assigned to a primary and secondary reviewer by the IACUC staff under the delegated authority of the Chair. All members will have access to the protocol prior to the meeting to review and submit questions via the online system.

2. Committee members will review the protocol(s) to ensure that they are consistent with the guidelines, regulations, and campus policies pertaining to live, vertebrate animal research and teaching.
3. Questions from the IACUC members will be compiled by the assigned IACUC Specialist and forwarded to the PI for response.
4. The protocol will then be discussed by a quorum of IACUC members at a convened meeting.
5. After discussion, the members will have the following options:
    a. Approve the protocol as presented.
    b. Table (protocol remains in FCR) until the next convened meeting to gather additional information or require modifications.
    c. Vote to send to DMR for additional review (see process below).
    d. Withhold approval.
6. If the IACUC votes to withhold approval, the PI will be provided written notification of the IACUC's decision along with a list of concerns regarding why the protocol or amendment was denied. The PI has an opportunity to respond in person (virtually) or in writing with a point-by-point plan to address each issue, and with an opportunity to discuss their plan with the IACUC at a convened meeting. The revised protocol or amendment is then submitted for IACUC review using the same method as any new protocol or amendment.

D. DMR

1. New Animal Care and Use Protocols and amendments to existing approved protocols will undergo initial review using the established pre-review process described above. If the request is eligible for DMR, the following procedure will be enabled:
    a. A DMR team or single member reviewer will be recommended by the IACUC staff on behalf of the IACUC Chair. If the recommended reviewer(s) requires modification, the IACUC staff will communicate the request to the PI. A single member reviewer may be used for non-invasive clinical trials and staff roster protocols and amendments.
    b. IACUC staff will send DMR requests to the committee by electronic mail. The email will contain the following:
        - DMR request, the one or more recommended designated reviewers, and the assigned IACUC Specialist.
        - A brief description of the protocol/amendment.
        - The assigned pain category.
2. Committee members will have two working days to request that the protocol be removed from DMR and placed on an agenda for FCR or request that they be added to the DMR team.
3. After two working days, if there are no objections to the DMR request, the members of the DMR team have the option to:
    a. Recommend approval of the protocol/amendment as presented.
    b. Request modifications.
    c. Request FCR.
4. All members of the DMR team must approve the protocol/amendment. If one DMR reviewer does not approve, the proposal must be moved to FCR.

5. An amendment or protocol that was reviewed by FCR may be assigned to DMR at a convened meeting if additional information is needed to secure approval and the members present vote unanimously to send the protocol/amendment to DMR. This provides the DMR team the authority to approve the protocol/amendment outside of a convened meeting. The protocol/amendment can be approved by DMR as soon as committee members receive the required information and there are no additional questions. The responses are not required to be reviewed by the entire committee. However, any member can request that a protocol or amendment be reviewed by the full committee at any time prior to approval.

E. Administrative Verification of Significant Changes
    1. OLAW/USDA allows certain significant changes to be approved administratively after the Attending Veterinarian or designee (e.g., Campus Veterinary Services, VMTH Field Services for agricultural species, CNPRC staff veterinarians for nonhuman primates at the Primate Center) verify the modification is consistent with IACUC approved policies, guidance documents, SOPs, and/or drug formularies. These changes include:
        a. Changes in anesthesia, analgesia, or sedation provided they are not used in conjunction with neuromuscular blocking agents. Changes in antimicrobials and contrast agents. Examples of changes which may be approved under this category are:
            i. Anesthetics, analgesics, sedatives, antimicrobials, and contrast agents using referenced dosages, routes, durations, and frequencies for the species and within acceptable and known veterinary parameters. Reference materials may include, but are not limited to, textbooks (such as Harkness and Wagner's Biology and Medicine of Rabbits and Rodents; Flecknell's Laboratory Animal Anesthesia; Plumb's Veterinary Drug Handbook; Hawk and Leary's Formulary for Laboratory Animals; Fowler's Zoo and Wildlife Medicine; Lumb and Jones Veterinary Anesthesia and Analgesia; Quesenberry and Carpenter's Ferrets, Rabbits and Rodents Clinical Medicine and Surgery; Fish and Danneman Anesthesia and Analgesia of Laboratory Animals); peer reviewed journal publications; personal communications with veterinary anesthesiologist(s), and IACUC approved formularies.
            ii. Switching from one approved analgesic, anesthetic, sedative, antimicrobial, or contrast agent to another.
            iii. Addition of a drug or compound used routinely in veterinary practice and/or the laboratory animal medicine field at dosages, volumes, and routes consistent with the above references.
            iv. Changes in euthanasia using any species appropriate method approved in the AVMA Guidelines for the Euthanasia of Animals.
        a. Animal number change <10% of the original approved animal number, cumulatively over all protocol amendments as noted above.
        b. Changes in duration, frequency, type, or number of approved procedures performed on an animal provided the changes do not result in greater pain,

distress, or degree of invasiveness. Typical examples under this category may include:

i. Blood collection frequency, site, and volume.
ii. Number, timing, or method related to in *vivo* imaging procedures.
iii. Non-invasive tissue sample collection (i.e., oral, ocular, nasal, auricular, rectal, and vaginal swabbing; dermal swabbing or scraping that does not cause more than momentary surface bleeding; hair, feather, or scale removal that does not impact physiological or functional performance).
iv. Method of identification including addition of rodent genotyping if the change is consistent with IACUC policy.
v. Routes of administration, volumes, dosages, durations, and frequencies of previously approved experimental compounds that does not exceed IACUC policy guidelines.
vi. Changes in timing of previously approved procedures.
vii. Additional strains and/or sources of animals.
viii. Change in animal disposition consistent with the Animal Tracking System (ATS) and the IACUC Adoption of Animals Used in Research and Teaching Policy.
ix. Changes in acquisition, disposition, or acclimation periods are consistent with established policy.

F. Administrative Amendments
1. The following categories of protocol amendments are viewed as minor changes, therefore acceptable for the IACUC staff to review and approve:
    a. Relocation to approved animal housing and approved day use areas.
    b. Roster additions with documented training according to IACUC policy.
    c. Roster deletions.
    d. Change in source of the animal(s) if it is to an approved vendor.
    e. Changes to the protocol title as long as the change proposed does not change the original objectives.
    f. Addition of a funding agency.
    g. Modifications to observational studies when there will be no impact on the animals.
    h. Change in disposition for animals that have not been used in any procedures.
    i. Corrections of grammar or typographical errors.
    j. Contact information updates.
    k. Changes to VMTH Clinical Trial Review Board Client Consent Form that does not affect the protocol (i.e., change in cost to client, inclusion criteria).
    l. Changes due to updates in IACUC approved policies.

G. Protocol Expiration Date
1. Three years after the initial date of IACUC approval, a protocol will expire and cannot be renewed through the annual renew process. If the project is still active, the PI must submit a new protocol to the IACUC requesting review and

approval. The new protocol should be submitted to the IACUC at least six weeks before the current protocol expires.

2. Prior to the protocol anniversary date of the third year, electronic reminder messages are sent 90, 60, 30, and 14 days prior to protocol expiration date.
3. If a new protocol is not approved by the expiration date, and there are still animals on the protocol when the protocol expires, the animal(s) will be transferred to a holding protocol (Campus Holding Protocol or unit-specific Holding Protocol) until a new protocol is approved. **No animal research or teaching may be performed using animals on the holding protocol.** Regular per diem charges will still apply and remain the responsibility of the PI. In accordance with the Animal Holding protocol: "*Transgenic and/or other unique and valuable animals may be maintained in a breeding colony to prevent loss of the line/traits of interest. If continued breeding is required to prevent loss of lines, the investigator must reach out to the Attending Veterinarian (or designee) for approval. Husbandry or veterinary staff will maintain the breeding colony if authorized by the Attending Veterinarian/IACUC. The campus policy on genotyping, sampling, identifying and breeding colony maintenance and all facility SOPs will be followed*."

H. Annual Protocol review

1. Renewal notices
    a. The IACUC Office will send renewal notices annually to the PI and Alternate Contact by electronic mail at the end of year 1 and year 2.
    b. Electronic mail messages will be sent before the protocol anniversary date reminding the PI that the protocol is due to expire soon unless renewed. Electronic messages for annual renewals are sent approximately 60, 30, and 14 days before the anniversary date, and require a response through the online system.
    c. Final expiration notifications will be sent at the same time intervals.
2. Responses by the PI
    a. The PI has the following response options:
        i. The project is still active and requests renewal.
        ii. The project is no longer active (or will be completed prior to the annual renewal date), and the protocol can be allowed to expire.
3. The PI will also be prompted to make any necessary changes to the personnel listed on the staff roster, changes in procedures, animal numbers, or other project aspects.
4. The PI will be prompted to verify animal usage numbers for accuracy.
5. The PI will be prompted to verify there have been no adverse events associated with the protocol.
6. If the PI does not respond to the renewal notice by the anniversary date, and there are still animals on the protocol, the animal(s) will be transferred to a holding protocol (Campus Holding Protocol or unit-specific Holding Protocol) until the protocol is renewed.
7. If an Annual Renewal request is not submitted, the protocol will be allowed to expire. If IACUC Staff are able to confirm with personnel associated with the project that the protocol is still active or can be allowed to expire, the

IACUC Staff member may respond to the Annual Renewal request on behalf of the PI.

8. Annual renewal reviews will be conducted at the end of year 1 and year 2. Reviews must be completed by the end of the calendar month the protocol was originally approved. IACUC review may occur via FCR at a convened meeting or using the DMR process described above with at least one member assigned as a designated reviewer.
9. IACUC annual renewal of a protocol extends the expiration to the next anniversary date of the protocol.
10. Protocols are approved for a three-year period, after which time a new protocol must be submitted for a de novo/triennial review.

I. Notifications

1. Electronic mail notification of the Committee's decision is sent to the PI following DMR, FCR, administrative changes, and annual reviews.
2. The finalized approved copy of the protocol or amendment is maintained on file in the IACUC Office and is available online for review by the PI and research staff. It is the responsibility of the PI to update the funding agency of any significant changes to the scope of the grant or contract proposal that is represented in the approved IACUC Protocol.

V. Resources:

1. Animal Welfare Act and Regulations
   https://www.nal.usda.gov/awic/animal-welfare-act
2. ILAR, Guide for the Care and Use of Laboratory Animals
   https://grants.nih.gov/grants/olaw/guide-for-the-care-and-use-of-laboratory-animals.pdf
3. PHS Policy
   https://olaw.nih.gov/policies-laws/phs-policy.htm
4. AVMA Guidelines for the Euthanasia of Animals: 2020 Edition
   https://www.avma.org/sites/default/files/2020-01/2020-Euthanasia-Final-1-17-20.pdf
5. All IACUC Policies and Guidelines
   https://research.ucdavis.edu/research-support/animal-care-use/iacuc/iacuc-policies-and-guidelines/
6. All Standards of Care Program Policies
   https://research.ucdavis.edu/research-support/animal-care-use/campus-veterinary-services/standards-of-care-program-policies/
7. U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training
   https://olaw.nih.gov/policies-laws/gov-principles.htm
8. PHS FAQs
   https://olaw.nih.gov/guidance/articles/ilar91.htm