VA NEBRASKA-WESTERN IOWA HEALTH CARE SYSTEM

Omaha, NE (636)

SUBCOMMITTEE OF ANIMAL STUDIES (IACUC)

STANDARD OPERATING PROCEDURES

A MANUAL

for

Principal Investigators

IACUC Members

& Staff

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REGULATIONS, GUIDELINES AND DOCUMENTS

All animal care, husbandry and animal research practices at Omaha VA animal facilities must be in accordance with the following laws, regulations, guidelines and documents. The full text of these references can be obtained from the internet web site established at: http//www.researchtraining.org.

- Department of Veterans Affairs VHA Handbook 1200.7, Use of Animals in Research
- Animal Welfare Act, Public Law 89-544 as amended; codified at 7 U.S.C. 2131 -2159.
- USDA Animal Welfare Act Regulations and Standards, 9 CFR Parts 1,2,3 and 4.
- The Health Research Extension Act of 1985, Public Law 99-158, as amended, "Animals in Research," codified at 42 U.S.C. Section 289d.
- PHS Policy on Humane Care and Use of Laboratory Animals, NIH, Office of the Director, Revised September, 1986, and reprinted October, 2000.
- 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, and originally published Federal Register, May 20,1985, Vol. 50, No. 97, by the Office of Science and Technology Policy.
- Guide for the Care and Use of Laboratory Animals. National Research Council, 2010 (or most recent edition).
- Report of the AVMA Panel on Euthanasia. Journal of the American Veterinary Medical Association, Volume 218 (5): 671-696, 2001.
- Biosafety in Microbiological and Biomedical Laboratories. CDC and NIH. 4th edition (or most recent revision).
- NIH Guidelines for Research Involving Recombinant DNA Molecules. NIH, 1994, and as subsequently amended.
- AAALAC, International. "Rules of Accreditation," revised January 2001.
- Nuremberg Code of 1947.
- VHA Handbook 1108.1, Controlled Substances.
- VA Handbook 0730, Security and Law Enforcement.
- VHA Handbook 1108.2, Inspection of Controlled Substances.
- M-2, Part VII, Pharmacy Services.
- VA Handbook 5005, Staffing, Part II, Appendix F32.
- VHA Handbook 1200.6, Control of Hazardous Agents in VA Research Laboratories.
- VHA Handbook 1200.8 Safety of Personnel Engaged in Research.
- VHA Directive 1105.1, Procedures for Management of Radioactive Materials.
- Other laws, regulations, guidelines, or documents that impact the use of radiographic equipment, endangered species, and work place safety, as well as any others added by the CRADO or his designee.

References to these resources are made throughout these procedures and guidelines.

ACRONYMS/DEFINITIONS

AAALACI - Association for Assessment and Accreditation of Laboratory Animal Care, International . AAALAC is the accrediting body for animal research programs recognized by VA.

ACLAM – American College of Laboratory Animal Medicine. ACLAM is the specialty certification board for laboratory animal veterinarians, recognized by the American Veterinary Medical Association.

ACORP - Animal Component of Research Protocol. The ACORP, the official VA animal protocol form is the set of questions that must be considered during a review of animal protocols. It must be used by VA Institutional Animal Care and Use Committees (IACUC).

APHIS – Animal and Plant Health Inspection Service. The USDA agency that protects and promotes U.S. agricultural health, regulates genetically engineered organisms, administers the Animal Welfare Act and carries out wildlife damage management activities.

ANIMAL - 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.

ARF – Animal Research Facility. Facility located on the 1st floor of Research Building 15.

AVMA – American Veterinary Medical Association. AVMA is the principal professional organization for veterinarians engaged in any specialty of the practice of veterinary medicine.

AWAR – Animal Welfare Act Regulation. Federal law in the United States that regulates the treatment of animals in research, exhibition, transport, and by dealers.

CRADO – Chief Research and Development Officer . The CRADO is the VA Central Office research administrator given the authority and the responsibility for managing all human, animal, and laboratory VA research activities. Responsibilities include policy, portfolio, and budget management. The CRADO directs the Office of Research and Development (ORD), VA Central Office.

CVMO – Chief Veterinary Medical Officer. The VA Central Office veterinarian given the primary responsibility for formulating VA animal research policy, advising senior VA administrators on animal research issues and providing support and guidance as needed to field research personnel conducting animal research. Veterinary medical and laboratory animal concerns and issues are the purview of the CVMO.

DVA – Department of Veterans Affairs.

IACUC – Institutional Animal Care and Use Committee. The IACUC is the local committee charged with ensuring compliance with animal research regulations and guidelines. In the VA system, the IACUC is organized administratively as a subcommittee of the Research and Development Committee.

OLAW – Office of Laboratory Animal Welfare. OLAW is the PHS Office responsible for administering PHS Policy on Humane Care and Use of Laboratory Animals.

IO – Institutional Official. The IO is the VA official responsible for ensuring that the animal research program has the resources and support necessary to comply with all Federal regulations and guidelines that govern the use of laboratory animals. At our VA, this individual is the Medical Center Director.

JIT – Just-in-Time. JIT refers to the review system that requires proof of IACUC approval and a copy of an ACORP, only if an application has received favorable scientific review and is likely to receive funding.

OH – Occupational Health

ORD – Office of Research and Development. The Office of Research and Development aspires to lead the Veterans Health Administration in providing unequaled health care value to veterans.

ORO – Office of Research Oversight. ORO serves as the primary Veterans Health

Administration Office in advising the Under Secretary for Health on all matters of compliance and assurance regarding human subjects' protection, animal welfare, research safety, and research misconduct.

PHS Assurance – Public Health Service Assurance. The documentation submitted to the OLAW by an institution that pledges that the institution will comply with PHS Policy.

R&D Committee – Research and Development Committee. The R&D Committee is charged with overseeing and approving all research projects at this Medical Center. In the VA system, committees such as the IACUC, the Subcommittee for Research Safety (SRS) and the Institutional Review Board (IRB) are technically subcommittees of the R&D Committee.

USDA – United States Department of Agriculture. USDA is charged with enforcing the Animal Welfare Act Regulations and Standards. The USDA Animal Care Section in the Animal and Plant Health Inspection Service is the administrative unit given the responsibility for monitoring compliance with USDA Animal Welfare Act Regulations.

VACO – Veterans Affairs Central Office.

VHA – Veterans Health Administration.

VMC – Veterinary Medical Consultant. The facility veterinarian who provides adequate veterinary care to the animals in compliance with regulations.

VMU – Veterinary Medical Unit. The VMU consists of the animal research facility plus the husbandry and veterinary technical personnel assigned to care for animals.

INTRODUCTION

The Veterans Health Administration (VHA) Handbook sets forth the principles and guidelines that govern research involving animals in the Department of Veterans Affairs (VA). The VA's Institutional Animal Care and Use Committee (IACUC), known as the Subcommittee of Animal Studies (SAS)*, is dedicated to the humane care and use of animals in activities related to research and teaching conducted at the VA or by individuals associated with the VA. All research involving vertebrate animals that is conducted or authorized under the jurisdiction of VA is subject to review by the IACUC. All VA animal facilities and affiliate or other animal facilities that house animals purchased with VA funds or used for VA or VA foundation projects must be accredited by Association for Assessment & Accreditation of Laboratory Animal Care, International (AAALACI) or an approved waiver must be in place. In the VA system, the IACUC reports to the Institutional Official (IO) and to the Research and Development (R&D) Committee as a subcommittee.

ETHICAL CONSIDERATIONS

Animal research contributes 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 disease that currently lack cures or effective treatments, 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 will be conducted according to the highest ethical and legal standards. The basic principles governing animal research in VA are as follows:

(1) Animal experiments are undertaken only after due consideration of their relevance for human or animal health and the advancement of biological knowledge.
(2) The fewest number of animals needed to achieve scientific objectives should be used.
(3) The least sentient species that will permit the attainment of research objectives should be used.
(4) The least painful or distressful procedures needed to meet research objectives should be used.
(5) All reasonable measures to minimize pain and distress to animals should be used.
(6) The principles of replacement, reduction, and refinement should always be considered when planning and conducting studies.
(7) Procedures that would be considered painful in a human should be considered painful in an animal.
(8) The best reasonable 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.

*For continuity of terminology, SAS will be referred to as IACUC.

(9) Personnel need to have appropriate qualifications, training, and experience when conducting procedures on animals. Opportunities for hands-on training need to be provided as necessary.

AUTHORITY TO CONDUCT ANIMAL RESEARCH

VA Authority

Animal research requires an extensive fiscal investment in facilities (space, staff, equipment, etc.) as well as extensive labor investments in the form of committee and administrative support. No VA medical center may initiate a new program of animal care and use unless approved by the Chief Research and Development Officer (CRADO), in consultation with the Chief Veterinary Medical Officer (CVMO) and affected Office of Research and Development (ORD) Service Directors. VA must ensure that animal research is conducted in environments where proper facilities, professional staff, and administrative support will foster the highest standards of animal care and use. VHA ORD is responsible for establishing policy for laboratory animal use in the VA system.

Authority to Suspend Individual Animal Research Protocols: If significant animal or human health and welfare concerns are noted in information presented in an Animal Component of Research Protocol (ACORP) submitted "Just-in-Time" as part of an application eligible for VA funding, CRADO, or designee, may:

1) Suspend local conduct of the animal research component of that application ("place a veterinary hold") until concerns are addressed adequately, and/or
2) Withhold funding until all VA Central Office concerns about the ACORP are addressed to the CVMO's satisfaction.

Public Health Service (PHS) Authority

According to Office of Laboratory Animal Welfare (OLAW) IACUC Guidebook each institution that receives PHS support for activities involving vertebrate animals or is subject to the authority of the Animal Welfare Act (AWA) must operate an animal care and use program with clear lines of authority and responsibility. IACUCs derive their authority from the law. They are mandated by the Health Research Extension Act (HREA-codified at 42 U.S.C. Section 289d) of 1985 and the PHS Policy on Humane Care and Use of Laboratory Animals (PHS Policy) and the AWA. All VA animal research must be covered by a PHS Assurance.

United States Department of Agriculture (USDA) Authority

By law, all VA animal research must comply with the AWA (7USC 2131-2156) and USDA AWA Regulations and Standards (Title 9, CFR, subchapter A, parts 1,2,3,4 and subsequent amendments) and with 42 C.F.R. 73, "Possession, Use and Transfer of Select Agents and Toxins" promulgated to enforce the Act.

THE IACUC STRUCTURE

Institutional Official (IO) Responsibilities

As stated in the VHA Handbook 1200.7, the Medical Center Director is appointed as the IO for USDA, PHS, and AAALAC correspondence. All of these organizations expect the IO to be a person who has the administrative and monetary authority to commit engineering, safety, employee health, and other resources as needed to correct any programmatic or facility deficiencies identified. The IO is responsible for officially appointing members in writing to the Medical Center's IACUC.

Research & Development (R&D) Committee Responsibilities

The R&D Committee is charged with overseeing and approving all research projects at the medical center. In the VA system, committees such as the IACUC are technically subcommittees of the R&D Committee. The R&D Committee shall establish an IACUC to deal with different aspects of research involving the use of live vertebrate animals. The R&D Committee will approve and forward the names of nominees for IACUC members (regular and alternate, as well as the Chair and Vice Chair nominee) to the IO.

Professional Staffing

Veterinary medical services will be provided through appointment of a qualified veterinary medical consultant (VMC).

The VMC qualifications are:

1) Must have a degree of Doctor of Veterinary Medicine or Veterinary Medical Doctor from an AVMC-approved school of veterinary medicine or have a certificate issues by AVMC's Commission for Foreign Veterinary Graduates. A VMC must be licensed to practice veterinary medicine in at least one state in the U.S.
2) Must meet at least one of the following criteria as evidence of adequate training and experience in laboratory animal medicine:
    a. Be an ACLAM diplomate
    b. Have completed at least 2 years of formal postdoctoral or residency by ACLAM or
    c. Have at least 4 years of on-the-job training and experience as a laboratory animal veterinarian at an institution with a biomedical research program involving laboratory animals.

The primary duties include, but are not limited to:

		Plans/Oversees/ Advises	Monitors	Conducts
1)	Disease detection and surveillance, prevention, diagnosis, treatment, and resolution	✓	✓	✓
2)	Handling and restraint; anesthetics, analgesics and tranquilizer drugs; and methods of euthanasia	✓	✓	
3)	Surgical and postsurgical care	✓	✓	✓
4)	Promotion and monitoring of animal=s physical and psychological well-being	✓	✓	
5)	Oversees adequacy of the husbandry program	✓	✓	
6)	Involved in the review and approval of all animal care and use, e.g., via a role on the IACUC	✓	✓	✓
7)	Training of institutional staff in the care and use of laboratory animals	✓	✓	✓
8)	Assists in establishment and/or monitoring of occupational health and safety program	✓		
9)	Monitors for zoonotic diseases	✓	✓	✓
10)	Advises on and monitors biohazard control policies and procedures relevant to the animal care and use program	✓	✓	

Principal Investigator (PI) Responsibilities

The PI is responsible for the following:

1) Submitting a completed Animal Component of Research Protocol (ACORP) using the most recent version with each research proposal involving the use of live vertebrate animals for funding. The IACUC shall review the ACORP form matching the proposal to the ACORP.

2) Assuring that all active protocols and new projects involving the use of live vertebrate animals have been reviewed by the IACUC.

3) Training and supervising laboratory staff to ensure compliance with all applicable regulations, policies, and guidelines for all research involving live vertebrate animals, including annual continuing education.

4) Reporting problems and concerns about the use of laboratory animals to the VMC and the IACUC Chair.

5) Securing approval through the IACUC for changes made in the original research plan.

6) Completing the Certification of Storage & Security of VA Research Information for each protocol.

7) Completing the Conflict of Interest Statement for each protocol.

NOTE: High school age personnel can be considered for approval on a protocol. However, the PI is responsible to make certain these individuals go through the same credentialing process, training and requirements as all staff. These individuals operate under the direct supervision of the ARF supervisor. All regulatory requirements apply. They must be listed on the protocols and approved by the IACUC before beginning work.

IACUC Responsibilities

The IACUC is responsible for the following:

1) Performing the review and oversight functions required by PHS Policy, the *Guide for the Care and Use of Laboratory Animals (Guide)*, the USDA Animal Welfare Act Regulations, the VHA Handbook 1200.7, and any other federal regulations that impact IACUC function.
2) Reviewing and approving, requiring modifications (to secure approval), or withholding approval of all research proposals involving species and activities included within the definition of an "animal" provided by Section III in PHS Policy. Recording in the minutes if progress was made in protocol after review of the abstract. All research projects involving animals must be approved by the IACUC and then by the R&D Committee prior to commencement.
3) Reviewing 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 and only non-protocol related issues may be discussed. Members who have a conflict of interest may not be counted toward a quorum and may not vote.
4) Providing written notification of the results of the IACUC review to the R&D Committee and the PI.
5) Reviewing at least annually all research programs involving the use of live vertebrate animals. The date of continuing review will be based on the date of IACUC approval.
6) Holding IACUC meetings monthly or more often if deemed necessary by the Chair. IACUC meetings are scheduled for the 2nd Thursday of each month at 1:00 in the Research Conference Room, R308 or other pre-determined designated area. Consistent parliamentary procedures must be used to conduct business. If needed, the Chair may call a Special Meeting. All members shall be notified of a Special Meeting. All regulations for Special Meetings are the same as the regularly scheduled convened meeting. In addition, at the discretion of the Chair, a meeting may be canceled. Tele-conference is allowed, where real time interaction opportunity is given for comments and vote for all those participating.
7) Performing semi-annual program and facilities self-assessment reviews. As part of the program review, the IACUC shall randomly review IACUC records representing at least 5% of the total active projects (a minimum of five) to determine if appropriate documentation of initial review, approval letters, annual and triennial approvals, modification, and investigator correspondence are present.
8) With the assistance of the veterinarian, as well as the Administrative Office, the IACUC is notified of per diem changes and forwards these changes to the R&D Committee. The R&D Committee should approve the rates before they are finally adopted.
9) Reviewing annually a report of response to elevations in animal room temperatures from Facilities Management personnel and results will be included in the minutes.
10) Reviewing at each regularly scheduled monthly meeting progress toward completing corrections of deficiencies previously noted in semi-annual reviews.

11) Reviewing and approving annually the Animal Research Facility SOP as well as the IACUC SOP.

12) Approving written disaster plans to protect personnel and animals.

13) Complying 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.”

14) Review Occupational Health records at semi-annual reviews.

IACUC Staff

The Administrative Officer (AO), Research Service provides support to the IACUC and R&D Committee. Responsibilities are:

1. Directing and overseeing all IACUC support functions and operations
2. Training, supervising and evaluating IACUC staff
3. Developing and implementing procedures to effect efficient document flow and maintenance of all IACUC records.

The IACUC Coordinator/staff's responsibilities include:

1. Maintaining the official roster of IACUC members
2. Scheduling IACUC meetings
3. Verifying that all required documents have been received, contacting PI if additional documents are needed
4. Maintaining a computerized database for tracking purposes
5. Providing IACUC meeting agenda items to all IACUC members no later than 3 business days before the meeting, but routinely one week before the scheduled meeting to allow for sufficient review time. Items must include an agenda with all business items listed, all required protocol submission forms, including an ACORP. The agenda will include reviewer assignments (2 voting members for new protocols) for all protocols being reviewed.
6. Providing the IACUC with the continuing review submission form, the project data sheet, and the updated abstract
7. Compiling the minutes of IACUC meetings in compliance with regulatory requirements
8. Maintaining all IACUC documentation and records in accordance with regulatory requirements
9. Assisting new IACUC members in completing orientation procedure and meeting required education standards
10. Ensuring that all IACUC records are secured and properly archived
11. Facilitating communication between investigators and the IACUC and communicating with affiliates as necessary
12. Tracing the progress of each research protocol submitted to the IACUC
13. Serving as a resource for investigators on general regulatory information, and providing guidance about forms and submission procedures
14. Maintaining training documentation and reference material related to IACUC requirements.
15. Maintaining and updating the IACUC investigator submission packets and IACUC forms
16. Drafting reports and correspondence to research investigators on behalf of the IACUC or

IACUC Chair regarding the status of research projects and conditions for approval of projects, including assurance that all staff listed on the protocol have completed mandatory web-site training before approval is granted

17. Drafting report and correspondence directed to research facility officials, federal officials and others on behalf of the IACUC or IACUC chair
18. Keeping manuals, procedures and guidelines up to date
19. Assisting during regulatory inspections and site visits

IACUC Membership

The VA Nebraska-Western Iowa Health Care System IACUC follows these guidelines:

1. The composition of the IACUC meets existing requirements set forth in PHS Policy and the USDA Animal Welfare Act Regulations. The IACUC consists of a minimum of 5 members who are required to serve as voting members to constitute the IACUC, of varying professional and personal backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. Only a properly constituted IACUC may conduct official business.

2. The required voting members include a Chair (preferably a more senior scientist with animal research experience and good committee management skills), the Veterinarian Medical Consultant, one scientist with animal research experience, a non-affiliated member (non-lab animal user and meets the criteria in subpar.8a [3] of the VHA Handbook 1200.7) and a lay member (non scientist) who must not be involved in animal research.

3. The Associate Chief of Staff for Research and Development (ACOS/R&D) and Administrative Officer for Research and Development (AO/R&D) are non-voting, ex-officio members on the IACUC.

4. At least one member of the IACUC is a member of the R&D Committee.

5. The IACUC appoints one person from among its members as Vice Chair of the IACUC. The Vice Chair serves as the IACUC Chair in the temporary absence of the Chair and may sign committee letters in the absence of the Chair. When the Chair and Vice-Chair are absent, a senior member of the committee may serve as Chair in their absence.

6. Alternate members are appointed to substitute in the absence of primary members. A specific alternate is designated to substitute for a specific primary member. The alternate member will receive and review the same materials that the primary member received or would have received. The IACUC minutes will document when an alternate member replaces a primary member. An alternate may only contribute to a quorum and function as an IACUC member if the regular member for whom they serve as alternate is unavailable.

7. Members other than those who are designated ex-officio may serve terms of up to 3 years, on staggered appointments. Members may be re-appointed without lapse in service to the IACUC.

8. The IACUC Chair shall be appointed by the Medical Center Director (through the R&D Committee) for a term of 1 year and may be re-appointed without any lapse in time. The

IACUC Chair shall not simultaneously chair the R&D committee or another subcommittee thereof.

9. Confidentiality: Members are expected to hold in confidence all matters coming before the IACUC.

10. Attendance of visitors at IACUC meetings: Persons who are not IACUC members may, at the discretion of the Chair, attend a meeting and their attendance will be noted in the minutes of the meeting.

CONFLICT OF INTEREST

IACUC Investigators

VA Nebraska Western Iowa Health Care System Memorandum No. 151-11 establishes policy and procedures regarding Conflict of Interest (COI) in research which will enable investigators (i.e., principal investigators, co-principal investigators, investigators, and collaborators with five percent [5%] or more effort) and immediate family members of investigators to comply with applicable VA and other federal and state regulations regarding conflicts of interest in research.

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).

The investigator is responsible for disclosing any COI. This disclosure must be documented through the use of the COI Statement, which must be submitted as a component of the research application.

IACUC MEMBERS

Both the USDA AWAR (see 9 C.F.R. 2.31(d)(2) and PHS Policy (IV.C.2) stipulate that no IACUC member may participate in the IACUC review, or in the approval of a research project in which the member is personally involved in the project, except to provide information requested by the IACUC. Thus, 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. **IACUC members should not participate in the IACUC review or approval of a research project in which the member or any member of his/her family has a personal or financial conflict, except to provide information requested by the IACUC.**

The minutes of the meeting will reflect that the member having the conflict of interest has left the room during the discussion and vote, and that their absence must not compromise the presence of a quorum for conducting business.

The ACOS/R&D and AO/R&D (non-voting members on the IACUC), 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.

IACUC APPROVAL PROCESS

The following describes the procedures for review and approval of **all** research (includes VA-funded and non-VA funded) regardless of performance location (includes research performed at the VA), and includes pilot studies and/or internally funded studies.

Full Committee Protocol Review

IACUC primary reviewers describe the protocol and their review of the ACORP, lead the discussion and note any needed changes and makes recommendation for IACUC action. Secondary reviewers and other members also offer additional comments as necessary.

The primary and secondary reviewer will complete a Reviewer's Checklist for initial and triennial reviews which helps to confirm the PI has reported the animals in the appropriate pain category. During the review of proposed animal studies, there must be adequate consideration for all issues that may compromise animal welfare, including prolonged distress without intervention. This checklist also documents any deviations from the Guide which can then be flagged and monitored during the semi-annual review and during the post approval monitoring.

The IACUC Chair opens the floor to discussion and review; when completed, the Chair requests one of the following motions and members' vote:

1. Approval – approved as submitted with no modification required.
2. Requires modification (to secure approval) – The Chair will notify the PI in writing of the required clarification. The PI will be notified by written notice once the revisions have been approved by the assigned reviewer and when the ACORP has been signed by the Chair, Veterinarian and others if necessary. In the event the modification(s) have not been addressed by the PI within 90 days of committee review, the protocol will be withdrawn and the submission process for initial review will be required.
3. Tabled – IACUC requires additional information and/or has a concern.
4. Withhold Approval – there are significant questions that the IACUC feels approval of the proposal/ACORP to be unwarranted.

Designated-Member Review

The use of the designated member subcommittee reviewer system allowed by PHS Policy and the USDA Animal Welfare Act Regulations may be used provided that all IACUC members receive complete copies of all protocol forms to aid them in deciding whether or not to request full committee review. When this method is used, the following will apply:

All IACUC members receive a list of proposed research projects and access to the necessary information on the protocol to be reviewed. If any member feels that the protocol should go before a full committee, then its review must be deferred to the next full IACUC meeting. Any member can make the decision to send the protocol to full-committee review at any time during

the time period designated for providing this opportunity. If no member calls for a full-committee review, then the Chair can refer the protocol in question to a designated reviewer. The Chair may select one or more members, qualified to review this specific protocol, who will act on behalf of the entire IACUC to:

1) approve the protocol
2) require modifications to secure approval, or
3) request full committee review.

The designated reviewer does not have the power to withhold approval, however, in such cases must refer the protocol for full-committee review.

The designated reviewer's approval has equal validity to full-committee review approval and does not require subsequent reapproval at a convened meeting. All reviews by this method will be listed on the next month's IACUC meeting agenda and minutes.

Locally, designated member review will be used primarily for amending an ACORP. The Chair will decide if the amendment requires approval by the designated member review process.

Note: If any IACUC member is not present at a convened meeting the quorum of members present may decide by unanimous vote to use DMR subsequent to FCR when modifications are needed to secure approval. However, any member of the IACUC, at any time may request to see the revised proposal and/or request FCR of the protocol.

Requirements for Approval

All IACUC actions are communicated to the PI in writing.

The protocol/ACORP must not be initiated until complete IACUC approval is received by the PI. This includes approval by the Research and Development Committee.

Research that has been approved by the IACUC is subject to review and approval, contingent approval or disapproval by the Research & Development committee and/or IO, but those officials **may not** approve research that has been disapproved by the IACUC.

The IACUC must review the conduct of all animal protocols at least annually. At the first and second anniversaries, the IACUC may accept a simple signed certification by the investigator addressing questions asked on the continued review form. The "Findings" portion of the abstract must be updated. Prior to the third anniversary, the IACUC must conduct a re-review of the protocol (triennial review). A new ACORP (latest version) must be submitted at the time of triennial review.

At any time a request for approval (initial, annual continued review, triennial review, amendments, etc.) comes before the IACUC, the PI and all team members on the protocol being reviewed must have all mandatory web-based animal training up to date before final approval is granted.

The IACUC shall 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 and only non-protocol related issues may be discussed.

Just-In-time (JIT) Review

JIT is a type of research proposal submission within the VHA R&D program that is limited to the receipt of compliance and assurance documentation. A JIT submission allows for the delay of all subcommittee and final R&D Committee Approval(s) when submitting a project for review. Even though JIT is used, all VA research proposals must be sent to R&D Committee before submission. Biomedical Laboratory Research and Development (BLR&D)/Clinical Science Research and Development (CSR&D) services require JIT submission of compliance for animal studies. The compliance documents should be submitted only after specific documents are requested by the VA JIT Document Manager. When submitting a proposal to Rehabilitation Research and Development Service (RR&D), please see the Research Administrative Office regarding submission requirements.

NOTE: Compliance and assurance documentation approved by the subcommittee must be approved by Central Office prior to their releasing any funds for approved projects.

IACUC REVIEW PROCESS

Protocol Submission Deadline

The complete protocol application including all attachments and appropriate signatures are due in the Research Administrative Office to the IACUC Coordinator by the **25th** day of the month for the following month's review. This deadline is also applicable for all annual protocol continued reviews.

Initial Protocol Review

Prior to the convened IACUC meeting, all members receive initial review materials consisting of the Request to Review Protocol, abstract, protocol narrative and the most recent version of the VA ACORP form as well as any other information which will help make the review substantive. The IACUC protocol submission checklist should be completed with all applicable items addressed. A primary and secondary reviewer is assigned to each initial protocol. This assignment takes into account appropriate reviewer's expertise based upon protocol content. Each reviewer will complete the IACUC Reviewer's Checklist.

Ad hoc reviewers (i.e. consultants with special expertise) with competence in specific areas may be asked to assist when the IACUC encounters studies involving science beyond the expertise of the members. These individuals may not vote with the IACUC. These individuals are subject to the same conflict of interest policies as IACUC members.

Investigators are encouraged to attend the meeting at which their proposal is being initially reviewed so that any questions from committee members can be answered at that time.

Continuing Protocol Review

Continuing review by the convened IACUC must be substantive and meaningful. Continuing review must be conducted at least annually from the initial IACUC meeting approval date. Prior to the convened IACUC meeting, all members will receive continuing review materials consisting of the project data sheet, an updated abstract and completed continued use form.

The same considerations apply for continuing review as initial review. Primary and secondary reviewers are assigned to review the updated abstract, project data sheet and continued use form.

The PI is responsible for:

Ensuring that reports are made to the IACUC of changes in research activity and ensuring that these changes in approved research, during the period for which IACUC approval has already been given, will not be initiated without IACUC review and approval except where necessary to eliminate apparent immediate hazards to the animals.

A Conflict of Interest question on the annual continuing review form must be answered by the PI. This question addresses any possible conflict of interest issues that may have developed since the beginning of the proposal. The PI should identify any co-investigators or research team members who develop a conflict of interest at the time of continued review.

Triennial Review

Prior to the third anniversary, the IACUC must conduct a complete re-review of the protocol. This will be accomplished by performing a new review of the protocol, a new ACORP (latest version), abstract and continued use form. Two reviewers are assigned to review all triennial reviews. Each reviewer will complete the IACUC Reviewer's Checklist.

Amendments

IACUC approval is required for significant changes to approved animal research protocols prior to implementing these changes. With the exception of Personnel Additions to a protocol, the Amended Protocol Reporting Form should be used when submitting changes. A separate amendment form is used for reporting personnel additions (see below*).

Some examples of changes to be reported include but are not limited to the following:

1. Use of additional animal species (a new ACORP is required), increase in the number of animals used, or increase in the number of procedures performed on individual animals;
2. Use of a procedure that might increase the pain/distress category in which the animals are placed, or might otherwise be considered a significant departure from the written protocol;
3. Use of a procedure not described in the ACORP;
4. Allowing other investigators to use animals or animal tissue on other protocols, or use these animals on another IACUC-approved protocol if you are changing your procedures to accommodate tissue sharing. If there are no new procedures, an amendment is not necessary; however, you must complete the tissue transfer form. (See section below)

When submitting an amendment to the committee for review, the most recently approved ACORP with all appendices must be submitted with the amended changes highlighted. Full committee amendments are sent to all members with two members assigned as reviewers. IACUC members look at the complete ACORP during an amendment review; however, only revisions relating to the present amendment should be addressed **unless** the revision impacts the welfare of the animal; then it is the IACUC's responsibility to address the concern.

When a PI is requesting a post award change, it is the PI's responsibility to get approval through proper channels if this change constitutes an action requiring NIH prior approval.

*Amendment Form for New Personnel should be used when reporting new personnel on an approved protocol. This form must be completed and signed by the Principal Investigator. All new personnel must have educational requirements met before submitted for IACUC review and approval. Personnel must not begin work on a protocol until an approval letter has been received from the IACUC. It is the PI's responsibility to verify completion of credentialing before team members begin work in the lab.
NOTE: High school age personnel can be considered for approval on a protocol. However, these individuals are responsible for going through the same credentialing process, training and requirements as all staff. These individuals operate under the direct supervision of the ARF supervisor. All regulatory requirements apply. They must be listed on the protocols and approved by the IACUC before beginning work.

POST APPROVAL MONITORING (PAM)

The purpose of post-approval monitoring and auditing is to reinforce the need for regulatory compliance as well as a means to improve ongoing communication between the IACUC and Research teams. It is a process to actively compare what is occurring during the conduct of a study in comparison to the conditions outlined in the approved written protocol. Prevention is key to maintaining institutional accountability and animal safety. At NWIHCS, the Post-Approval Monitoring Program (PAM) will ensure that all active animal protocols are reviewed at least once each calendar year in addition to their initial or continuing review done by the IACUC (Please see IACUC SOP for detail).

Membership

A Post-Approval Monitoring Team will be established as a subgroup of the IACUC. It will consist of a minimum of 3-4 IACUC members and, when necessary, Principal Investigators who have appropriate scientific expertise and knowledge of animal regulations and procedures. A PAM Team member will be expected to recuse themselves if they have a conflict of interest with a study or investigator. All team members will be instructed on how to use the PAM audit form, the importance of their responsibilities as an auditor, and the need for confidentiality.

Audit Process

1. All active animal protocols will be reviewed at least once each calendar year.
2. The IACUC Coordinator will work with the IACUC Chair before the end of the year to create the annual PAM schedule for assigning audits for the following year
3. The PI will be notified at least 2 months prior to the month when the audit will occur and will be given an electronic copy of the Audit form at that time.
4. A meeting time between the PAM Team members, the PI and support personnel will be established and a location determined – preferably in or close to the animal laboratory. The PAM member should schedule sufficient time to ensure that opportunities to observe activities associated with the protocol (when possible) are included in the PAM audit. Visual inspection of the lab, surgical room and recover areas should also occur at the time procedures are being reviewed.
5. Prior to the meeting, the PAM Team members should begin their audit of the animal protocol assigned to them by familiarizing themselves with the protocol. They should review the protocol file in the Research Administration Office and access any additional information included on the audit form that is maintained by the ARF director and/or the IACUC Coordinator. The PAM Team member can begin to generate additional questions they may have for the PI and/or his/her staff personnel at this time.
6. The PAM Team member meets with the PI and his/her staff personnel to discuss and confirm that the actual work being done corresponds to the written protocol. The PAM team member should be completing the form during this process.
7. If the PAM Team member finds that the work being done corresponds to the written protocol, the audit report will be presented at the next IACUC meeting and a copy of the completed audit will be provided to the PI.
8. If the PAM Team member finds that the work being done does not correspond to the written protocol or that animal safety is being negatively impacted, the PAM Team member should submit his/her audit findings and form immediately to the IACUC Chair who will then discuss the issue with the ACOS/Research to determine if this represents an issue of non-

compliance. The process of investigation of an allegation of non-compliance, definitions of non-compliance and actions to be taken if non-compliance occurs, are all explained in the IACUC SOP Memorandum 151-10 Research Service Policies and Procedures for Complaints and Allegations of Non-Compliance. If, as a result of the process, the allegation of non-compliance is not substantiated, the audit report will be presented at the next IACUC meeting and a copy of the completed audit will be provided to the PI. If, as a result of the process, it is determined that issues of non-compliance were present, the completed audit form will become part of any written correspondence sent by the IACUC to the PI in addition to any corrective actions that must be taken.

Review of the Audit Process

The IACUC will review the auditing process annually, or sooner if needed, to assess whether or not is should be modified to accommodate program resources and needs. Input from PI receiving the audits should also be considered during this review.

Animal Tissue Transfer

The Tissue Transfer Form is used to permit transfer of animal tissue/parts to an investigator from another investigator who is willing to share them. The donor, recipient and IACUC Chair or Vice-Chair must sign the form. Tissue sharing may begin upon concurrence by the Chair or Vice-Chair of the Subcommittee of Animal Studies. The complete, signed form must be submitted to the Subcommittee of Animal Studies for review and discussion. If the recipient investigator is from an outside institution, an official from that institution must provide a letter documenting approval to conduct research at that institution. Tissues/parts must be collected post-mortem, and no additional procedures can be performed on the animals before euthanasia.

Animal Transfer Form

The Animal Transfer Form is used to permit transfer of animals to an investigator from another investigator, both internally (within our facility) and externally (to off-site facilities). For animals being transferred off-site, the recipient PI will provide the IACUC with a letter from an official from their institution documenting approval to conduct research at their institution (e.g., the IACUC Chair) as well as a statement confirming the recipient PI will accept responsibility for the animals' care and welfare as the new owner of the animals.

All federal regulations relating to animal transportation standards apply and must be followed.

Offsite Animals

According to VHA Handbook 1200.7, "Use of Animals in Research", section 7.e., all VA animal facilities and affiliates or other animal facilities that house animals purchased with VA (including VA Foundation) funds must be accredited by AAALACI. Under exceptional circumstances, a waiver may be requested in writing from CRADO, or designee, through the CVMO's office.

A Memorandum of Understanding (MOU) is in effect for personnel who plan to house or use animals at any OVAMC facility where such animals are purchased with UNMC or Creighton University funds as part of UNMC-sponsored or Creighton University-sponsored research and to personnel who house or use animals at UNMC or Creighton University where such animals are purchased with VA or VA Nonprofit-sponsored research. For more specific information regarding the MOU between VA and the affiliated universities, please contact the Research Administrative Office.

Suspension of Projects

The IACUC may suspend an activity that is previously approved if it determines that the activity is not being conducted in accordance with the description of that activity provided by the PI and approved by the IACUC. In consultation with the veterinarian, it may also require any animal procedures not approved by the IACUC to stop. Unless the IO has granted additional authority, the IACUC may suspend an activity only after review of the matter at a properly-convened IACUC meeting and with the suspension vote by a majority of a quorum.

If the IACUC suspends an activity involving animals, the Director (IO), in consultation with the IACUC and ACOS/Research Service, shall review the reasons for suspension, take appropriate corrective action, and report that action with a full explanation in writing within 5 business days of the suspension to:

1. CVMO
2. OLAW
3. ORO
4. USDA
5. AAALACI
6. The affiliate's IACUC, if the project involves animals purchased with funds awarded to the affiliate.

REPORTING ANIMAL CONCERNS

The humane care and use of animals in research and teaching at Omaha VAMC is of paramount importance to the IACUC. Concerns regarding the health and welfare of animal subjects used here can be reported anonymously and without fear of reprisal. Concerns should be reported to the IACUC by contacting the Research Administrative Office. Memo No. 151-10 establishes policy and procedures with respect to protection of whistle-blowers from discrimination and internal and external allegations of improper animal care. Flyers detailing this policy/procedure are posted throughout the animal facility and research building.

CONTINUING EDUCATION/TRAINING

The USDA Animal Welfare Act Regulations (section 2.32, Personnel qualifications), the U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training (Principle VIII), PHS Policy (see Sec. IV.1.g), and the *Guide for the Care and Use of Laboratory Animals* mandates training for all personnel who work with laboratory animals. This includes laboratory animal veterinarians, ARF Supervisor and other husbandry staff, as well as IACUC members, PIs and their research team members. Accordingly, it is critical that local funds be allocated for continuing education activities for the veterinarian, ARF Supervisor and husbandry staff, IACUC members and appropriate administrative staff.

The mandated training site can be accessed at http://www.citiprogram.org. Investigators and research staff who utilize laboratory animals must pass the exam entitled "Working with the VA IACUC", exams for specific species used in their research protocols and the post procedure care course when using mice or rats. A Biosecurity Curriculum is also mandated as a one-time exam for all staff. These mandated exams must be completed every two years from the date first taken. All IACUC protocol approvals require that this training for PI and team members be up to date before final approval can be granted.

All IACUC members must pass the exam entitled "Essentials for IACUC Members" which is accessed at the site http://www.citiprogram.org. New members will be given a copy of the IACUC and ARF Standard Operating Procedures manual as part of their orientation, as well as a sample of a recent IACUC agenda and minutes. A good resource for IACUC members is available at htttp://grants.nih.gov/grants/olaw/references/outline.htm. The IACUC Chair also meets with the prospective member indicating what their role will be on the IACUC and answers any questions they may have.

Animal care and use videos can also be checked out for viewing from the Animal Facility Supervisor. The American Association for Laboratory Animal Science (AALAS) has created a website (www.aalaslearninglibrary.org) with many useful training courses for all personnel.

All personnel listed on an active animal protocol must have an annual Occupational Health screening. This is also a requirement and expectation of our AAALAC accreditation. The month of April was designated "Research Occupational Health Month". At that time all personnel listed on an active animal protocol will be required to complete a screening during the month of

April regardless of when the previous screening was completed.

SEMI-ANNUAL PROGRAM AND FACILITY SELF-ASSESSMENT REVIEWS

Review Process

The VA IACUC must perform a self-assessment review of the program of animal care and use, and an inspection of the animal facilities and husbandry practices at least every 6 months. The self-review is conducted using the standards established in the most current *Guide for the Care and Use of Laboratory Animals,* PHS Policy, USDA regulations promulgated in accordance with the Animal Welfare Act and this Handbook.

The semi-annual self-review must include all facilities and investigator areas where laboratory animals purchased with local VA funds are used in procedures, or housed longer than 12 hours. A Memorandum of Understanding has been initiated between the VA IACUC and our affiliates' facility to house animals at the off-site facility; the VA IACUC will accept the semiannual inspection conducted by the IACUC of the other facility in lieu of sending a VA IACUC review team to the facility. The affiliates' animal care and use program and facility evaluation will be included as part of our semi-annual self-review. All deficiencies affecting animals purchased with VA funds must be noted and corrections tracked to assure optimal care for the animals.

The following information must appear in the Program and Facility Self-assessment Review report (our facility uses the checklist [Forms 1, 2 and 3] as furnished by the CVMO):

1. VA Nebraska-Western Iowa Health Care System (636), 4101 Woolworth Avenue, Omaha, NE and the date(s) that the self-assessment was performed.
2. If program or facility deficiencies are noted, the report must contain a reasonable and specific plan and schedule with dates for correcting each deficiency.
3. The report form must distinguish significant deficiencies from minor deficiencies. A significant deficiency is one which, in the judgment of the IACUC, is or may be a threat to the health or safety of the animals. Examples of such deficiencies are animal facility heating and cooling equipment that cannot maintain consistent temperatures in the ranges specified in the *Guide*, an inadequate program for the care of surgical patients, an inadequate program for the medical care of animals, conduct of research not approved by the IACUC, inadequate caretaker staffing, and inadequate IACUC administrative support such that the IACUC cannot fulfill its regulatory mandates. A minor deficiency is one that does not fit the definition above of a significant deficiency.
4. Any minority opinions and views.
5. A list of IACUC members present during the self-assessment with name, degree(s) and IACUC role of each member. All IACUC members are strongly encouraged to participate in the self-assessment, but the review team must include at least three IACUC members (two voting) for program review, and three IACUC members (two voting) for facility review. Attendance by the non-affiliated member is especially encouraged.
6. After a majority of voting IACUC members have voted to approve the report by signing next to their typed names, the report will be discussed in a meeting of the Medical Center Director, the VMC, the IACUC Chair and one or more research administrators (other IACUC members may also attend). The Medical Center Director must then sign the

report, indicating he has reviewed it, after which it is forwarded to the CVMO within 60 days of the self-review date. A copy should also be sent to the local R&D Committee for review, but R&D Committee approval is not needed before the document is sent to the CVMO.

7. The report must not be altered by any local official once a majority of voting IACUC members have voted to approve the report.
8. The report must be retained on file for at least 3 years by the Research Administrative Office.
9. If corrections of significant deficiencies are not completed according to the plan and schedule set by the IACUC as part of the semi-annual self-review report, the IACUC must notify ORD (by contacting the CVMO's office) through the ACOS/R&D and the Medical Center Director within 5 business days of the missed deadline. The following organizations must also be notified:
    a. OLAW, as required by PHS Policy.
    b. The Animal Care Section at USDA APHIS, as required by AWAR, if the deficiency involves a species meeting the definition of an animal in the AWAR, or if the deficiency impacts the care or use of such a species.
    c. AAALACI, as required by AAALACI rules of accreditation
    d. The affiliate's IACUC, if a joint IACUC is not present and the project involves animals purchased with funds awarded to the affiliate; or if an agreement between the VA and affiliate requires such notification.
    e. The VA ORO, as required by ORO policy
    f. Any Federal agency (other than the VA) funding an activity that has been suspended.
10. As part of the semi-annual Program review, the IACUC shall randomly review IACUC records representing at least 5% of the total active projects (a minimum of five) to determine if appropriate documentation of initial review, approval letters(s), annual and triennial approvals, modifications, and investigator correspondence are present.
11. As part of the semi-annual program review, the IACUC shall review and offer suggestions for further compliance of Occupational Health Records for personnel listed on active animal protocols.
12. As part of the semi-annual report sent to CVMO, Central Office, significant accomplishments, as well as any new programmatic goals the committee has identified, will be documented for review with the Institutional Official.

Mandated Reporting of Deficiencies

The main categories of deficiencies that must be reported within 5 days to outside authorities (agencies are listed on page 30, #9.a.-f) are as follows:

a. Any serious or continuing non-compliance with VA or PHS Policy (including any serious deviation or continuing non-compliance with the provisions of the *Guide*, as required by the PHS Policy) or USDA AWAR.

b. Suspensions of protocols previously approved or stopping of procedures or studies never given IACUC approval.

c. Failure to correct a significant deficiency (identified during a semi-annual IACUC program or facility self-assessment review) according to the schedule approved by the IACUC.

IACUC RECORDKEEPING

The VA Nebraska-Western Iowa Health Care System IACUC shall prepare and maintain adequate documentation of IACUC activities.

1. Minutes of IACUC meetings must be published within three weeks of the meeting date and must include the following:

   a. IACUC members present, absent or excused. For each member, their role on the committee must be noted, include whether they are voting or non-voting.

   b. Date of the meeting and a heading/title as follows:

   Subcommittee of Animal Studies (IACUC)
   Omaha VA Medical Center (636)
   Research Service (151)
   4101 Woolworth Avenue
   Omaha, NE 68105-1873

   c. Whether a quorum is present. A quorum is defined as a majority (more than 50%) of voting members.

   d. Three sections:

   - Review of minutes
   - Old business
   - New business

   e. For each project under consideration, first and last name of the PI and the complete name of the project.

   f. For each project being reviewed, the motion passed by the committee must be recorded with the exact vote, which must include the number voting for the motion, the number voting against, the number abstaining, and who, if anyone, was recused or excused. It must be stated which member(s) will review revisions and have the authority to grant final approval for the committee.

   g. Minority opinions

h. A description of committee deliberations of each project reflecting in lay language the issues discussed, and specific revisions and clarifications requested.

i. A notation of which members were recused during project review and vote to prevent conflicts of interest.

j. Records of continuing review activities and amendments

2. A copy of the minutes will be submitted to the IO and R&D Committee monthly.

3. Copies of all research proposals reviewed (approval and disapproval determinations), scientific evaluations that accompany proposals, approved and signed ACORP forms, progress reports and amendments submitted by the PIs and any reports associated with the protocol shall be retained indefinitely **after completion** of the research. All records shall be accessible for inspection and copying by authorized representatives at reasonable times and in a reasonable manner.

4. Minutes of IACUC meetings and semi-annual reports will be maintained for indefinitely until otherwise designated by VA Central Office.

5. The Research Administrative Office will maintain adequate documentation, including all PHS, USDA, AAALACI, and other reports/correspondence of all IACUC activities for indefinitely until otherwise designated by VA Central Office.

DETERMINATION FOR ACORP COMPLETION

All studies will be brought before the full committee at a convened meeting. The following will help in determining the necessity for ACORP completion as well as future review responsibilities.

A. The IACUC **will** require completion of an ACORP if:

1. Animals purchased with VA or non-VA funds would be used primarily or exclusively for experiments proposed in the application, whether the animals are housed on or off-site, and regardless of whether funds for animal purchase appear in the budget.
2. Animal tissues or primary cell lines purchased with VA or non-VA funds would be derived from animals sacrificed primarily or exclusively for use in the experiments proposed in the VA application, whether or not funds for animal purchase are included in the budget.
3. A Breeding Colony is initiated. This will be treated as a new protocol and will be assigned a separate protocol number.

When an ACORP is required using criteria 1-3 above, the protocol will be followed by the IACUC.

B. The IACUC **will not** require an ACORP if:

1. Only immortal animal cell lines or immortal explants would be used in the proposed experiments such that no additional animals would be needed to meet application objectives.
2. Animals on other IACUC-approved projects would be used for the proposed work, and these animals would be utilized for the other project even if the need for the animals by the proposed VA project did not exist (with the exception of a Breeding Colony).
3. Animal tissues, blood, and other body fluids, or primary cell lines would be obtained exclusively from live animals on other IACUC-approved protocols. Although an ACORP is not required for submission, local IACUC approval for such use is required.
4. Animal tissues, blood and other body fluids, or primary cell lines would be obtained exclusively from euthanized animals, and those animals would be euthanized even if the need for the tissues or cell lines by the proposed VA project did not exist. This provision applies to the use of tissues collected from USDA-licensed slaughterhouses. Although an ACORP is not required for submission, local IACUC approval for such use may be required.
5. Use of animals would be limited to animal-derived reagents or products such as serum, antibodies, and mediators purchased as a standard catalog item from a USDA-licensed commercial vendor.
6. Use of animals would be limited to non-standard reagents such as custom antibodies, or other tissue products must be purchased from a vendor, and additional animals must be used to generate these reagents at the vendor's facility. PHS Policy dictates that an IACUC review and give approval for the use of animals in this scenario, and that an assured performance site be used.

When an ACORP is not required using criteria 1-6 above, exclusion from future IACUC review may, when appropriate, be made and annual review will be deferred to the R&D Committee.

BREEDING COLONY GUIDELINES

The following is a guideline for PIs and IACUC members to use when preparing and reviewing breeding protocols. In particular, this guide lists items that need to be addressed in the ACORP that specifically concern breeding protocols that is above and beyond what is asked for in the current general ACORP form.

Overall, a new ACORP must be submitted, this will be considered an initial review and assigned a separate protocol number. All of the questions on the ACORP form need to be answered and for breeding protocols the following additional information needs to be added under the headings highlighted below.

B. Lay Description:

1. Describe the use of the particular breeding protocol in lay language and the benefits of using the particular mice for experiments and why the use of these mice in proposed experimentation might benefit the heath of people or animals.

C. Experimental Design:

1. Describe in lay language the experimental protocol that will be used for starting and maintaining the breeding protocol.

2. Describe in scientific language outside your discipline the experimental protocol that will be used for starting and maintaining the breeding protocol. Include the following detailed information as to how the breeding colony will be managed:

    a. Indicate what the genotype of breeding males and females will be.
    b. Describe the breeding scheme for each strain that will be bred. Indicate how many females per male will be housed and the mating system planned (brother-sister mating, back-cross, etc).
    c. Estimate the number of litters a female will produce during her lifetime.
    d. Estimate the age the breeders will be started and retired.
    e. State how you will monitor and check for pregnancy.
    f. State and justify at what age the animals will be weaned (standard weaning age is 21 days).
    g. Describe the criteria you will use to select which animals are transferred to an approved experimental IACUC protocol.
    h. Describe the genetic testing used (i.e. tail snipping). Describe associated tissue collection procedures, including the use of local or general anesthesia that will be used prior to tissue collection.
    i. Describe how the census of the colony is managed and recorded. Include a description of the laboratory records that will be maintained to track (i.e. the number transferred to experimental protocol, euthanized, died or retained for future breeding stock). Also how will the animals be identified (by cage tags, ear punch).

j. Provide the best estimate of yearly needs which would include the following:
   i. the number of breeders needed per year (those retained for breeding and not transferred to experimental protocols)
   ii. the number of weanlings that will be euthanized because of improper genotype or gender per year
   iii. the number of breeding cages needed per year
   iv. the number of weanlings that will be used in experiments per year

D. Describe the characteristics of the selected species and justify its use.
List the species and stain of animals. List whether there is a functional deficit in these mice that would cause more that momentary pain or distress (i.e. tumor formation, diabetes, glaucoma). List where you will obtain the adult breeders to start the colony. Give information as to how the colony contributes to the overall objectives of your research and why animals from commercial vendors cannot be used. Note: Cost alone is not considered a justification for breeding.

Also, provide the currently approved and/or pending IACUC protocol number or title that the offspring of this breeding colony will be transferred to for experiments.

E. Personnel- Names of staff that will work with the breeders. List education, training and experience with animals in general and experience doing exact procedures for this breeding ACORP. Include who will be working with the breeders, and what experience they have for all appropriate procedures (i.e. tail snipping, euthanasia, ear punching).

F. Personnel- training. If personnel listed in E do not have experience, how and who will train them?

K. Justification for the number of animals
Provide the rational/scientific justification for the number of animals you have requested in Section C2. You probably cannot give specific statistical justification, as this is a request for breeding animals. However, you should be able to give an estimate of the number of animals you intend to breed and the reasoning behind that number.

N. Housing Sites
In question 2 also respond as to how long you intend to maintain the breeding

ACQUIRING AND DISPENSING NARCOTICS

The PI is required to sign up on the designated sheet in the ARF office indicating type, strength, volume and, appropriate ACORP for required narcotics. The VMO will order the narcotic on the hospital electronic computer system (VISTA). Once ordered, the Research Drug Officer will pick up the drug at pharmacy, log in, and place in lock box in R104. The VMO acknowledges receipt of drug by electronic signature through VISTA. The drug is dispensed as needed to the approved PI or Personnel on ACORP. The hospital assigns designees to inspect the lock box monthly for correct inventory, records, and expiration dates.

REPORTING

1. A USDA Annual Report of Research Facility is completed and submitted by December 1 each year using the USDA website. A copy of this report is not needed in the CVMO office if filed electronically.
2. AAALACI 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 AAALACI. These reports are sent to the CVMO.
3. Semi-annual self-assessment reports. No later than 60 days after the self-review date, an approved report signed by a majority of a convened quorum must be forwarded to the CVMO's office through the ACOS/R&D and the Medical Center Director.
4. An annual VA VMU report, which includes mice and rats, is submitted to the CVMO.
5. A PHS Assurance to conduct animal studies is required if the medical center accepts any PHS funds. New PHS Assurances and annual updates are sent to OLAW documenting program changes & dates of the IACUC's semi-annual reviews and inspections. PHS assurance, annual updates and correspondence to and from OLAW are sent to the CVMO.
6. The United States PHS regulation, "Responsibility of PHS Awardee and Applicant Institutions for Dealing With and Reporting Possible Misconduct in Science." At 42 C.F.R. 50103(b), requires that all institutions renew their research misconduct assurance by annually submitting a report to the Office of Research Integrity (ORI) on the allegations, inquiries, and investigations they handled in the previous year and other matters related to the regulation.
7. "What to Report to ORO" clarifies current requirements for reporting research-related issues to the ORO.

RESOURCES

1. VHA Handbook 1200.7, Use of Animals in Research

- Website: http://www.research.va.gov

2. Animal Component of Research Protocol (ACORP) – Latest Version

- Intranet Website: vaww.nwihcs.med.va.gov
- Internet Website: www.researchtraining.org

3. Office of Laboratory Animal Welfare (OLAW)

- http://grants.nih.gov/grants/olaw/olaw/htm

4. Guide for the Care and Use of Laboratory Animals

- Website:http://www.nap.edu/readingroom/books/labrats/contents.html

5. Association for Assessment and Accreditation of Laboratory Animal Care, International (AAALACI)

- Website:http://www.aaalac.org