

Table of Contents

IACUC Standard Operating Procedures

PARAGRAPH	PAGE
Institutional Animal Care and Use Committee (IACUC)	1
Ethical Principles Governing the IACUC	1
The Regulatory Mandates for Animal Experimentation	1
Definition of Animal Subject and Research	2
Subcommittee on Animal Research (SAR) Roles and Authorities	2
The Membership of the SAR	5
IACUC/SAR Record Keeping and Required Documentation	6
VA Pittsburgh Healthcare System IACUC Review Process and Approval Considerations	7
Required Training	9
Managing Conflicts of Interest	10

Standard Operating Procedures for the VA Pittsburgh Healthcare System Animal Care and Use Committee (IACUC)

Introduction

This VA Medical Center Institutional Animal Care and Use Committee (IACUC) Standard Operating Procedure (SOP) is a reference for IACUC members and investigators. This SOP details the policies and procedures specifying the regulations and policies governing animal research and the requirements for submitting research proposals for review to the IACUC [or Subcommittee on Animal Research (SAR)].

1. Ethical Principles Governing the IACUC

Animal subjects contribute immeasurably to advancements in medical science. Most research and testing involving human patients is based on the results of animal experimentation. To provide hope for veterans suffering from diseases that currently lack cures or effective treatments, the VA actively supports the use of animals in research, teaching, and testing. However, the use of animals in VA research is a privilege granted with the understanding and expectation that such research is conducted according to the highest ethical and legal standards.

2. The Regulatory Mandates for Animal Experimentation

All animal care, husbandry, and animal research practices at VA animal facilities must be in accordance with applicable laws, regulations, and policy. The basic principles governing animal research in VA are found in the United States (U.S.) Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training, which include the following imperatives:

- a. Animal experiments are undertaken only after due consideration of their relevance for human or animal health and the advancement of biological knowledge.
- b. The fewest number of animals needed to achieve scientific objectives is to be used.
- c. The least sentient species that will permit the attainment of research objectives is to be used.
- d. The least painful or distressful procedures needed to meet research objectives are to be used, and all reasonable measures to minimize pain and distress should be utilized.
- e. When planning and conducting studies, the principles of replacement, reduction, and refinement need to always be considered.
- f. Procedures that would be considered painful in a human need to be considered to be painful in an animal.

g. The best possible living conditions need to be maintained for animals kept for research, training, or testing purposes. Animal care needs to be supervised by a veterinarian experienced in laboratory animal medicine. Housing needs to ensure that the general health of animals is safeguarded and that undue stress is avoided, with appropriate attention paid to environmental factors such as temperature, ventilation, and humidity.

h. Personnel need to have appropriate qualifications, training, and experience when conducting procedures on animals. Opportunities for hands-on training need to be provided as needed.

3. Definition of Animal Subject and Research

Animal research refers to any use of laboratory animals in research, testing, or training.

The term “**animal**” is defined as any live vertebrate animal used or intended for use in research, research training, experimentation, or biological testing, or for a related purpose (see PHS Policy on Humane Care and Use of Animals, Sec. III). For the purpose of compliance with the Animal Welfare Act Regulations an animal is defined as any live or dead cat or dog, non-human primate, guinea pig, hamster, rabbit, or any other warm-blooded animal which is being used, or is intended for use in research, teaching, testing, or experimentation. The term excludes birds, rats of the genus *Rattus* and mice of the genus *Mus* bred for use in research, and horses not used for research purposes and other farm animals, such as, but not limited to livestock or poultry, used or intended for use as food or fiber, or livestock or poultry used or intended for use in improving animal nutrition, breeding, management, or production efficiency, or for improving the quality of food or fiber.

4. Subcommittee on Animal Research (SAR) Roles and Authorities

A. Authority to Conduct Animal Research

Because this VA conducts animal research according to the highest ethical and regulatory standards, all animal research must comply with the Health Research Extension Act (codified at 42 U.S.C. Section 289d) and the Public Health Services (PHS) Policy. The PHS Policy includes the U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training (prepared by the Interagency Research Animal Committee), The Guide for the Care and Use of Laboratory Animals (prepared by the National Research Council; henceforth called the Guide and the Report of the AVMA Guidelines on Euthanasia). *NOTE: Compliance with PHS Policy is mandated by VA policy, whether or not PHS funds are accepted by an individual VA facility.* All animal research must be covered by a PHS Assurance. By law, all animal research must comply with the Animal Welfare Act (codified at 7 U.S.C. Sections 2131-2159), the USDA AWAR (Animal Welfare Act Regulations and Standards) (Title 9 Code of Federal Regulations (CFR) Parts 1-4), and 42 CFR 73, Possession, Use, and Transfer of Select Agents and Toxins. All VA animal research involving infectious or recombinant agents must also comply with guidelines found in the latest editions of the Centers for Disease Control and

Prevention (CDC)-National Institutes of Health (NIH) publication entitled “Biosafety in Biomedical and Microbiological Laboratories” and the NIH publication entitled “NIH Guidelines for Research Involving Recombinant DNA Molecules.”

B. Designation of Institutional Official

The Medical Center Director is responsible for all research activities conducted under medical center auspices, and serves as the Institutional Official (IO). The IO is the responsible official for correspondence related to animal research with AAALAC, USDA, and the PHS. The R&D Committee, which reports to the VAMC Director, oversees the IACUC. The VAPHS operates one IACUC.

C. Functions of the IACUC

The VAPHS IACUC must perform the review and oversight functions required by PHS Policy (Sec IV.B., IV.C, and IV.F), the Guide (see monitoring the Care and Use of Laboratory Animals), the Animal Welfare Act (see 7. U.S.C. §2143[b][1]), the USDA AWAR (see 9. C.F.R. §2.31), VA policy, and any other Federal regulations that impact IACUC function.

(1) Semi-Annual Program and Facility Self-Assessment Reviews. According to the USDA Animal Welfare Act Regulations and Standards (see 9 C.F.R. §2.31(c)(1)) and PHS Policy, the designated VA IACUC must perform a self-assessment review of the program of animal care and research use, and an inspection of the animal facilities, husbandry practices, and laboratories where animal procedures are performed at least every 6 months. This self-assessment review must be conducted using the standards established in the most current Guide (see “Institutional Animal Care and Use Committees”), PHS Policy (see Sec. IV.B), the Animal Welfare Act (see 7 U.S.C. §2143[b][3] and [b][4]), USDA AWAR (see 9 C.F.R. §2.31[c][2]), and this VA policy.

(2) Research Proposal Review. The IACUC must review and approve, require modifications in (to secure approval), or withhold approval of all research proposals involving species and activities included within the definition of an “animal”. All research projects involving animals must be approved by the IACUC and then by the R&D Committee prior to commencement. The date of continuing review is based on the date of IACUC approval. The IACUC must review proposed research at convened meetings at which a quorum (a majority of voting members) is present. In order for the research to be approved, it must receive the approval of a majority of those voting members present at the meeting. A quorum must be maintained for each vote to occur. If a quorum is not maintained, the proposal must be tabled although suggestions for review may be recorded and communicated to benefit the investigator.

5. The Membership of the SAR

The members of the IACUC, which is designated as the SAR at the VAPHS are recommended by the Associate Chief of Staff for Research and Development (ACOS/R&D), confirmed by the

R&D Committee and appointed by the Institutional Offices (IO)/Medical Center Director. The IACUC consists of at least five members, and its membership meets the composition requirements set forth in the PHS Policy at IV.A.3.b and Animal Welfare Act (see 7 U.S.C. §2143[b][1]). A minimum of five members are required to serve as voting members to constitute an IACUC. Only a properly constituted IACUC may conduct official business. The required voting members include a Chairperson, one Veterinarian, one scientist with animal research experience, a non-affiliated member, and a lay member. The IACUC chairperson can not simultaneously chair another subcommittee of the R&D Committee. The Chairperson needs to be a more senior scientist with animal research experience and good committee management skills. The non-affiliated member is not otherwise affiliated with the VA medical center, and is not part of the immediate family of a person who is affiliated with the medical center. The designation of lay members as both the lay member and the non-affiliated member is discouraged. Recruitment of separate individuals to fulfill these roles is a best practice. Non-affiliated and lay members of the IACUC may be compensated for travel expenses and time, as long as such reimbursement can not be construed as compromising their ability to fulfill their independent respective roles on the IACUC. At least one member of the IACUC needs to be a member of the R&D Committee. The Veterinary Medical Officer (VMO), Veterinary Medical Consultant (VMC), or a member of the IACUC needs to be a member of the Institutional Biosafety Committee. The IACUC Chairperson must be appointed by the medical center Director annually, without a lapse in service. There is no limit to how many times a chairperson may be reappointed, but it is Best Practice to rotate the Chairperson position to develop a cadre of research staff with experience in filling that role. Members other than those who are designated ex officio (appointed on the basis of their position, such as the institutional veterinarian) may serve terms of up to 3 years, on staggered appointments. Members may be reappointed without lapse in service to the IACUC.

6. IACUC/SAR Record Keeping and Required Documentation

The IACUC/SAR meets on the third Thursday every month. The research office provides agenda packets to IACUC members at least 3 business days before the IACUC meeting. This packet includes an agenda with all business items listed, including reviewer assignments for all new protocols and copies of all protocol forms. Reviews of new and three-year renewals of protocols are performed by the Consulting Veterinary Medical Officer (Consulting VMO) and one other member of the SAR by submitting written comments and then later reviewing the changes made by the PI until both are satisfied that the protocol can be approved by the SAR. The two reviewers lead the review of the protocol at the SAR meeting. The parliamentary system used needs to allow for discussion of each item, motions, seconds to motions, and official votes tallied by yeas, nays, and abstentions. A majority of the SAR members must be present to conduct a convened meeting. In order for research to be approved, it must receive the approval of a majority of the quorum present at the meeting. A quorum equals more than half of voting members. The Research Office Staff member taking the minutes at the meeting will track the quorum throughout the meeting. To protect anonymity, the identity of the members making a motion, seconding a motion, and voting yea, nay, or abstain should not be recorded. A motion must be seconded for a vote to occur. For a motion to pass, a majority of a quorum present must vote affirmatively. For any business item, any member may request that a minority opinion be

submitted for placement in the minutes. The committee may review the minority opinion as part of the review of minutes at the next meeting, but may not vote to remove or revise (to change the meaning) the minority opinion so as to give the appearance of suppressing dissent. Minority opinions addressing individual protocols must be included in the ACORP or other animal form used for review.

The IACUC minutes must be written and published within 3 weeks of the meeting date. Since this VA medical center has its IACUC, the IACUC minutes are formatted in compliance with the VA Handbook 1200.7. For VA projects under consideration, the minutes of joint or affiliate IACUC need to contain the same information somewhere in the document.

At the top of the first page, on separate lines in a large typeface, place the bolded name of the facility and facility number, the official address, the official committee name, and the date of the meeting. Abbreviations are not acceptable. Subsequent pages are to be numbered. List all voting members present and absent (non-voting members may be listed separately). For each voting member, note the voting member's appointed role on the committee to establish that the IACUC is properly constituted (see subpar. 8a (I) for required voting members). Use the term "ex-officio" only when the member's office or legal role (such as the institutional veterinarian) dictates a member's presence on the committee. Indicate if a quorum is present. A quorum is defined as a majority (more than 50 percent) of voting members. Arrange the minutes into at least three sections: review of previous minutes, old business, and new business. At each meeting, a review of semi-annual review schedules for correction needs to be conducted to monitor progress toward completing corrections of deficiencies previously identified. Business items need to be retained under old business in subsequent minutes until the final approval is given by the IACUC, the project is disapproved by the IACUC, or the project is withdrawn from consideration by the investigator. The final disposition of each project needs to be clearly stated in the minutes. For each project under consideration, list the first and last name of the principal investigator, and the complete name of the project. For each new project, the motion passed by the committee (approved, approved pending clarification, deferred, disapproved) must be recorded with the exact vote, which must include the number voting for the motion, the number voting against, and the number abstaining. Committee deliberations on each project must be reflected in the minutes so that an outside observer can understand the issues discussed, and recognize the specific revisions and clarifications requested for each protocol under consideration. Experience has shown that if IACUC members are asked to provide written or electronic copies of their reviews, their comments can be used to document deliberations and greatly streamline the process of writing the minutes as well as communicating IACUC decisions in writing to investigators. The minutes must note which members recused themselves for which project(s) to prevent conflicts of interest. If they are important to understanding the conduct of business, copies of any internal or external reports or correspondence with outside agencies referenced in the minutes need to be attached to the minutes.

Once IACUC minutes are approved at the following meeting, the IACUC Chairperson needs to sign and date them at the bottom. No local official may alter the IACUC minutes once signed by the IACUC Chairperson, and no local official may exert pressure on any IACUC member to change the wording in the minutes to language more favorable to the institution. If requested by the Chief Veterinary Medical Officer (CVMO) or other VA Central Office official, complete copies of the signed minutes need to be sent through the ACOS for R&D and the medical center Director. The R&D Committee needs to review a copy of the signed minutes as an item of

business, but R&D Committee approval is not necessary prior to sending minutes to ORD for review, i.e., if ORD requests a copy for review.

The following reports and correspondence must be forwarded to the CVMO's office or ORD, as indicated:

1. USDA Annual Report of Research Facility. This report (required by the USDA Animal Welfare Act Regulations and Standards, see Sec. 2.36) must be completed and submitted to ORD by November 15 each year as a component of Part II of the Research and Development Information System (RDLS).
2. AAALAC Reports. Every third year a comprehensive AAALAC Program Description must be completed prior to the scheduled triennial AAALAC site visit and annually, an abbreviated report also must be submitted to AAALAC.
3. IACUC Semi-Annual Self-Assessment Reviews. Semi-annual Self-assessment Reviews must be prepared by the IACUC no later than 60 days after the self-assessment review date. A copy of the approved report signed by a majority of IACUC members and the medical center Director must be forwarded to the CVMO's office through the ACOS for R&D and the medical center Director.
4. Annual VA Veterinary Medical Unit (VMU) Report. An annual VA VMU Report for the previous fiscal year must be completed using the website designed for that purpose by January 15.
5. PHS Assurances and Annual Assurance Updates
6. A copy of all correspondence between Office of Laboratory Animal Welfare (OLAW), USDA, AAALAC and VA facilities must be forwarded to the CVMO and ORO within 15 business days of receipt or mailing.

This institution will maintain all reports for at least three years.

7. VA Pittsburgh Healthcare System IACUC Review Process and Approval Considerations

Principal Investigators (PI) new to the Pittsburgh VA should arrange for a pre-submission meeting with the Consulting VMO. This can occur in the afternoon of any IACUC meeting date. Investigators with a currently approved animal protocol from the University of Pittsburgh should follow the guidance in the "Addendum for Investigators with an Approved University of Pittsburgh Protocol". New PIs, or those proposing a significant change/increase in use of the Animal Research Facility (ARF), should meet with the Animal Research Facility Supervisor, to evaluate availability of space and facility accommodation of any special needs of their projects. Investigators and research staff who utilize laboratory animals must pass the exam covering the "Working with the VA IACUC" web course plus the exam for any species-specific web course that covers the species proposed for use [8.k.(2)(a)]. The VA IACUC currently recognizes the University of Pittsburgh's Animal training for staff working with animals, however anyone involved in the preparation and submission of an Animal Component of Research Protocol (ACORP) to the VA IACUC must present certification of completion of the VA Training found on the VA Training website.

A. Submission Process:

When a PI submits an ACORP to the Research Office it is electronically forwarded to the Chair to determine whether the ACORP qualifies for designated review or full committee review. The Chair will assign one member from the Institutional Animal Care and Use Committee (IACUC) and the Consulting VMO as the reviewers of the ACORP. The Program Clerk will electronically mail the submission to the reviewers to review the ACORP for completeness of the application and compliance with information requirements. The reviewer's written comments/recommendations will be requested within 5 working days and electronically mailed to the Research Office. The Program Clerk will assemble all of the comments/recommendations into one Microsoft Word document and forward it to the PI. The PI should respond to the Program Clerk within 5 working days of receiving the comments by addressing each item with a written response and by highlighting the recommended changes on the revised ACORP and appendices as applicable. The Program Clerk will electronically mail the revised ACORP and the PI's comments to the two reviewers and the Consulting VMO for verification that the comments/recommendations have been adequately addressed and notify the Program Clerk within 5 business days. Any additional comments/recommendations from the reviewers are sent to the Program Clerk to forward to the PI to make additional changes (with changes highlighted) and if the PI has any other modifications to the ACORP they should be italicized, and this revised ACORP should be resubmitted to the Program Clerk within 5 business days. The reviewer and the Consulting VMO must all be satisfied with the PI's response and revised ACORP in order to recommend approval. A reviewer can request a full committee review and/or discussion of the ACORP at a regularly scheduled meeting. Before final approval can be granted each member of the IACUC must have the opportunity to review the ACORP and the opportunity to request a full committee review. The revised version of the ACORP will be provided to the IACUC members as part of the monthly meeting's agenda packet and each member's decision with regard to the ACORP will be recorded at the meeting. If the revised version is approved by the IACUC, it may be finalized with the signatures of the IACUC chair and the VMC.

B. Review Systems

The use of the designated review system may be used. VA policy stipulates that all IACUC members receive complete copies of all protocol forms to aid them in deciding whether or not to request full committee review.

C. Research Conducted at Contract Facilities

The only "contract" facilities used are those of the School of Medicine, University of Pittsburgh which are AAALAC accredited. VA staff members who choose to do their animal research at the University Facilities have faculty appointments at the School of Medicine, University of Pittsburgh. The Memorandum of Understanding (MOU) for Collaborative Research executed between the University of Pittsburgh and VAPHS describes in detail the structure for the coordination of oversight of VA-funded research carried out in University facilities (implemented, February, 2004). Briefly, the VA IACUC reviews all animal study protocols involving research at VAPHS and VA funded research at the University of Pittsburgh. The VA IACUC receives copies of the semi-annual program review and facility reviews and the annual

USDA report from the animal facility at the University of Pittsburgh. The VA IACUC Chair, who presents any significant findings or the lack thereof at the next IACUC meeting, reviews these reports

C. IACUC Considerations

In order to approve proposed research projects, the SAR will conduct a review of those components related to the care and use of animals and determine that the proposed research project is in accordance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals. The SAR confirms that the research project will be conducted in accordance with the Animal Welfare Act, PHS Policy, the *Guide for the Care and Use of Laboratory Animals*, the VA Handbook, and other federal regulations or guidelines that impact the conduct of business. All research projects involving animals are approved by the SAR and the R&D Committee prior to commencement. All research proposals that involve the use of animals are peer reviewed for scientific merit by the Research and Development Committee at this institution. Those research proposals that are funded by the VA are also reviewed for scientific merit by VA Central Office established review committees and the animal protocols are reviewed by the VA Chief Veterinary Medical Officer.

In accordance with VA Handbook 1200.7 (Appendix D), The IACUC needs to consider the following topics in the preparation and review of animal care and use protocols:

1. Rationale and purpose of the proposed use of animals.
2. Justification of the species and number of animals requested. Whenever possible, the number of animals requested should be justified statistically.
3. Availability or appropriateness of the use of less-invasive procedures, other species, isolated organ preparation, cell or tissue culture, or computer simulation.
4. Adequacy of training and experience of personnel in the procedures used.
5. Unusual housing and husbandry requirements.
6. Appropriate sedation, analgesia, and anesthesia.
7. Unnecessary duplication of experiments.
8. Conduct of multiple major operative procedures.
9. Criteria and process for timely intervention, removal of animals from a study, or euthanasia if painful or stressful outcomes are anticipated.
10. Post-procedure care.
11. Method of euthanasia or disposition of animal.
12. Safety of the working environment for personnel.

D. Annual Reviews:

The IACUC must review the conduct of all animal protocols annually. At the first and second anniversaries of approval, the IACUC will review a the continuing review submission form giving current basic information, such as IACUC approval number, IACUC approval date, title of project, and species used. The investigator then notes that either no changes have taken place, or describes any proposed changes. Responses are reviewed by the IACUC, or an IACUC-designee, for assessment of the changes reported. Any changes to the approved activity which

are deemed of sufficient magnitude to merit further consideration may then be presented to the IACUC for continued review approval. If a study is no longer active the investigator uses this form to notify the IACUC.

Prior to the third anniversary, the IACUC must conduct a complete re-review of the protocol. This is accomplished by requiring the PI to submit a new protocol utilizing the latest version of the protocol forms. This Three-Year renewal submission is subjected to the IACUC review process and approval procedures.

E. Terminations and Suspensions

The SAR may suspend an activity that it previously approved if it determines that the activity is not being conducted in accordance with applicable provisions of the Animal Welfare Act, the Guide, the institution's Assurance, or IV.C.1.a.-g. of the PHS Policy. The SAR may suspend an activity only after review of the matter at a convened meeting of a quorum of the SAR and with the suspension vote of a majority of the quorum present. If the SAR suspends an activity involving animals, or any other institutional intervention results in the temporary or permanent suspension of an activity due to noncompliance with the Policy, Animal Welfare Act, the *Guide*, or the institution's Assurance, the Institutional Official in consultation with the SAR shall review the reasons for suspension, take appropriate corrective action, and report that action with a full explanation to OLAW.

The CVMO must be notified of any SAR suspensions of animal protocols in writing through the ACOS/R&D and IO within 5 business days of the action. The Office of Laboratory Animal Welfare is also notified of the suspension to comply with PHS Policy. In the spirit of self-regulation, AAALAC is also notified.

F. Notifications

The IACUC has the responsibility of informing the ARF supervisor when animal protocols have been approved and when they have expired. The supervisor of the ARF is a member of the IACUC and therefore is kept up to date on which protocols are about to expire so that he/she will not approve animal orders until the ACORP is renewed.

8. Required Training

Personnel must have appropriate qualifications, training, and experience when conducting procedures on animals. All animal personnel, investigators and their technical staff who are employees of the VA and who have contact with animals are given a medical examination. The qualifications and experience of technicians and fellows with the particular procedures to be employed on the animals are checked and verified as compliant. If it is lacking, the committee requires that the employee obtain the requisite training through any of the courses that are offered or by other training method.

Certificates of required training are submitted to the Research Office upon completion. The research office requires all applicable training certificates for each researcher listed on the Research Staff Form to be included with all submissions. The SAR will not review an Investigator's protocol unless all of the staff listed has completed the required training. The certificates must be dated within at least one year of the submission. These certificates serve as documentation of completion of required training and are maintained in the Research Office. A listing of all required training is available on the Research Office website at <http://www.vaphs.research.med.va.gov/>.

9. Managing Conflicts of Interest

As a public agency, the VA has an obligation to preserve public trust in the integrity and quality of research carried out by its investigators, among its patients, and in its facilities, and to exercise prudent stewardship of public resources, including public funds that support research programs. Appropriate mechanisms must be in place to ensure that actual or perceived financial conflicts of interest do not undermine that trust. With regard to conflicts of interest, all VA employees must comply with the criminal statute pertaining to acts affecting personal or imputed financial interest (18 U.S.C. Section 208) and the Standards of Ethical Conduct for Employees of the Executive Branch (5 CFR Part 2635). VA Regional Counsels are authorized to interpret these provisions.

A. Member Conflicts:

The IACUC is responsible for ensuring that the protocol review process is not compromised by conflicts of interest arising from members participating in animal research reviewed by the IACUC. Therefore, no IACUC member may participate in the IACUC review, or in the approval of a research project in which the member is either personally involved in the project, and/or has a financial conflict, except to provide information requested by the IACUC. Voting members who have conflicts of interest are required to recuse themselves from deliberations and are not counted toward the quorum for that specific protocol.

B. Investigator Conflicts:

Each PI, co-investigator, consultant and collaborator who plans to devote five or more percent effort to the project will submit a Department of Veterans Affairs Research and Development Conflicts of Interest Survey for all projects submitted for review by the IACUC. Use of the information on the survey is for the review and approval of this proposed research project only.

C. Non Voting Member Conflicts:

The ACOS for R&D and Administrative Officer (AO) for R&D (or equivalents) should not serve as voting members on the IACUC, and when in attendance, need to be very sensitive to the occurrence or appearance of conflict of interest relative to their supervisory, managerial, or fiscal authority. They should avoid intervention or participation in deliberations involving entities in which they have financial or economic interests, except to provide information as requested by the IACUC.