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VA Pittsburgh Healthcare System

Institutional Animal Care and Use Committee (IACUC)

Standard Operating Procedures

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**IACUC Standard Operating Procedures**

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

## Introduction

This VAPHS 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.

***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 Governing the IACUC***

Because this VA conducts animal research according to the highest ethical and regulatory standards, all animal research must comply with the VHA Handbook 1200.07, Health Research Extension Act (codified at 42 U.S.C. Section 289d; Public Law 99-158) 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 U.S. Interagency Research Animal Committee), The 8th edition of the Guide for the Care and Use of Laboratory Animals (prepared by the National Research Council; henceforth called the Guide), and the American Veterinary Medical Association (AVMA) Guidelines for the Euthanasia of Animals. *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 United States Department of Agriculture (USDA) Animal Welfare Act Regulations and Standards (AWAR) (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 Microbiological and Biomedical Laboratories (BMBL)” and the NIH publication entitled “NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.”

The basic principles governing animal research in the 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.

**Animal use** is defined as the proper care, use, and human treatment of laboratory animals produced for or used in research, testing, or teaching.

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. IACUC Roles and Authorities***

1. **Institutional Authority of the IACUC**

The Medical Center Director is responsible for all research activities conducted under the auspices of this VA Medical Center (VAMC) and serves as the Institutional Official (IO). The IO is the responsible official for correspondence related to animal research with Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC), USDA, and the PHS. The Research and Development (R&D) Committee reports to the VAMC Director and oversees the IACUC. The VAPHS operates one IACUC.

1. **Roles and Responsibilities of the IACUC**

The IACUC is responsible for the oversight and review of the VAPHS Animal Care and Use Program in accordance with 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. Specifically the IACUC is responsible for the following oversight functions:

1. Conduct a review of the animal care and use program at the VAPHS at least once every six months pursuant to standards established in the most current issue of the 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. Inspect the animal facility and laboratories where animal procedures are performed at least every 6 months using the aforementioned policies as guidance.

3. Review and approve, require modifications (to secure approval), or withhold approval of all research proposals involving animals. The IACUC must review proposed research at convened meetings at which a quorum (a majority of voting members) is present.

4. Review and evaluate non-compliance issues involving the care and use of animals at the VAPHS.

5. Suspend activity involving animals that it previously approved if it determines that the activity is not being conducted in accordance with applicable provisions of the [Animal Welfare Act](http://www.nal.usda.gov/awic/legislat/awa.htm), the [Guide](http://www.nap.edu/readingroom/books/labrats/), the institution's Assurance, or IV.C.1.a-g of the PHS Policy.

***5. Membership of the IACUC***

A properly constituted IACUC as set forth in PHS Policy (see subpar.IV.A.3b) and the Animal Welfare Act (see 7 U.S.C. §2143[b][1]) must have at least five voting members and must include a Chairperson, one Veterinarian, one scientist with animal research experience, a non-affiliated member, and a lay member not involved in animal research. Only a properly constituted IACUC may conduct official business

**A. Appointment of the Chairperson and Vice Chairperson, Length of Service and Duties**

The Chairperson must be a senior scientist with animal research experience and good committee management skills.

**Appointment:** The IACUC Chairperson and Vice Chairperson are 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.

The IACUC Chairperson is automatically nominated as a voting member of the R&D Committee. The IACUC chairperson cannot simultaneously chair another subcommittee of the R&D Committee.

**Qualifications:** The IACUC Chair and Vice Chairperson shall have an MD, PhD, or equivalent advanced degree and 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 IO.

**Authority:** The IACUC Chairperson and Vice Chairperson are authorized to approve the agenda of IACUC meetings and can call ad-hoc IACUC meetings as needed. The chair of the IACUC also represents, or delegates IACUC members to represent the IACUC to institutional administrators and the research staff.

**B. Appointment of IACUC Members, Length of Service and Duties**

**Appointment:** Nominees for the IACUC, are recommended by the ACOS/R&D in consultation with the IACUC, are approved by the R&D Committee and appointed by the IO in writing for terms of up to 3 years. Reappointment to the IACUC may be granted at the end of the term without a lapse in service.

The committee members receive an appointment letter from the IO, which includes a hyperlink to the Office of Laboratory Animal Welfare (OLAW) website to access the following: 1) The PHS Policy for the Humane Care and Use of Laboratory Animals, 2) The National Research Council (NRC) Guide for the Care and Use of Laboratory Animals, and 3) The Applied Research Ethics National Association (ARENA)/OLAW IACUC Guidebook. Each IACUC member is instructed to review these documents. Additionally, a copy of our Animal Welfare Assurance is sent to the member with the appointment letter. When new committee members are appointed, the IACUC Coordinator conducts a brief orientation and provides an IACUC Member Information document to the new member. The document summarizes the committee processes and provides guidance on member expectations. This information is to be used by the members as reference and guidance for the IACUC review process.

**Qualification of Members/Composition of Boards:** In addition to the chair, a properly constituted IACUC must contain the Attending Veterinarian (AV), a scientist with animal experience, a non-affiliated member, and a lay member not involved in animal research. The non-affiliated member is not otherwise affiliated with the VAMC, and is not part of the immediate family of a person who is affiliated with the VAMC. 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 cannot 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 (IBC).

**C. Alternate Members**

Alternate members of the IACUC may substitute for a specific member of the IACUC when that member is not in attendance and are nominated and appointed by a procedure similar to that in place for regular members.

**D. Ex Officio Members**

Ex Officio members include the Attending Veterinarian (voting), the Medical Center Director (non-voting), Chief of Staff (non-voting), Associate Chief of Staff (ACOS) R&D (non-voting), Deputy ACOS (non-voting), Biosafety Officer (non-voting), Industrial Hygienist (non-voting), Business Manager R&D (non-voting), and the Administrative Officer (AO)/ACOS R&D (non-voting).

Role of Research Compliance Officer(s) (RCO):The RCO may not serve as a voting member of the IACUC but may attend IACUC meetings upon request by the IACUC.

**E. Conflict of Interest**

No IACUC member (voting or non-voting) may participate in the IACUC review, or in the approval of a research project in which the member is either personally involved 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.

The ACOS for R&D and 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.

***6. IACUC Record Keeping and Required Documentation***

**A. Record Retention**

All records will be maintained in accordance with the current VA Records Control Schedule 10-1 and applicable local policies.

Investigators should notify the VAPHS Research Office as soon as possible, but no less than 30 days prior to his/her departure. The investigator must ensure that a plan has been developed and approved by all relevant parties to account for his/her research records/data. *REMINDER: If the investigator is leaving the VA entity this means that the records must remain at the VA and may either be transferred to another VAPHS Investigator or come under the custodianship of the Research Office.*

For detailed information related to research records/data, please refer to VAPHS R&D Policy #017, Research Information Protection Program.

**B. Access to IACUC Records**

Access to IACUC records is limited to voting and non-voting members of the IACUC, the IACUC Coordinator, authorized VA representatives, and officials of Federal and State regulatory agencies, including but not limited to Office of Research Oversight (ORO), Office of Research and Development (ORD), AAALAC, OLAW and Chief Medical Veterinary Officer (CMVO). Research investigators will be provided reasonable access to files associated with their research. Access to IACUC records can be granted to entities beyond those indicated above by the Medical Center Director, the R&D Committee, and/or VA Central Office.

If the IACUC receives a request or comments and/or questions from the general public, the information must go through the VAPHS Freedom of Information Act (FOIA) Officer. A formal FOIA request must be submitted. Redaction of any information, including the monthly minutes, is carried out before information is provided to the public.

**C. Required Qualifications, Training, and Training Records**

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 offered enrollment in the Animal Exposure Preventive Medicine Program (AEPMP). The qualifications and experience of investigators, technicians and fellows with procedures to be employed on the animals are checked and verified. If qualifications or experience is lacking, the committee requires that the employee obtain the requisite training through any of the courses that are offered or by other training methods.

Investigators and research staff who utilize laboratory animals must pass the exam covering the "Working with the IACUC" web course plus the exam for any species-specific web course that covers the species proposed for use [VHA Handbook 1200.07 8m(1)].

The Research Office maintains a database of all training requirements and completion information for all research personnel. The Research Office will verify training completion of each researcher listed on the Research Staff Form. The IACUC will not approve an investigator’s protocol unless all of the staff listed has completed the required training. All training completion dates must be current at the time of the submission. A listing of all required training is available on the VAPHS Research Office website for Research Professionals at https://www.pittsburgh.va.gov/Research/Employment\_Credentialing\_and\_Training.asp

**D. Research Tracking System**

The IACUC uses a computerized tracking system, Manage Institutional Review Board database (MIRB™), to track protocols. Upon receipt, all proposals are entered into the database and assigned a unique identification number. MIRB includes the following information:

1) Title of the Research (Protocol)

2) Names of the PI and co-investigators where appropriate

3) Funding source (if any)

4) Date of initial approval

5) Date of most recent continuing approval

6) End of current approval period

7) Current status (under review, approved, suspended, closed)

**E. Written Standard Operating Procedures**

SOPs pertinent to IACUC function, animal facility operation, and animal care and welfare are available to all investigators on the Research Office website, SharePoint, or from the IACUC Coordinator. The SOPs are reviewed annually by the IACUC and approved by the R&D Committee, per VHA Directive 1200.01 (section 9b).

**F. Documentation of Convened IACUC Meetings**

The IACUC meets on the second Thursday of each month. The agenda and all meeting documents are posted on SharePoint one week prior to the meeting. SharePoint will contain copies of all business item documents, the previous month’s meeting minutes, initial review submissions, three-year renewal submissions, and modifications/amendments (if applicable). At the time the agenda is posted to SharePoint, the IACUC Coordinator also sends a separate email to all committee members to notify them that the agenda is available on SharePoint. A follow-up email with the agenda documents as an attachment is also sent to those members who do not use SharePoint. Each new and three-year renewal protocols are assigned to one voting IACUC member and either the AV or the Consulting Veterinarian (CV). The two reviewers are expected to lead the discussion of the protocol review at the IACUC meeting. Consistent parliamentary procedures must be used to conduct committee business. 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 IACUC 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 voting members present at the meeting, provided there is a quorum. A quorum equals more than half the number 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 Animal Component of the Research Protocol (ACORP) or other animal form used for review.

The IACUC minutes must be written in compliance with VA Handbook 1200.07 and published within 3 weeks of the meeting date. At the top of the first page, on separate lines in large typeface, are placed 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. All voting members present and absent (non-voting members may be listed separately) are listed. For each member, his or her role on the committee and whether they are voting or non-voting is noted to establish that the IACUC is properly constituted. The term “ex-officio” is used only when the member’s office or legal role (such as the institutional veterinarian) dictates a member’s presence on the committee. Whether or not a quorum is present is also documented. The minutes are arranged into at least three sections: review of previous minutes, old business, and new business. 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, the first and last name of the principal investigator, and the complete name of the project is also listed. For each project, the motion passed by the committee (approve, require modifications (to secure approval) or withhold approval) must be recorded with the exact vote, which must include the number voting for the motion, the number voting against, and the number abstaining. 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. 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.

The IACUC minutes are reviewed and approved at the next convened meeting. After approval by the IACUC, the IACUC Chairperson signs the minutes and they are forwarded to the ACOS/R&D, Chief of Staff and the Medical Center Director for signature and approval, prior to being forwarded to the R&D Committee for their review and approval. The minutes must be reviewed by the R&D within 60 days of finalization. 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 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.

Copies of committee minutes are maintained for three years.

**G. Required reports**

The reports are prepared by the Research Office in consultation with the IACUC. They are reviewed and approved by the committee at a convened IACUC meeting prior to the submission due date.

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 the USDA by December 1st each year.
2. AAALAC Annual Report: This report is completed annually for each fiscal year. Additionally, every third year a comprehensive Program Description must be completed prior to the scheduled triennial AAALAC site visit.
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 is submitted to the Chief Veterinary Medical Officer (CVMO).
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 of each year.
5. Office of Laboratory Animal Welfare (OLAW) Annual Report: The report is a key document pertaining to the Public Health Assurance (PHS) Animal Welfare Assurance. The report is due by January 31 of each year. Assurance renewals applications are submitted four months prior to the expiration of the PHS-approved Assurance.

A copy of all correspondence between OLAW, USDA, AAALAC and VA facilities must be forwarded to the CVMO and ORO within 15 business days of receipt or mailing.

***7. IACUC Protocol Review Process and Approval Considerations***

Principal Investigators (PIs) new to the VAPHS must arrange for a meeting with the Animal Research Facility (ARF) Supervisor to evaluate availability of space and facility accommodation of any special needs of their projects before submitting their protocol.

**A. Review Systems**

Generally, the Full Committee Review (FCR) method is used for reviewing and approving all animal study protocols. However, should a situation warrant it, the institution, or IACUC may want to use the designated-member review (DMR) method. In such instances, the protocol is electronically mailed to all IACUC members to allow all members the opportunity to call for a FCR. The IACUC Coordinator polls members to obtain concurrence to use the DMR method, or concurrence by silent assent after 5 working days. If FCR is not requested, at least one member of the IACUC, designated by the chairperson, is assigned to review the protocol and has the authority to approve, require modifications (to secure approval) or request FCR of that protocol. If multiple designated reviewers are used, their decisions must be unanimous; if not unanimous, the protocol will be referred for FCR. If the review of a protocol is conducted by DMR, that action is documented in the minutes of the next convened IACUC meeting. If FCR is requested, approval of those protocols may be granted only after review at a convened meeting of a quorum of the IACUC and with the approval vote of a majority of the quorum present. The approval of the protocol is finalized with the signatures of the IACUC Chair and the Veterinarian.

**B. Initial or Three-year renewal Submission Process**

When a PI submits a new or three year renewal animal protocol to the Research Office, the IACUC Coordinator conducts an administrative review of the documents for completeness. Additionally, the IACUC Coordinator verifies the training requirements for the PI and his/her staff. The PI will be instructed to address any issues prior to committee member review. The IACUC Coordinator consults with the Chair to assign the primary reviewer. The Chair will assign one voting member from the committee and either the AV) or CV as the reviewers of the ACORP. The IACUC Coordinator electronically mails the submission to the reviewers to review the ACORP for completeness of the application and compliance with animal welfare requirements. If applicable, a copy of the research plan from the funded grant is also sent to the reviewers to match the ACORP against the experiments outlined in the funded application. The reviewers’ written comments/recommendations are requested within 10 calendar days and electronically mailed to the Research Office. The IACUC Coordinator assembles all of the comments/recommendations into one document and forwards it to the PI. The PI must respond to the IACUC Coordinator within 10 calendar days of receiving the comments by addressing each item with a written response and by highlighting the recommended changes in the revised ACORP and appendices, as applicable. The IACUC Coordinator electronically mails the revised ACORP and the PI’s response to the reviewers for verification that the comments/recommendations have been adequately addressed. This information should be communicated to the IACUC Coordinator within 5 business days. Any additional comments/recommendations from the reviewers are sent to the IACUC Coordinator to forward to the PI to make additional changes (with changes highlighted), and should be resubmitted to the IACUC Coordinator within 5 business days. The reviewer(s) and the Veterinarian must all be satisfied with the PI’s response and revised ACORP before the project is recommended for review at the next convened meeting. If there is an impasse issue, the matter is discussed by the full committee to determine how to move forward. Once the reviewers are satisfied with the PI’s response to the comments, each IACUC member is provided copies of the protocols in their agenda packet for discussion at the next convened meeting in which a quorum of the IACUC is present. The protocol, along with the comments and the response by the PI, are discussed by the assigned reviewers. During this FCR, any IACUC member is encouraged to provide additional comments or suggestions. After the discussion is complete, a full committee vote is taken to approve, require modifications (to secure approval) or withhold approval. The committee’s decision to approve, require modifications (to secure approval), or withhold approval 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 the committee’s decision is to approve the protocol, the study is finalized with the signatures of the IACUC Chair and the Veterinarian. The complete study will go to the next convened R&D Committee meeting for final approval and notification that the research project can be initiated by the ACOS/R&D. The investigator will receive the subcommittee approval letters, the combined R&D approval letter and ACOS notification once they have all been obtained.

For initial protocol reviews, work cannot be initiated until all approval letters and notification from the ACOS have been received by the PI. For three-year renewals, notification of approval of the three-year renewal should be received prior to the expiration date of the previous approval period; work will continue without interruption. However, if notification of approval of the three-year renewal is not received prior to the expiration date of the previous approval period, work cannot continue beyond the expiration date and cannot be resumed until notification that the three-year renewal has been approved.

If the protocol is not approved at the meeting, a letter from the IACUC describing the committee’s action is sent to the PI. This letter includes the result of the IACUC review, which may include one of the following: require modifications (to secure approval) or withhold approval. If the decision of the IACUC is to require modifications, the PI is given instructions to secure approval and must respond within 6 weeks of the meeting date. When the IACUC requires modifications of a protocol to secure approval, such modifications are reviewed as follows:

1. If approved unanimously by all members at the meeting at which the required modifications are identified, and documented, the Chair or designee will review the investigator’s response and modifications required to secure approval. However, if any member calls for FCR of the modifications, such modifications can only be reviewed and approved by FCR.

2. Minor modifications of an administrative nature (typographical or grammatical errors, required signatures, etc.) may be confirmed by IACUC Coordinator.

If the revised versions of the applicable forms are approved, they will be finalized with the signatures of the IACUC Chair and the Veterinarian. The complete study will go to the next convened R&D meeting for final approval and notification by the ACOS/R&D. The PI will receive the subcommittee approval letters and the combined R&D approval letter and ACOS notification that the project has been approved and research can begin on the project.

If the decision of the IACUC is to withhold approval, the PI is given instructions for re-submission. This re-submission undergoes the same review process as when initially submitted.

**C. Research Conducted at Contract Facilities**

The only "contract" facilities used are those at the University of Pittsburgh, which is AAALAC accredited. VA staff members who choose to do their animal research at the University Facilities have a faculty appointment at the University of Pittsburgh. The VA IACUC reviews all animal study protocols of VA funded research being performed at the University of Pittsburgh. In addition, the VA IACUC receives notification of approval by the University of Pittsburgh’s IACUC for those VA funded studies that are being performed in the University of Pittsburgh facilities.

The VA IACUC receives copies of the sections from the University of Pittsburgh’s semi-annual program and facility reviews pertaining to the VA funded investigators conducting VA funded research at the University. The VA IACUC Chair reviews these reports and presents any significant findings, or the lack thereof, at the next IACUC meeting.

**D. IACUC Considerations**

To approve proposed research projects, the IACUC 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 PHS Policy on Humane Care and Use of Laboratory Animals. The IACUC 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 IACUC and the R&D Committee and the ACOS prior to commencement. 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 CMVO.

In accordance with VA Handbook 1200.07 (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. Documentation of availability or appropriateness of the use of less-invasive procedures, other species, isolated organ preparation, cell or tissue culture, or computer simulation.
4. Unnecessary duplication of experiments.
5. Conduct of multiple major operative procedures.
6. Criteria and process for timely intervention, removal of animals from a study, or euthanasia if painful or stressful outcomes are anticipated.
7. Post-procedure care.
8. Safety of the working environment for personnel.
9. Procedures with animals will avoid or minimize discomfort, distress, and pain to the animals, consistent with sound research design.
10. Procedures that may cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedation, analgesia, or anesthesia, unless the procedure is justified for scientific reasons in writing by the investigator.
11. Criteria and process for timely intervention, removal of animals from a study, or euthanasia if painful or stressful outcomes are anticipated. Animals that would otherwise experience severe or chronic pain or distress that cannot be relieved will be painlessly euthanized at the end of the procedure or, if appropriate, during the procedure.
12. The living conditions of animals will be appropriate for their species and contribute to their health and comfort. The housing, feeding, and nonmedical care of the animals will be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied.
13. Medical care for animals will be available and provided as necessary by a qualified veterinarian.
14. Personnel conducting procedures on the species being maintained or studied will be appropriately qualified and trained in those procedures.
15. Methods of euthanasia used will be consistent with the current recommendations of the [American Veterinary Medical Association (AVMA) Guidelines for the Euthanasia](http://www.avma.org/resources/euthanasia.pdf) of Animals, unless a deviation is justified for scientific reasons in writing by the investigator.
16. The ACORP of animal research conducted at the VAPHS is matched against the funded application.

**E. Amendment Reviews**

To amend a study, the investigator must complete an amendment request form. The amendment request form, along with the revised ACORP and/or appendices (per the requested changes), must be submitted to the Research Office.

The changes listed below, must be approved by either FCR or DMR:

 1. From non-survival to survival surgery

 2. Resulting in greater pain, distress, or degree of invasiveness

3. In housing and/or use of animals in a location that is not part of the animal program overseen by the IACUC

 4. In species

 5. In study objectives

 6. In Principal Investigator (PI)

 7. That impact personnel safety

 8. Anesthesia, analgesia, sedation, or experimental substances

9. Euthanasia to any method approved in the AVMA Guidelines for the Euthanasia of Animals

 10. Duration, frequency, type, or number of procedures performed on an animal

 11. An increase in previously approved animal numbers

The IACUC Coordinator will send the amendment request submission electronically to all members of the IACUC. The committee members are given 3 working days to communicate their request for FCR to the IACUC Coordinator. If none of the members request a FCR, the modification may be reviewed and approved via the DMR mechanism. If DMR is the method for review, the Chair or designee and veterinarian will review the investigator’s amendment request and revised documents for approval. The elements of this process will be documented in the minutes of the next convened IACUC meeting.

If a member does request FCR of the modification, the amendment request will be added to the next meeting agenda. The Chair may act as the primary reviewer or assign a committee member to act as primary reviewer. The IACUC Coordinator will electronically mail the amendment submission to the assigned primary reviewer and veterinarian to present the amendment at the next convened IACUC meeting in which a quorum of the IACUC is present. Each IACUC member will receive a copy of the amendment submission in their agenda packet for discussion at the meeting. After the committee review and discussion is complete, a vote is taken to approve, require modifications (to secure approval) or withhold approval. The committee’s decision 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.

Changes that may be handled administratively include:

 1. Correction of typographical errors

 2. Correction of grammar

 3. Contact information updates

4. Change in personnel, other than the PI. (The IACUC Coordinator will conduct an administrative review to ensure that all such personnel are appropriately identified, adequately trained, enrolled in occupational health and safety programs).)

The Chair, the veterinarian, and/or the IACUC Coordinator will review the investigator’s amendment request and revised documents for administrative approval. The elements of this process will be documented in the minutes of the following next convened IACUC meeting.

**F. 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 the continuing review submission form containing 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. Submission of a brief protocol progress report is also required. Additionally, the PI must also list the rooms/areas where animal work/procedures were performed, the number of animals which were approved for this study, the number of animals that have been used since this protocol was approved, and report any unexpected complications or deaths not previously reported. The continuing review form and responses are reviewed by the IACUC, or an IACUC-designee, for assessment of the changes reported. The annual protocol review process is documented on the agenda for the following IACUC meeting and these actions are acknowledged by the committee members as part of the minutes. The IACUC meeting minutes are reviewed and approved by the Committee. Any non-approved or proposed changes to the originally approved activity that are deemed to be 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 (as described in Section 7B).

**G. Study Closure**

If the PI decides to close an approved protocol, he or she is required to submit the Research Project Study Closure form to the IACUC Coordinator. This should be submitted prior to the current approval expiration. If the project has not been audited within the last three years of this study closure request, the investigator must contact the RCO to schedule an audit. The study closure request form and any other necessary documentation (e.g., audit report) are electronically mailed to the IACUC Chair for review and approval. The elements of this process will be documented on the agenda for the following IACUC meeting. The study file folder is maintained in the Research Office for at least three years.

**H. Notifications**

The IACUC has the responsibility of informing the ARF Supervisor when new protocols, three-year renewals, and amendments have been approved. The ARF Supervisor is also informed when a protocol has expired. As a member of the IACUC, the ARF Supervisor is kept informed as to which protocols are about to expire so that he/she will not approve animal orders until the ACORP is renewed. The IACUC Coordinator electronically mails a copy of the approved ACORP and/or amendment to the investigator and the ARF Supervisor.

***8. Reporting and Review of Compliance Issues***

In accordance with VHA Handbook 1058.01, Research Compliance Reporting Requirements, the IACUC must be notified of, and conduct a review of, a variety of incidents related to animal research. Details regarding those incidents, the process for reporting them and for the IACUC’s review are described in Sections 8.A through 8.C. below.

**A. Incidents Requiring Reporting to the IACUC**

The VAPHS IACUC must be notified of the following types of animal research related incidents:

1. Unanticipated Death of Research Animals:VA personnel, including Without Compensation (WOC) and Intergovernmental Personnel Act (IPA) Agreement appointees, must ensure written notification of the IACUC within 5 business days after becoming aware of any apparent unanticipated death(s) of animals used for research including, deaths due to physical plant deficiencies, engineering failures, worker errors, test article toxicity, anesthetic or surgical complications, and other mishaps. NOTE: The IACUC is not required to respond to reports of experimental animal deaths that are within expected mortality ranges, normal mortalities that occur in large rodent colonies, or individual deaths due to aggression when incompatible rodents are inadvertently housed together. However, these types of losses should be monitored and periodically reported to the IACUC, as part of an animal health surveillance program.

2. Animal Theft, Escape, or Unexplained Disappearance:VA personnel, including WOC and IPA appointees, must ensure written notification of the IACUC within 5 business days after becoming aware of any theft of research animals or of the escape or unexplained disappearance of research animals that could potentially pose a danger or risk to workers, the public, or the environment.

3. Human Deaths: VA personnel, including WOC and IPA appointees, must ensure oral notification of the IACUC immediately upon becoming aware of any human death that may be the result of working with, caring for, or other contact with research animals.

(1) The IACUC must alert ORO by e-mail or telephone within 2 business days after receiving such notification. The Medical Center Director and the ACOS/R&D must receive concurrent notification.

(2) VA personnel, including WOC and IPA appointees, must ensure written notification of the IACUC within 5 business days of becoming aware of the death.

4. Human Accident, Injury, Illness, or Exposure: VA personnel, including WOC and IPA appointees, must ensure written notification of the IACUC within 5 business days after becoming aware of any serious accident, injury, illness, or exposure of a human (other than resulting in death) that may be the result of working with, caring for, or other contact with research animals.

5. Reportable Incidents Under Applicable Federal Standards:VA personnel, including WOC and IPA appointees, must ensure written notification of the IACUC within 5 business days after becoming aware of any incident that is reportable under relevant VHA Handbooks or applicable Federal requirements related to laboratory animal welfare or research safety.

**B. Submission and Review of Reported Incidents**

1. Submission Procedures: In the case of a reportable event as listed in Section 8.A, investigators and/or research staff or any other individual aware of the incident should make a written report (via email) to email address VHAPTHIACUCReporting@va.gov within 5 business days of becoming aware of the event (**\*NOTE**: Emails sent to this address can only be sent from the VA Network. If you are unable to send from a VA email address, please call the IACUC Coordinator at 412-360-2382 or the Biosafety Officer at 412-360-2842). The report should include the date of the event, affected protocol(s) by name and MIRB number and a detailed summary of the event. Complainants may submit concerns anonymously or explicitly request confidentiality under the Whistleblower Protection Act of 1989. There is a lockable steel box located in the ARF for individuals to submit an anonymous concern or report. The ARF Supervisor will check the contents of the box daily. If a report is submitted, the ARF Supervisor will send it to the IACUC Chair and AV for review. Determination of additional action pertaining to an anonymous report will be handled in the same manner as any other reported incident or concern.
2. Preliminary Investigation: Upon receipt of a report of an incident, a review and discovery of salient information will be conducted by appropriate personnel (e.g., ARF Supervisor & staff, AV, or IACUC Chair, etc.) at the direction of the Chair or Vice Chair for presentation at the next convened meeting. The Chair or Vice Chair will be responsible for overseeing the investigation. The investigation process may include discussion with the alleged offender and (if involving research personnel), the associated PI of the project. Whenever feasible, the PI of the project or supervisor will be given written notice of the allegation prior to the meeting and be given an opportunity to provide a written response. The PI may petition the IACUC Chair to appear directly before the committee either to present information salient to the case, or to appeal a sanction against him/her. The determination as to granting such an audience will be at the discretion of the Chair.
3. IACUC Review: The IACUC will review any reported incident at its next convened meeting.  Incidents that involve a human death or present a significant risk to the safety of research personnel, live animals used in research, or the environment, may call for immediate attention and require the IACUC to convene an emergency session prior to the next scheduled meeting.  During the meeting, a summary of the event(s) and information gathered from the review will be presented to the full committee.  The Committee will determine if a reportable incident has occurred or not.  In addition, the Committee will consider whether or not additional action needs to be taken, and if so, who will be responsible for completing those actions. Possible actions may include, but are not limited to: sanctions against the individual/group, implementation of a corrective action plan, suspension or termination of the research, etc. This determination will be documented in the meeting minutes. ***NOTE:*** *If the significance of a reported event is not clear, the IACUC Chair, or designee, should consult the ORO Associate Director for Research Safety and Animal Welfare. Questions about reporting to OLAW or other Federal agencies must be referred directly to the relevant agency or to the ORO Associate Director for Research Safety and Animal Welfare who will confer with the ORD Chief Veterinary Medical Officer (CVMO) as appropriate.*
4. Reporting: The IACUC must notify the Medical Center Director and the ACOS/R&D within 5 business days after reaching a determination that a reportable incident has occurred. Per VHA Handbook 1200.07, no official or committee may reverse or overrule the IACUC’s determination that a reportable incident has occurred. The Medical Center Director must report the incident to ORO within 5 business days after receiving the IACUC’s notification. Additional details regarding the reporting to ORO and other regulatory agencies are outlined in VAPHS R&D Policy #001. If the IACUC determines that an incident is not reportable, the IACUC must also notify the Medical Center Director and the ACOS/R&D within 5 business days after any determination. Regardless of the determination reached by the IACUC, the responsible party will be informed, in writing, of the committee’s decision. If the IACUC is unable to make a determination within 60 calendar days after receiving notification of the relevant event, it must immediately notify the Medical Center Director who, within 5 business days after receiving the IACUC’s notification, must provide ORO with an acceptable justification for the delay and an acceptable completion timeline.
5. **Incidents Related to Research Information Security**

VA personnel, including WOC and IPA appointees, must ensure notification of the ACOS/R&D, Information Security Officer (ISO), Privacy Officer (PO), and relevant investigators immediately (i.e., within one hour) upon becoming aware of any information security incidents related to VA research. Reporting of these incidents must occur in accordance with the procedures outlined in VAPHS R&D Policy #014, Research Information Protection Incident Reporting.

When such incidents involve one or more VAPHS animal research studies, the ACOS/R&D must immediately notify the IACUC. Notifications of information security incidents must be reviewed by the IACUC, when relevant, at its earliest practicable convened meeting, not to exceed 30 business days from the date of notification. The IACUC must determine whether or not the incident constitutes a serious problem and in conjunction with the ISO and/or the PO, whether and what remedial actions are warranted by the facility or the relevant investigator(s). If the IACUC determines that the incident constitutes a serious problem, then the committee must notify the Medical Center Director and the ACOS/R&D within 5 business days. If the IACUC makes additional determinations under its authority, any reporting requirements pertinent to such determinations must also be satisfied. Procedures related to the reporting of the IACUC’s determination to the Medical Center Director and other regulatory agencies are described in VAPHS R&D Policy #001.

1. **Other Reporting and Review**

In addition to the requirements outlined in Sections 8.A through 8.C, the following types of events may also require reporting to the VAPHS IACUC and/or facility officials and oversight agencies.

1. Failure to correct a significant deficiency (identified during a semi-annual IACUC program or facility self-assessment review).

The IACUC is charged with assigning a schedule by which any significant deficiencies identified during a semi-annual IACUC program or facility self-assessment review must be corrected. According to the USDA AWA (see 9 CFR 2.31(c)(3)), failure to correct a significant deficiency by the deadline imposed by the IACUC, must be reported, in writing, within 15 business days of the deadline. The report must be made to the USDA and any Federal agency funding that activity, through the IO.

1. Compliance issues identified by the University of Pittsburgh (for VA-funded investigators conducting VA funded research at the University).

As the funding agency, the VAPHS needs to be aware of non-compliance activities identified by the University of Pittsburgh’s IACUC involving a VA study and/or VA employees. As such, the University of Pittsburgh Research Conduct and Compliance Office notifies the VAPHS Research Office of all reportable non-compliance events involving VA-funded research activities at the time they are reported to the appropriate regulatory agencies. The VAPHS IACUC will review the notification and make any additional reports as described in Section 8.B.

In an effort to capture non-compliance events that do not reach the “reportable” threshold, investigators who conduct their VA-funded animal research studies under an approved University of Pittsburgh protocol are required to notify the VA IACUC of such issues related to these projects. If a VA Investigator is cited by the University of Pittsburgh Research Conduct and Compliance Office for a minor compliance issue, he/she must submit this information to the VA IACUC upon receipt of the non-compliance sanction letter. The Investigator will submit a copy of the sanction letter and the required corrective action plan to the VAPHS IACUC Coordinator for committee review at their next scheduled meeting. Additionally, the Investigator will report all non-compliance issues, both reportable and those deemed non-reportable, which occurred during the past year at the time of their annual VA IACUC Continuing Review submission

***9. Managing Conflicts of Interest***

**Investigator Conflicts**

All PIs, co-PIs, and investigators are required to complete a Department of Veterans Affairs Research Financial Conflict of Interest (FCOI) Statement at the time of initial review, at continuing review, and any time they are being added to an IACUC protocol (as a PI, co-PI or investigator). A FCOI statement must also be submitted when there is a change to the current statement on file with the Research Office. The revised FCOI statement is necessary when an answer on Section I changes to “yes” or when there is a change in the reasoning for a “yes” answer. FCOI statements are submitted to the IACUC Coordinator and are reviewed in accordance with VAPHS R&D Policy #010, Financial Conflict of Interest.

Non-financial conflicts of interest may also occur. Such conflicts are identified as outlined in VAPHS R&D Policy #008, Non-Financial Conflicts of Interest. Conflicts of interest related to VA administrative duties that involve research project or contract management responsibilities will be reviewed by the IACUC.