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

I. **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.

II. **Policy:**

The Animal Welfare Regulations (AWRs) and the Institute for Laboratory Animal Resources (ILAR) Guide for the Care and Use of Laboratory Animals (Guide) require that the IACUC review and approve all proposals for animals used in research, teaching, or testing, any change to existing approved proposals, as well as annual reviews of existing protocols.

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 for approval any proposed change(s) to approved protocols prior to implementing the change. The IACUC will review the request to ensure that the protocol/amendment is in accordance with the Public Health Service (PHS) Policy, AWRs, US Government Principles Regarding the Care and Use of Animals, ILAR Guide, and the Federation of Animal Science Societies Guide for the Care and Use of Agricultural Animals in Research and Teaching (Ag Guide). In accordance with Federal AWRs the IACUC must also review annually all approved protocols pertaining to regulated species. UC Davis has applied this requirement to all species used by UC Davis faculty and research/teaching personnel.

III. **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 and a Staff Veterinarian for review.
3. The veterinarian has the option of contacting the PI directly with questions or forwarding their questions to the assigned IACUC Specialist.
4. The assigned Specialist will review the request to ensure it is complete and communicate questions/suggestions to the PI to finalize the request for IACUC review.
5. The IACUC staff will request specific portions of a newly submitted or newly funded NIH grant to compare to the Animal Care and Use Protocol.
6. Other funding agencies may require a grant comparison (e.g., DoD, VA).
7. Once all necessary revisions have been made, the protocol/amendment is placed on the next IACUC agenda for review.

B. IACUC Review

The IACUC may either review the protocol/amendment by Designated Member Review (DR) or Full Committee review. Any IACUC member may request that a protocol be reviewed by the full committee.

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
- Nonhuman primate protocols with the exception of:
  - Observational studies in which there is no behavioral or environmental manipulation.
  - Field studies not regulated by USDA.
- Nonhuman primate protocol amendments with the exception of:
  - Animal number additions of approximately 25% greater than the originally approved number.
  - Survival Surgeries
  - Terminal Surgeries
  - Any invasive procedure not approved in a CNPRC/CNS SOP

Protocols falling into the above categories may only be assigned to DR if an exception is approved by the IACUC chair or designee.

Members who are associated with a protocol or have a related conflict of interest must abstain from voting on the protocol or amendment.

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

If project funding is listed as departmental or has not been peer reviewed, the IACUC may request an outside expert be consulted.

1. Full Committee Review

   a. Full committee protocols will be placed on an IACUC agenda and assigned to a primary and secondary reviewer. All members will have access to the protocol prior to the meeting to review and can ask questions via the online system.
   b. Committee members will review the protocols to ensure that they are consistent with the guidelines, regulations, and campus policies pertaining to animal research.
   c. Questions from the IACUC members will be compiled by the assigned Specialist and forwarded to the PI for response.
   d. The protocol will then be discussed by a quorum of IACUC members at a convened meeting. After discussion, the members will have the option of:
      i. Approve as presented.
ii. Approve with a condition (e.g. veterinarian to be present during first procedure).
iii. Table until the next meeting to gather additional information.
iv. Send to DR for additional review (see process below).
v. Withhold approval.

2. Designated Member Review

a. New Animal Care and Use Protocols and amendments to existing protocols will undergo the initial review using the established pre-review process described above. If the request is eligible for DR, the following procedure will be enabled:
   i. A designated review 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 Chair will notify the IACUC staff of the necessary change(s).
   ii. A single member reviewer may be used for non-invasive and clinical trials protocols and amendments.
   iii. IACUC staff will send DR requests to the committee by electronic mail. The email will contain the following:
      - DR request, the one or more recommended designated reviewers, and the assigned Specialist.
      - A brief description of the protocol/amendment.
      - The assigned pain category.
   b. Committee members will have two working days to request that the protocol be removed from DR and placed on the next agenda for full committee review or request that they be added to the DR team.
   c. After two working days, if there are no objections to the DR request, any member of the DR team can recommend:
      i. Approve the protocol/amendment as presented.
      ii. Request modifications.
      iii. Request full committee review.
      All members of the DR team must approve the proposal.
   d. An amendment or protocol that was reviewed by the full committee may be assigned to DR at a convened meeting if additional information is needed to secure approval and the members present vote unanimously to send the protocol/amendment to DR. The protocol/amendment can be approved by the designated reviewers as soon as they receive the required information and provided there are no additional questions. However any member can request that a protocol or amendment be reviewed by the full committee at any time prior to approval.
   e. If significant requirements or modifications are made to a protocol or amendment during the review process, notification will be sent to the full committee and two additional days will be allowed for review.

3. Administrative Verification of Significant Changes

OLAW/USDA allow certain significant changes to be approved administratively after the Attending Veterinarian or designee (Campus Veterinary Services, VMTH Field Services for agricultural species, CNPRC staff veterinarians for nonhuman primates at the Primate Center or the CTRB for VMTH clinical trials) verify the modification
is consistent with IACUC approved policies, guidance documents, standard operating
procedures (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); journal
      publications peer reviewed from PubMed and CAB database; Diehl et al. J Ap
      Tox. 2001; 21:15-23, 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.

b. Changes in euthanasia using any species appropriate method approved in the
   AVMA Guidelines for the Euthanasia of Animals.

c. Changes in duration, frequency, type, or number of already 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 site and volume.
      iii. Number, timing, or method in imaging procedures.
      iii. Non-invasive tissue sample collection (i.e., oral, ocular, nasal, auricle, 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 genotyping contingent upon the
          change being consistent with IACUC policy.
      v. Routes of administration, volumes, dosages, durations, and frequencies of
         previously approved experimental compounds that does not exceed 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 that are consistent
          with established policy.

4. Administrative Amendments:
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–02 “Training Requirements for Personnel Exposed to Live, Vertebrate Animals” policy.
c. Roster deletions.
d. Change in source of the animal(s) if it is to an approved vendor. This will be done in consultation with the Health Monitoring Coordinator.
e. Changes to the protocol title as long as it 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 invasive procedures.
i. Corrections of grammar or typographical errors.
j. Contact information updates.
k. Changes to VMTH CTRB Client Consent Form that do not affect the protocol (i.e.; change in cost to client, inclusion criteria).

C. Protocol Expiration Date

1. Three years after the initial date of IACUC approval, a protocol will expire and cannot be renewed. 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 the 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. Only animal husbandry and necessary veterinary care may be performed while the animals are on the Holding Protocol. Breeding colonies may be maintained to prevent loss of the lines. Husbandry or veterinary staff will maintain the breeding colony if authorized by the Attending Veterinarian or IACUC. No research or teaching may be performed with animals while maintained on the Holding Protocol. Regular per diem charges will apply, and are the responsibility of the PI.

D. 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 on 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 would like to request its 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.
b. The PI will also be prompted to make necessary changes to personnel on the staff
roster, changes in procedures, animal numbers, or other project aspects.
c. The PI will be prompted to verify animal usage numbers for accuracy.
d. The PI will be prompted to verify there have been no adverse events associated
with the protocol.
e. 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. Only animal husbandry and necessary veterinary care may be
performed while the animals are on the Holding Protocol. Breeding colonies may
be maintained to prevent loss of the lines. No research or teaching may be
performed with animals while maintained on the Holding Protocol. Regular per
diem charges will apply, and are the responsibility of the PI.

3. If an Annual Renewal request is not submitted, the protocol will be allowed to expire.
If the IACUC Staff is able to confirm with personnel associated with the project the
protocol is still active or can be allowed to expire, the IACUC Staff may respond to
the Annual Renewal request on behalf of the PI.

4. 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 full committee review at a convened
meeting or using the designated member review process described above with at least
one member assigned as a designated reviewer.

5. IACUC annual renewal of a protocol extends the expiration to the next anniversary
date of the protocol.

F. Notifications

0. Electronic mail notification of the Committee’s decision is sent to the PI following
DR, full committee review, or annual review.
1. 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.
3. It is the responsibility of the PI to update the funding agency of any significant
changes to the scope of the grant proposal that is represented in the IACUC Protocol.