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USE OF ANIMALS IN RESEARCH

1. REASON FOR ISSUE. This Veterans Health Administration (VHA) Handbook sets forth the principles and procedures that govern research, testing, and teaching activities involving laboratory animals in the Department of Veterans Affairs (VA).

2. SUMMARY OF MAJOR CHANGES. This constitutes a complete revision of existing policy.

3. RELATED ISSUES. VHA Directive 1200.

4. RESPONSIBLE OFFICE. The Office of Research and Development (12) is responsible for the contents of this VHA Handbook. Questions may be addressed to 404-728-7644.

5. RESCISSIONS. VHA Manual M-3, Part 1, Chapter 12, Animal Subjects in Research, dated September 1990, and VHA Program Guide 1200.5, dated March 1996, are rescinded.

6. RECERTIFICATION: This document is scheduled for recertification on or before the last working date of April 2010.

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USE OF ANIMALS IN RESEARCH

1. PURPOSE

This Veterans Health Administration (VHA) Handbook sets forth the principles and procedures that govern research, testing, and teaching activities involving laboratory animals in the Department of Veterans Affairs (VA).

2. BACKGROUND

Animal research contributes immeasurably to advancements in medical science. As recognized by principle #3 of the Nuremberg Code of 1947, it is often a moral imperative to perform research or testing on animals before subjecting humans to new procedures, pharmacologics, or devices. Most research and testing involving human patients continue to be based on the results of animal experimentation. To provide hope for veterans suffering from diseases 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 is conducted according to the highest ethical and legal standards. The basic principles governing animal research in VA are found in the United States (U.S.) Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training, which include the following imperatives:

a. Animal experiments are undertaken only after due consideration of their relevance for human or animal health and the advancement of biological knowledge.

b. The fewest number of animals needed to achieve scientific objectives is to be used.

c. The least sentient species that will permit the attainment of research objectives is to be used.

d. The least painful or distressful procedures needed to meet research objectives are to be used, and all reasonable measures to minimize pain and distress should be utilized.

e. When planning and conducting studies, the principles of replacement, reduction, and refinement need to always be considered.

f. Procedures that would be considered painful in a human need to be considered to be painful in an animal.

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

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

3. DEFINITIONS

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

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

c. **Animal.** The term “animal” is defined in this Handbook is 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). An animal for purposes of compliance with the Animal Welfare Act Regulations (see Sec. 1.1) is 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.

d. **Animal Research.** Animal research, as used in this Handbook, refers to any use of laboratory animals in research, testing, or training.

e. **Association for Assessment and Accreditation of Laboratory Animal Care, International (AAALAC).** AAALAC is the accrediting body for animal research programs recognized by VA.

f. **Animal Component of Research Protocol (ACORP).** 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) when a project involving animal research is submitted for consideration of VA funding. **NOTE:** See subparagraph 8d (2)(e) for guidelines for determining when an ACORP is needed when submitting applications for VA funding.

g. **Chief Executive Officer (CEO).** As the highest ranking administrative official at the local VA medical center, the Director must serve as the CEO, and appoint IACUC members to the VA (or joint VA affiliate) IACUC as required by the Animal Welfare Act (7 U.S.C. § 2143[b][1]) and the Health Research Extension Act (42 U.S.C. §289d).

h. **Chief Research and Development Officer (CRADO).** 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. **NOTE:** *The CRADO directs the Office of Research and Development (ORD), VA Central Office.*

i. **Chief Veterinary Medical Officer (CVMO).** 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. **NOTE:** *CVMO contact information is in Appendix A.*

j. **Institutional Animal Care and Use Committee (IACUC).** 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.

k. **Institutional Official (IO).** 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. The IO is the point of contact for correspondence addressing animal care and use issues with the United States Department of Agriculture (USDA), the Public Health Service (PHS), AAALAC, VA ORD, and VA Office of Research Oversight (ORO). As mandated by this Handbook, the medical center Director must fulfill the role of IO for VA research programs except when a VA medical center does not have its own PHS Assurance, or when it is accredited by AAALAC as part of an affiliate's program. In such cases, an administrator at the affiliate institution must assume the role of the IO for PHS correspondence to comply with PHS Policy (see Sec. II and Sec. III.G) and/or the role of IO for communication with AAALAC regarding accreditation matters.

l. **Just-in-Time (JIT).** JIT refers to the ORD review system (for VA applications involving animals) 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. Guidance on submission of JIT ACORPs is provided in subparagraphs 8d(2)(f) and (g) in this handbook. **NOTE:** *VHA Handbook 1202.1 provides details on the JIT submission process.*

m. **Office of Laboratory Animal Welfare (OLAW).** OLAW is the PHS Office responsible for administering PHS Policy on Humane Care and Use of Laboratory Animals (henceforth referred to as PHS Policy).

n. **Office of Research Oversight (ORO).** ORO serves as the primary VHA office in advising the Under Secretary for Health on all matters of compliance and assurance regarding human subjects' protections, animal welfare, research safety, and research misconduct.

o. **Public Health Service Assurance (PHS Assurance, or Animal Welfare Assurance).** PHS Assurance is the documentation submitted to the OLAW (USDA), by an institution that pledges that the institution will comply with PHS Policy.

p. **Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy).** PHS policies require institutions to establish and maintain proper measures to ensure the appropriate care and use of all animals involved in research, research training, and biological testing activities conducted or supported by PHS (see subpar. 3m). VA policy requires compliance with PHS Policy even if PHS funds are not received.

q. **Reduction.** Reduction is minimizing the number of animals needed for research, testing, or training. Reduction may include optimizing a study to utilize animals as their own controls, gathering a maximum amount of data from each animal subject (e.g., by gathering data for more than one experiment concurrently, or designing experiments to prevent the need for duplicate control groups), and using more sophisticated measuring techniques to improve precision and to reduce the sizes of the groups needed.

r. **Refinement.** Refinement is modification of experimental protocols to minimize pain or distress, whenever possible. Examples include:

(1) Identifying ways to prevent or relieve pain or distress likely to be caused by experimental procedures;

(2) Setting the earliest possible endpoints for the research;

(3) Using more appropriate analgesics and anesthetics for potentially painful procedures as they become available; and

(4) Increasing the effectiveness of post-surgical care with new technology.

s. **Replacement.** Replacement usually refers to the use of *in vitro* techniques or computer simulations in place of procedures on animals. Sometimes the term is applied to the use of less sentient species, such as invertebrates, birds, and reptiles, in place of more sentient animals such as mammals.

t. **Research and Development (R&D) Committee.** 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, the Subcommittee for Research Safety (SRS), and the Institutional Review Board (IRB) are technically subcommittees of the R&D Committee.

u. **Subcommittee for Research Safety (SRS).** SRS is the subcommittee of the R&D Committee that reviews and approves the use of hazardous substances in VA research. ***NOTE:*** *This subcommittee is also called the Institutional Biosafety Committee (IBC).*

v. **United States Department of Agriculture (USDA).** USDA is charged with enforcing the Animal Welfare Act Regulations and Standards (henceforth known as USDA AWAR). 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 AWAR.

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

4. SCOPE

a. Applicability

(1) The provisions of this Handbook apply to all research involving animals that is conducted completely or partially in VA facilities, or conducted in approved off-site locations and facilities by VA researchers while on VA official duty time. The research may be VA-funded, funded from extra-VA sources, or conducted without external funding. **NOTE:** *For clarification, an NIH-funded project for which the academic affiliate is the recipient of the grant, the research is conducted at the affiliate; and the investigator conducts the research on non-VA time would not be affected by this requirement.*

(2) Under exceptional circumstances, CRADO may grant a waiver from some, or all, of these provisions to individual investigators, provided that such a waiver is consistent with PHS Policy and the USDA AWAR. Requests for waivers need to be sent to the CVMO's office with a detailed justification.

b. Authority to Conduct Animal Research

(1) Pursuant to Title 38 United States Code (U.S.C.) Section 7303, VA is authorized to carry out a program of medical research in connection with the provision of medical care and treatment to veterans. VA must ensure that animal research is conducted in environments where proper facilities, professional staffing, and administrative support foster the highest standards of animal care and use. Animal research requires:

- (a) An extensive fiscal investment in facilities.
- (b) Extensive labor investments in the animal research facility.
- (c) Committee and administrative support.

(2) VA medical centers may not initiate a new program or restart a dormant program utilizing laboratory animals for research, testing, or training unless approved by CRADO, in consultation with the CVMO and the affected ORD Service Directors.

(3) If serious concerns about the health and welfare of animals exist, CRADO, in consultation with the CVMO, may suspend animal research activities at a station. **NOTE:** *Unless exceptional circumstances dictate otherwise, the input from the affected station and Veterans Integrated Service Network (VISN) management must be sought before major decisions to suspend field research are made.*

(4) Because VA conducts animal research according to the highest ethical and regulatory standards, all VA facilities conducting animal research must comply with the Health Research Extension Act (codified at 42 U.S.C. Section 289d) and the PHS Policy. The PHS Policy includes the U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training (prepared by the Interagency Research Animal

Committee), The Guide for the Care and Use of Laboratory Animals (prepared by the National Research Council; henceforth called the Guide), and the Report of the AVMA Panel on Euthanasia. **NOTE:** *Compliance with PHS Policy is mandated by VA policy, whether or not PHS funds are accepted by an individual VA facility.*

(a) All VA animal research must be covered by a PHS Assurance.

(b) Local VA medical centers may be covered by their affiliate's PHS Assurance in lieu of having their own PHS Assurance. The text in the affiliate's Assurance document must make it clear that the VA medical center animal research program is covered as part of the affiliate's Assurance.

(5) By law, all VA animal research must comply with the Animal Welfare Act (codified at 7 U.S.C. Sections 2131-2159), the USDA AWAR (Title 9 Code of Federal Regulations (CFR) Parts 1-4), and 42 CFR 73, Possession, Use, and Transfer of Select Agents and Toxins.

(6) All VA animal research involving infectious or recombinant agents must also comply with guidelines found in the latest editions of the Centers for Disease Control and Prevention (CDC)-National Institutes of Health (NIH) publication entitled "Biosafety in Biomedical and Microbiological Laboratories" and the NIH publication entitled "NIH Guidelines for Research Involving Recombinant DNA Molecules."

c. **VA Responsibility for Research Animals.** VHA ORD is responsible for establishing policy for laboratory animal use in the VA system. Local medical centers are responsible for ensuring proper oversight and care of all research animals housed on VA property, as well as research animals purchased with VA funds, no matter where they are housed.

d. **Authority to Suspend Individual Animal Research Protocols.** If significant animal or human health and welfare concerns are noted in information presented in an 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 ACORP are addressed to the CVMO's satisfaction.

5. CHIEF VETERINARY MEDICAL OFFICER (CVMO), VA CENTRAL OFFICE

a. **Qualifications.** See VA Handbook 5005, Staffing, Part II, Appendix F32.

b. **Primary Responsibilities.** Primary responsibilities include, but are not limited to:

(1) Advising CRADO, Deputy CRADO, and ORD Service Directors regarding animal welfare issues including: animal research facility operations, animal care and use issues, and the selection of veterinary medical personnel serving field facilities. **NOTE:** *The CVMO reports directly to the CRADO or designee.*

(2) Developing and implementing policies on a national level for improving laboratory animal medicine, and the care and use of laboratory animals in VA.

(3) Providing policy guidance to VA health care facilities on the role and function of animal research facilities.

(4) Acting as liaison with other government agencies and public and private institutions engaged in biomedical research involving animals.

(5) Participating as an expert in laboratory animal medicine with national and international scientific and professional organizations at conferences and meetings.

(6) Communicating with the media, special interest groups, and the general public concerning animal welfare issues and VA's commitment to quality animal care and research use programs.

(7) Monitoring compliance of VA medical centers with applicable Federal laws and guidelines pertaining to animal care and research use; and reporting and/or advising facilities to report, as required, incidents of non-compliance to internal and external oversight organizations.

(8) Providing guidance and assistance to VA medical centers in attaining and maintaining full accreditation by AAALAC.

(9) Interacting with research personnel to provide guidance and information about regulatory and policy matters that pertain to VA animal research.

(10) Coordinating the secondary veterinary medical review of protocols submitted for VA funding.

6. ORGANIZATION AT VA MEDICAL CENTERS

a. **Designation of Institutional Official (IO).** Each medical center Director must serve as the IO, which is the responsible official for correspondence related to animal research with AAALAC (the "Responsible Institutional Official," see item 1 in AAALAC Annual Report), USDA (the "Institutional Official" or "Chief Executive Officer," see Sec. 1.1), and the PHS (the "Institutional Official," see Sec. III. G) except in the following instances:

(1) If the medical center does not have its own approved PHS Assurance on file, but instead is covered by the affiliate institution's PHS Assurance, then an administrator at the affiliate institution must be appointed the IO for PHS correspondence concerning the animal care and research use program at both the medical center and the affiliated institution, in accordance with PHS Policy (see Sec. II and Sec. III G).

(2) If the medical center is accredited as a component of the affiliate's animal care and research use program, then an administrator at the affiliate institution must be appointed the IO for AAALAC correspondence to comply with AAALAC policy.

b. **Professional Staffing.** Veterinary medical services may be provided through appointment of a full- or part-time Veterinary Medical Officer (VMO), appointment of a qualified Veterinary Medical Consultant (VMC), or a combination of a qualified consultant and a clinical veterinarian. For the purposes of internal and external correspondence, the organizational title of a VMO is Chief, VMU. ***NOTE: Laboratory animal medicine is a recognized specialty within veterinary medicine that requires special training and experience.***

(1) **VMO and VMC Qualifications.** See VA Handbook 5005, Staffing, Part II, Appendix F32.

(2) **VMO Recruitment and Promotions.** The CRADO, or designee, must concur on: all new VMO and VMC appointments, regardless of the source of salary support; the recruiting of all laboratory animal veterinarians into government positions at the General Schedule (GS)-14 or GS-15 level; and promotions of laboratory animal veterinarians to the GS-14 or GS-15 level. A memo requesting concurrence on the appointment or promotion must be forwarded with the candidate's curriculum vitae to the CVMO, who makes a recommendation on the appointment or promotion to the CRADO.

(3) **Recruitment and Retention Incentives.** Of critical importance to a quality animal care and research use program is the participation of a qualified laboratory animal veterinarian. The National Research Council publication "National Needs and Priorities for Veterinarians in Biomedical Research," documents a continuing deficit of trained veterinarians entering the laboratory animal medicine specialty. Accordingly, to the extent allowed by VA policy, VA veterinarians need to be considered for recruitment, retention, and other types of incentive allowances to ensure the continued participation of qualified veterinarians in the VA system.

(4) **Supervisory Controls.** Locally, a VMO or VMC is supervised by the ACOS for R&D, the Chief of Staff (COS), or the medical center Director.

(5) **Duties.** Primary duties of VMOs and VMCs include, but are not limited to:

(a) Directing the operation of the animal research facility to ensure compliance with current animal welfare laws, regulations, and policies, and to support R&D programs using animal subjects.

(b) Providing professional guidance and technical support to the health care facility's investigators in planning, executing, and directing R&D activities using animals. This includes the establishment and execution of disease surveillance programs in the animal research facility.

(c) Ensuring adequate caretaker staffing and proper support of animal research projects at the facility. Once the annual proposed Veterinary Medical Unit (VMU) budget is prepared by research administrators with input from the VMO, the proposed budget should be submitted to the IACUC for comments, and then submitted to the R&D Committee for review and final approval.

(d) Initiating and/or reviewing requests for equipment used in the animal research facility

and plans for animal research facility construction and renovation.

(e) Serving as a member of the local IACUC.

(f) Performing mandatory veterinary consultations with investigators prior to the submission of their animal protocol forms to the IACUC.

(g) Participating in mandated semi-annual IACUC inspections of animal facilities and the animal care and research use program.

(h) Guiding the facility in preparations for AAALAC, international accreditation site visits, and compliance visits by regulatory agencies.

(i) Drafting or reviewing regulatory documents required for compliance with applicable regulations, guidelines, and policies. This includes AAALAC Program Descriptions, PHS Assurance documents, USDA Annual Reports (to be signed by the IO), and annual VA VMU reports.

(j) Serving as a source of guidance on animal research regulations, guidelines, and prevailing standards.

(k) Serving as a member of the Biosafety Committee as a liaison to the IACUC, if requested by the ACOS for R&D.

(l) Contributing to the promotion of favorable community and affiliate relations and increased public appreciation of the importance of animal studies in improving patient care.

(m) Participating in VA initiatives that contribute to improved animal research support of R&D programs throughout the VA health care system.

(n) Assisting the CVMO with special projects of system-wide importance.

(6) Use of a Clinical Veterinarian. If exceptional circumstances preclude the provision of adequate and timely veterinary medical care by a VMO or VMC, a local veterinarian without training and experience in laboratory animal medicine may be employed to provide clinical and other services commensurate with their training and skills. The clinical veterinarian in such cases functions within the written plan of veterinary medical care developed by the responsible VMO or VMC. Under such circumstances a clinical veterinarian supplements, but does not replace, services of the VMO or VMC.

(a) Visits by a clinical veterinarian do not reduce the minimum frequency of visits required for VMOs or VMCs.

(b) Duties of the clinical veterinarian may include emergency medical and surgical care of animals, diagnostic and therapeutic measures for sick or injured animals, and implementation of preventive medicine practices.

(c) Appointment of a clinical veterinarian must be approved in advance by CRADO, or designee. A letter requesting approval of a candidate must be forwarded with the candidate's curriculum vitae through the CVMO to the CRADO, or designee, for concurrence.

(7) **Continuing Education.** Training is mandated for all personnel who work with laboratory animals. This includes laboratory animal veterinarians. **NOTE:** *See USDA AWAR (9 C.F.R. §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.* Accordingly, it is critical that local funds be allocated for continuing education activities by veterinarians, preferably to fund travel to seminars or professional meetings that address topics of importance to animal research. **NOTE:** *It is an ethical and professional imperative that veterinarians continue to learn about advances in laboratory animal medicine and care to ensure the highest standards of care for animals, and the best possible support for animal research projects.*

(8) **VMC Contractual Agreements.** Contracts for veterinary medical consultants may be negotiated either with an organization or an individual, as long as the services are provided by a qualified VMC, or an individual supervised by a qualified VMC.

(a) When a VA medical center obtains veterinary medical services through a contract rather than employment of a VMO, arrangements must be made for regularly scheduled visits. The frequency of visits depends on the size and nature of research activity at a particular location, but under no circumstance will visits to a VA medical center with an ongoing program of animal research be less frequent than monthly. Supplemental visits, scheduled or unscheduled, must be arranged as required to ensure provision of adequate veterinary medical care.

(b) A written plan of providing adequate veterinary care to laboratory animals must be developed and approved by the VMC and ACOS for Research and Development (R&D). This plan must include the frequency of visits, provisions for after hours, weekend, and holiday veterinary coverage, and the VMC's role in VMU operations, as well as IACUC participation. A copy of this plan must be maintained locally, and be provided to the CVMO upon request.

(c) Visits by a VMC must be documented in writing.

c. **The VMU Supervisor.** Each facility with an active program of animal research must assign the responsibility of overseeing daily husbandry and other care duties to a single individual. The organizational title of this position is Supervisor, VMU.

(1) **Qualifications.** Through training and/or experience, the VMU supervisor must possess adequate knowledge and skills in laboratory animal science and technology, record keeping, and personnel management to direct the day-to-day operations of the VMU such that the food, water, and housing provided to all animals is appropriate.

(a) Although not a requirement, certification by the American Association for Laboratory Animal Science (AALAS) or Canadian Association for Laboratory Animal Science (CALAS) at any level is helpful in gaining needed knowledge and skills.

(b) Prior to appointment, it is strongly suggested that the supervisor have at least 1 year of experience working as a laboratory animal care technician, animal health technician, or veterinary technician with laboratory animals in a biomedical research setting.

(2) **Supervisory Controls.** The VMU Supervisor is supervised by the VMO when such a position exists. In the absence of a VMO, the VMU Supervisor is supervised by the VMC for issues related to animal care and use, but may be supervised by the Administrative Officer for Research (AO for R&D) for administrative issues not related to animal care and use.

(3) **Primary Duties.** The VMU Supervisor's responsibilities include, but are not limited to:

(a) Scheduling work assignments of the VMU staff and monitoring the quality and quantity of work performed.

(b) Providing orientation and training for employees, preferably with the goal of preparing the employees to take and pass AALAS certification examinations.

(c) Instructing and assisting research technicians and investigators in the performance of routine techniques for animal experimentation.

(d) Maintaining essential records (e.g., animal and equipment inventories, procurement records, etc.).

(e) Ensuring the maintenance of a sound program of animal husbandry.

(f) Ensuring the maintenance of a stable animal environment (temperature, lighting, and ventilation) and promptly reporting malfunctions to proper authorities.

(g) Noting and reporting abnormal behavior or illness in animal subjects to the designated veterinarian (VMO, VMC, or Clinical Veterinarian).

(h) Recording and reporting misuse of animals during experimentation or deviation from approved protocols to the VMO, VMC, clinical veterinarian, or other member of the IACUC.

(4) **Continuing Education.** Training is mandated for all personnel who work with laboratory animals, including laboratory animal veterinarians, the supervisor, and husbandry care staff. **NOTE:** See USDA AWAR (9 C.F.R. §2.32, *Personnel qualifications*), the U.S. *Government Principles for Training (Principle VIII)*, *PHS Policy (see Section IV.1.g.)*, and the *Guide*. Accordingly, it is critical that local funds be allocated for continuing education activities on an annual basis. **NOTE:** *It is an ethical and professional imperative that veterinarians continue to learn about advances in laboratory animal medicine and care to ensure the highest standards of care for animals, and the best possible support for animal research projects.*

d. **Contact with CVMO.** If a VMO, VMC, clinical veterinarian, IACUC Chairperson, IACUC member, or any other VA employee has not been able to solve local problems regarding the ethical treatment and use of animals by working through local chains of command, the employee may contact the CVMO directly to discuss concerns, solicit guidance, or seek

information without requesting or receiving local permission to do so. **NOTE:** *Consistent with USDA AWAR (9 C.F.R. §2.32) and Title 5 (Pt. III, Subpt. A, Ch. 23, Sec. 2302), actions may not be taken against an employee for the act of contacting the CVMO.*

7. VMU OPERATIONS AT THE VA MEDICAL CENTER

VMUs must be operated as administratively-centralized facilities and services directed by a VMO or jointly by a VMC and a VMU supervisor. **NOTE:** *Under no circumstances may authority or responsibility for animal research conducted on VA property be ceded to non-VA entities, unless approved by CRADO.*

a. Equipment and Physical Plant

(1) **Request for VA Central Office or ORD Equipment Funds.** Funding for common use equipment needed in the animal research facility may be requested subject to the availability of funds and demonstrated need.

(2) **Animal Research Facility Heating, Ventilation, and Air Conditioning (HVAC) Equipment and Testing**

(a) All HVAC reheat boxes serving one or more rooms housing animals must be designed so that they fail in the “off” or “safe” position, to prevent the loss of animals due to excessive temperature. Laboratory animals can not be housed at any VA facility in rooms that are not so equipped.

(b) If an air handler serving one or more animal rooms contains a preheat coil or other equipment that could deliver excessive heat to animal rooms, engineering staff must determine if the equipment represents a potential threat to animals in case of a malfunction, and record findings in writing for IACUC review.

1. If such a threat is identified, preventative action such as installation of a preheat coil-fan interlock must be undertaken with due consideration of preventing damage to cooling coils or other air handler equipment.

2. Catastrophic air handler failures occur despite the presence of high-temperature alarms in animal rooms; thus the ability of facility personnel to detect high temperatures in animal rooms does not eliminate the need to comply with subparagraph 7a (2)(b).

(c) To test the ability of facilities management personnel to properly detect and respond to elevations in animal room temperatures, at least once every fiscal year research personnel must purposely overheat a temperature sensor (e.g., with a hair dryer, with input from facilities management personnel) in at least one animal room in each animal research facility without notifying engineering or facilities management personnel in advance. The response must be carefully noted, and reported to the IACUC by VMU staff at the next convened IACUC meeting.

1. The IACUC must decide if the response to the excessive temperature was timely and adequate. If the response is not deemed timely or adequate, corrective action must be taken

immediately by the medical center to ensure a proper emergency response.

2. Unannounced repeat tests must be conducted monthly until the IACUC approves the adequacy of the response. The IACUC minutes must reflect all reviews of testing. **NOTE:** *Repeated deficiencies may be considered reportable, as described in subparagraph 8g.*

(3) **Disaster Planning.** As required by the Guide, a disaster plan needs to be developed in order to protect the animals during a power loss. The plan needs to be in writing and approved by the IACUC. It is a “Best Practice” to connect the animal facility HVAC system to emergency power; however, alternate approaches to ensuring adequate temperature control after a power loss can be employed effectively. For instance, supplemental portable cooling and heating equipment can be available at the medical center, or from vendors on short notice.

(4) **Animal Facility Construction and Renovation.** To help ensure that costly mistakes are not made in the construction of new animal facility space, in the renovation of existing animal facility space, or in the renovation of non-animal facility space to animal facility space, the CVMO must approve the design plans for all animal facility construction or renovations costing more than \$100,000 (equipment purchases count toward the \$100,000 cut off). **NOTE:** *Construction and renovation activities must be conducted pursuant to existing VA policy when applicable (e.g. VHA Directive 1800.1, “Major Construction and Real Property Project Document Approval Level Procedures”).*

b. **Animal Care, Husbandry, and Animal Research Practices.** All animal care, husbandry, and animal research practices at VA animal facilities must be in accordance with applicable laws, regulations, and policy. **Regarding animal procurement:**

(1) Any laboratory animal used in a VA research facility must be acquired in accordance with Federal laws, regulations, and policy. For procurement opportunities for aged and other special groups of animals see Appendix B.

(2) No request for animal procurement may be approved or initiated until the veterinarian or VMU Supervisor determines that the source of animals is appropriate, that adequate and appropriate housing is available upon arrival, and that the animals are going to be used in a protocol approved by the IACUC. Upon arrival, the delivered animals must be subtracted from the animal use ceiling approved by the IACUC.

(3) Delivery of live animals must be made directly to the animal research facility, unless special arrangements have been made between the VMU staff and receiving staff. To avoid delay, whenever possible, the procurement document should show the specific location in the animal research facility where delivery is to be made. Appropriately skilled personnel must be designated in order to represent the contracting officer at the time of delivery, in receiving and inspecting live animals.

(4) These procurement activities must be conducted pursuant to existing VA policy (e.g. VA Directive and Handbook 7126.2, “Procurement Sources and Programs”) as is applicable.

c. **Standard Operating Procedures (SOPs).** The VMU Supervisor, with guidance and assistance from the VMO or VMC, must develop a manual of SOPs setting forth schedules and methods of cleaning animal housing and research areas, feeding and watering practices, staff training, equipment maintenance and related activities. At a minimum, the SOP manual must be reviewed annually by the VMU supervisor and the VMO, or VMC, to determine the need for any changes in procedures. ***NOTE: This SOP manual should be reviewed and approved by the IACUC at least annually.***

d. **Animal Health**

(1) Because the availability of healthy animals is a prerequisite for the modern use of animals in research, teaching, and testing, all research animals need to be as free as possible of infectious agents capable of adversely affecting:

(a) Experimental studies, or

(b) The ability of VA investigators to exchange animals with colleagues at other institutions as part of collaborative investigations.

(2) In general, if a practical means of diagnosing and eradicating an infection in an animal exists, steps need to be taken to do so, and the animal needs to be kept free from further infection.

e. **Accreditation.** All VA animal facilities and affiliates, or other animal facilities that house animals purchased with VA funds, or used for VA or VA research and education corporation projects must be accredited by AAALAC. Under exceptional circumstances, a waiver may be requested in writing from CRADO, or designee, through the CVMO's office. ***NOTE: To facilitate the accreditation of VA facilities, VA Central Office funds a contract with AAALAC for the accreditation of all facilities with VA animal research programs.***

NOTE: For clarification, an NIH-funded project for which the academic affiliate is the recipient of the grant, the research is conducted at the university, and the investigator conducts the research on non-VA time would not be affected by this requirement.

f. **Veterinary Care.** Adequate veterinary medical care must be provided for all animals maintained for research, testing, training, or educational purposes. The program of veterinary medical care must be planned and monitored by a laboratory animal veterinarian qualified by training and experience for this responsibility. The program must include:

(1) Frequent observation of animals by a person qualified to verify the health of each animal.

(2) Provision of veterinary medical care for animals found to be ill or injured.

(3) Application of currently accepted measures of prophylaxis and therapy.

(4) Consideration for humane aspects of animal experimentation such as the proper use of anesthetics, analgesics, and tranquilizers and the implementation of such measures as directed by the responsible veterinarian to alleviate unacceptable levels of pain or distress to animal subjects.

g. **Euthanasia.** Euthanasia of animal subjects must be performed in a manner that minimizes stress and discomfort to animals, and avoids undue psychological distress to persons performing this task. Methods of euthanasia must follow the recommendations present in the Report of the AVMA Panel on Euthanasia (see subpar. 11g, or most recent). Any exception to these recommendations must be project-specific, based on scientific necessity, and require advance approval of the IACUC.

h. **Adoption of Research Animals as Pets.** Unless a waiver is requested in writing and approved by the CVMO, research animals may be adopted as pets only if all of the following circumstances are true:

(1) The animal is found to be healthy after a complete physical examination by a veterinarian, a complete CBC and serum chemistry panel reveals no significant abnormalities, and a thorough exam for external and internal (fecal) parasites is negative.

(2) The animal does not exhibit aggressive or antisocial behavior that could represent a threat to children or adults.

(3) The animal has no implanted external or internal devices.

(4) The animal has no chronic health problems arising from natural causes or experimental manipulations.

(5) The animal has been or will be (as a condition of adoption) neutered or spayed. **NOTE:** *All exceptions must be approved by the CVMO.*

(6) The IACUC and R&D Committee have approved the adoption.

i. **Operating Costs Recovery.** Investigators using animals must be charged a pro-rated share of total animal care costs. An annual review of rates by the veterinarian and research administrators is recommended so that revisions can be made to maintain the financial health of the VMU, unless local subsidies are provided. Charges for animal care must be based on projected operating costs, plus caging and equipment replacement and other reserves, less the amount received in cost center 105 funding. Ordinarily projections of animal care costs are best made from records of previous year expenditures with inclusion of an inflation factor, such as an increase in the consumer price index. **NOTE:** *The NIH Manual on Cost Analysis and Rate Setting for Animal Research Facilities, is a good source of information when calculating per diem charges.*

(1) The IACUC, with the assistance of the veterinarian, is charged with recommending changes in per diem rates to the R&D Committee. The R&D Committee must approve the rates before they are finally adopted.

(2) The IACUC and/or research administrators must notify the R&D Committee when investigators become more than 3 months delinquent in per diem payments. **NOTE:** *Such information may be relevant to R&D Committee reviews of research projects, and discussions regarding budgetary issues in the research service.*

j. **Security.** Measures must be implemented to exclude the entry of unauthorized personnel into the animal research facility. Special attention to physical security is warranted by the threat of property destruction and theft by groups opposed to use of animals in research. Use of a computer-based system for tracking individual user entry through perimeter doors is highly recommended. Typically such systems rely on electric strike or magnetic locks opened by coded cards issued to each individual user. Propping of doors in the open position is to be strongly discouraged as it is considered a security lapse. Security cameras in the animal research facility monitored by facility security personnel are recommended when unusual security risks are present. **NOTE:** *VA Handbook 0730, Security and Law Enforcement, Appendix B, Physical Security and Options, contains additional security requirements for animal facilities.*

(1) Requests for tours of the animal research facility by members of the media and persons claiming to represent animal rights and animal welfare organizations need to be handled with discretion, and permitted only with the approval of the medical center Director.

(2) Inquiries regarding lost pets need to be handled with caution and sensitivity. Permission to search an animal research facility for a lost pet should be granted only after obtaining a detailed description of the missing pet including sex, color, markings, breed, approximate weight and age, and date last seen by the owner; and determining with reasonable certainty that the request is legitimate.

k. **Use of Explosive Agents in Animal Facilities.** Newer anesthetic agents have essentially eliminated the necessity of using explosive agents such as ether for anesthesia on any species. In general, the use of any explosive substance in an animal research facility is strongly discouraged due to the risk of injury and death to people and animals.

(1) Use of any explosive agent in the animal research facility is prohibited unless the IACUC and the Subcommittee on Research Safety (SRS) first grant local approval. Only under exceptional circumstances, when non-explosive alternatives cannot be used for scientific reasons, should the IACUC allow use of explosive agents in the animal research facility.

(2) The IACUC and SRS must ensure that all reasonable precautions to prevent explosions are planned before giving approval. Examples of such precautions include the following:

- (a) Procedures must be performed within a properly operating, ventilated safety hood.
- (b) All electrical equipment used with such agents must be located and powered outside the hood.
- (c) Containers of ether or other explosive agents must be placed in a safety hood throughout use and stored in an explosion proof refrigerator, or if completely used, discarded following use.

(d) Containers of an explosive agent and items containing traces of the agent must not be disposed of by incineration or by placement in waste receptacles in which contents are ordinarily incinerated.

(e) Care must be taken to ensure that all potentially explosive fumes have dissipated from animal carcasses and other objects before placement in storage. Explosion-proof refrigerators or freezers need to be utilized for such storage.

l. **Use of Patient Care Areas and Equipment for Animal Studies.** Patient diagnostic, treatment, and monitoring areas, and patient care equipment may be used for animal studies only when such use is of potential future value to human patients.

(1) Use of any patient care area for animal research is prohibited unless the IACUC and appropriate local clinical and administrative officials first grant approval. **NOTE:** *As part of the approval process, the IACUC must review and approve a completed ACORP Section 8, Request To Use Patient Care Procedural Areas for Animal Studies.* Only when reasonable alternative arrangements cannot be made should the IACUC allow use of human clinical areas or human equipment for animal research.

(2) Use of patient care equipment destined to return to patient care areas from the animal research facility must be approved by the IACUC and service chief responsible for this equipment. As part of the approval process, an SOP for properly cleaning and disinfecting the equipment prior to resumption of human patient use must be submitted and approved by the IACUC and the VMO or VMC.

NOTE: *ACORP Section 8 is not required if human clinical diagnostic equipment will be used in the animal facility or an animal procedure area, rather than in human clinical areas. In such circumstances, special emphasis must be placed on ensuring that the equipment is clean and free of animal body fluids, waste, or external parasites such as fleas, after use.*

m. **Use of Animal Research Facility for Studies Involving Human Cadavers or Human Tissues**

(1) Use of animal research facility rooms for studies involving human cadavers or human tissues can be considered disrespectful, and should not be permitted unless appropriate study facilities outside of the animal research facility are not available.

(2) Such studies must be approved by the local IACUC and the local Subcommittee on Research Safety (SRS) before they begin, with due consideration for maintaining institutional respect for the human cadaver or tissue at all times.

n. **Use of Controlled Substances.** As is true of all research areas in the medical center, the order, receipt, disbursement, and disposal of controlled substances of all classes is dictated by VA policy (see VHA Handbook 1108.1, VHA Handbook 1108.2, and M-2 Part VII).

(1) All controlled substances must be ordered by the local VA pharmacy, and also received by the pharmacy for disbursement to research personnel.

(2) Controlled substances may not be purchased by research personnel directly from a vendor or received directly from a vendor, and controlled substances not purchased and received by the VA pharmacy are not permitted on VA property.

8. INSTITUTIONAL ANIMAL CARE AND USE COMMITTEES

According to the USDA AWAR (9 C.F.R. §2.37) and PHS policy, each VA medical center with a program of research involving use of live vertebrate animals must establish an IACUC. The medical center Director is responsible for providing adequate administrative support for IACUC and personnel to support the review and record-keeping functions of the IACUC (to include timely preparation of minutes and timely preparation of investigator correspondence and other documents).

a. **Membership, Composition, and Terms of Service.** IACUC members in consultation with the R&D Committee must forward the name(s) of nominees for the IACUC to the medical center Director. The medical center Director must officially appoint members in writing, to include specifying the length of the appointments (see subpar. 8a (6), this handbook).

(1) **Composition.** The composition of the IACUC must meet existing requirements set forth in the Animal Welfare Act (see 7 U.S.C. §2143[b][1]) and PHS Policy (see subpar. IV.3b). At this time, a minimum of five members are required to serve as voting members to constitute an IACUC. Only a properly constituted IACUC may conduct official business. The required voting members include a Chairperson, the Attending Veterinarian, one scientist with animal research experience, a non-affiliated member (must meet the criteria in subpar. 8a[3], this handbook), and a lay member (who must not be involved in animal research). ***NOTE:** Changes in PHS policy or USDA AWAR that alter IACUC membership requirements will supersede the membership requirements in this paragraph.*

(2) **Chairperson.** The IACUC chairperson can not simultaneously chair another subcommittee. The Chairperson needs to be a more senior scientist with animal research experience and good committee management skills.

(3) **Non-Affiliated Members.** To comply with the USDA AWAR, each IACUC must include at least one member who is not otherwise affiliated with the VA medical center, and who is not part of the immediate family of a person who is affiliated with the medical center. The person chosen should provide representation for general community interests in the proper care and treatment of animals.

(a) A veteran who volunteers at the medical center is considered to have an affiliation with the institution and is disqualified from serving as the non-affiliated IACUC member; however, appointment of such veterans to the IACUC in another capacity, such as lay member is strongly encouraged.

(b) Veterans who do not use a VA medical center for medical care may serve as the non-affiliated member on that medical center's IACUC, as long as they have no other affiliation with the medical center and are not in the immediate family of a medical center employee.

(c) 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.

(d) Non-affiliated and lay members of the IACUC may be compensated for travel expenses and time, as long as such reimbursement can not be construed as compromising their ability to fulfill their independent respective roles on the IACUC.

(4) At least one member of the IACUC needs to be a member of the R&D Committee.

(5) **Subcommittee on Research Safety.** The VMO, VMC, or a member of the IACUC needs to be a member of the Subcommittee on Research Safety, unless exceptional circumstances prevent such participation.

(6) **Length of Terms**

(a) Chairperson. The IACUC Chairperson must be appointed by the medical center Director annually, without a lapse in service. There is no limit to how many times a chairperson may be reappointed, but it is Best Practice to rotate the Chairperson position to develop a cadre of research staff with experience in filling that role.

(b) Membership. Members other than those who are designated ex officio (appointed on the basis of their position, such as the institutional veterinarian) may serve terms of up to 3 years, on staggered appointments. Members may be re-appointed without lapse in service to the IACUC.

b. **VA-Affiliate IACUC Interactions**

(1) **Use of an Affiliate's IACUC as the VA IACUC.** An affiliated institution's IACUC may be used as the official VA IACUC subject to the provisions below:

(a) The affiliate's IACUC must agree to provide copies of IACUC minutes, semi-annual IACUC reports, AAALAC correspondence, USDA correspondence, copies of IACUC files on VA investigators, and other regulatory documents to the local station or VA Central Office if required to respond to queries by regulatory authorities. Documents must be provided in their entirety, or the affiliate must agree to allow review of un-redacted documents by VA personnel during normal business hours.

(b) The VMO, or VMC, and at least one other VA scientist with animal research experience must sit on the affiliate's IACUC as voting members with full committee privileges. A VA Clinical Veterinarian may sit on the IACUC as well, but the Clinical Veterinarian's presence cannot substitute for the VMO or VMC.

(c) The affiliate's IACUC must agree to review the VA animal research facility and program as part of its own facility and program review.

(d) The affiliate's IACUC must agree to review the VA ACORP during committee meetings for those VA investigators submitting VA applications to ORD.

(e) If the provisions in subparagraphs 8b(1)(a)- 8b(1)(e) cannot be met, either an independent VA IACUC at the medical center must be formed, or arrangements to use another IACUC must be made. If the option to use another IACUC is chosen, the details of the arrangement must be described in written correspondence forwarded to the CVMO. **NOTE:** *Use of a commercial IACUC is prohibited.*

(f) If the affiliate's IACUC is used as the VA IACUC, the VA medical center Director must officially appoint all members in writing.

(2) **Separate VA and Affiliate IACUCs.** If a VA medical center has its own VA IACUC distinct from the affiliate's IACUC, but the VA medical center animal care and research use program is covered under the affiliate's PHS Assurance for conducting animal research, the affiliate's designated PHS IO and the medical center Director must both appoint members of the VA IACUC in writing.

(a) When a VA investigator uses PHS funds administered by the affiliate institution for animal research, the VA IACUC may not supersede any adverse action taken by the affiliate IACUC against such a project. Also, the VA IACUC may not allow work on such a project to continue once approval by the affiliate IACUC lapses unless a formal agreement between the VA and affiliate (approved by OLAW) allows the VA IACUC to do so.

(b) Likewise, when a VA investigator uses PHS funds administered by a VA entity or a VA research and education corporation for animal research, the affiliate IACUC may not supersede any adverse action taken by the VA IACUC against such a project. Also, the affiliate IACUC may not allow work on such a project to continue once approval by the VA IACUC lapses unless a formal agreement between the VA and affiliate (approved by OLAW) allows the affiliate IACUC to do so.

(3) If a medical center maintains an IACUC separate from the affiliate IACUC and an agreement for partial or full-protocol reciprocity is in place, records must be kept at VA for protocols reviewed under such agreements to comply with NIH Notice NOT-OD-01-017 dated February 12, 2001 (see section entitled "No Requirement For Duplicate Review").

c. **Avoiding Conflicts of Interest in IACUC Reviews.** As a public agency, VA has an obligation to preserve public trust in the integrity and quality of research carried out by its investigators, among its patients, and in its facilities, and to exercise prudent stewardship of public resources, including public funds that support research programs. Appropriate mechanisms must be in place to ensure that actual or perceived financial conflicts of interest do not undermine that trust. With regard to conflicts of interest, all VA employees must comply with the criminal statute pertaining to acts affecting personal or imputed financial interest (18 U.S.C. Section 208) and the Standards of Ethical Conduct for Employees of the Executive Branch (5 CFR Part 2635). VA Regional Counsels are authorized to interpret these provisions. **NOTE:** *Additional policy guidance for the IACUC is provided in VHA Handbook 1200.13, "Financial Conflicts of Interest in Research."*

(1) The ACOS for R&D and Administrative Officer (AO) for R&D (or equivalents) should

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

(2) 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. **NOTE:** *The USDA Animal and Plant Health Inspection Service (APHIS) is the unit responsible for administering and enforcing the Animal Welfare Act Regulations and Standards. APHIS Animal Care Policy Manual, Policy 15, makes it clear that no IACUC member can review the IACUC member's own proposal. 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.*

(3) IACUC members should not participate in the IACUC review or approval of a research project in which the member has a financial conflict, except to provide information requested by the IACUC prior to the deliberations. **NOTE:** *A web course (located at: <http://www.researchtraining.org>) on avoiding financial conflict of interest in research settings has been prepared by the VA Office of General Counsel to help VA research staff avoid financial conflicts of interest.*

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

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

(a) The semi-annual self-assessment 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. If a formal arrangement has been made between the VA IACUC and a satellite or affiliate's facility, the VA IACUC may review that facility's semi-annual self-assessment review as an IACUC business item in lieu of sending a VA IACUC review team to the facility. If the VA IACUC does not set up such an agreement, the other facility and its animal care and research use program must be evaluated (by the VA IACUC), and a report of that facility's evaluation included as part of the semi-annual self-assessment review. In either case, all deficiencies affecting animals purchased with VA funds must be noted and corrections

tracked to ensure optimal care for the animals. **NOTE:** *Medical centers are strongly encouraged to describe in their PHS Assurance which approach will be taken.*

(b) As part of the Program review, the IACUC must randomly review IACUC records representing at least 5 percent of the total active projects (a minimum of five). The purpose of the review is to determine if appropriate documentation of initial review, approval letter(s), annual and triennial approvals, modifications, and investigator correspondence are present.

(c) Non-VA institutions that house animals purchased with non-VA funds on VA property must be given the opportunity to conduct their own IACUC semi-annual facility and program review, in the absence of a reciprocal agreement as described in preceding subparagraph 8d(1)(a).

(d) The compliance items found in the VA IACUC Program and Facility Self-Assessment Checklist (see App. E) must be covered by the IACUC. The items in Appendix E, the OLAW Semiannual Program and Facility Review checklist, or a similar checklist incorporating all the elements found in Appendix E need to be completed within a month of the self-review. Whichever checklist is used, the following must appear in the report:

1. The name, address, and facility number, with 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 must distinguish significant deficiencies from minor deficiencies.

a. 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:

(1) Animal research facility heating and cooling equipment that cannot maintain consistent temperatures in the ranges specified in the most current Guide.

(2) An inadequate program for the surgical care of animals.

(3) An inadequate program for the medical care of animals.

(4) Conduct of research not approved by the IACUC.

(5) Inadequate caretaker staffing.

(6) Inadequate IACUC administrative support such that the IACUC cannot fulfill its regulatory mandates.

b. A minor deficiency is one that does not fit the preceding definition of a significant deficiency. Examples of minor deficiencies are difficult to provide because local circumstances strongly influence whether a deficiency is considered significant or minor. **NOTE:** *For help*

with such decisions, contact the CVMO, who may recommend further consultations with OLAW or USDA.

4. The report must state any minority views.

5. A list of IACUC members present during the semi-annual self-assessment review with the name, the degree(s) held, and the IACUC role (veterinarian, scientist with animal research experience, lay member, non-affiliated member) of each member. At least three IACUC members (including the veterinarian) need to conduct the program and facilities review, unless exceptional circumstances prevent such attendance. All members of the IACUC are strongly encouraged to participate in the semi-annual self-assessment review; however, the review team must include at least two voting members of the IACUC. **NOTE:** *Attendance by the lay and non-affiliated members is especially encouraged.*

(e) A majority (of all voting IACUC members) must vote to approve the report; each member must indicate approval by signatures next to the typed name and committee role. Then the report must be discussed with the medical center Director by the IACUC Chairperson, veterinarian, and one or more research administrators (other IACUC members may also attend as dictated by local IACUC policy). The medical center Director then must sign the report indicating that the report has been reviewed. Once the medical center Director has signed the report, it must be sent to the CVMO through the medical center Director within 60 days of the self-review date. **NOTE:** *A copy needs to 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.*

(f) Under no circumstances may an IACUC semi-annual report be altered by any local official once a majority of voting IACUC members has voted to approve the report.

(g) Under no circumstances may local officials pressure IACUC members to change the wording of such reports to language more favorable to the institution. Local officials may comment or indicate their non-concurrence with information in the report in a cover letter.

(h) The report must be retained on file for at least 3 years by the research office.

(2) **Research Proposal Review.** The IACUC must review and approve, require modifications in (to secure approval), or withhold approval of all research proposals involving species and activities included within the definition of an “animal” (see subpar. 3c). All research projects involving animals must be approved by the IACUC and then by the R&D Committee prior to commencement. The date of continuing review is based on the date of IACUC approval. The IACUC must review proposed research at convened meetings at which a quorum (a majority of voting members) is present. In order for the research to be approved, it must receive the approval of a majority of those voting members present at the meeting. A quorum must be maintained for each vote to occur. If a quorum is not maintained, the proposal must be tabled although suggestions for review may be recorded and communicated to benefit the investigator.

(a) Evaluations. **NOTE:** *Evaluations of the animal protocol forms are based on standards promulgated by the USDA AWAR (see 9 C.F.R. §2.31(d), PHS Policy (see Sec. IV. C), the Guide (see “Monitoring the Care and Use of Animals”), VA policy, and other Federal regulations or*

guidelines that impact the conduct of IACUC business. The IACUC needs to consider the following topics in the preparation and review of animal care and use protocols (see App. D):

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

(b) If procedures are proposed that may cause more than momentary or slight pain or distress to the animals, it is mandated that an investigator consult the VMO, VMC, or designee, during the planning stages of a project (see the USDA AWAR; see 9 C.F.R. §2.31[d][iv][B]). Because it is often difficult for an investigator to predict which procedures might cause more than momentary pain or distress without consulting a laboratory animal veterinarian, the provision for a consultation in the USDA Animal Welfare Act Regulations and Standards is amended in this Handbook to extend to all projects with the requirement that the VMO, VMC, or another qualified laboratory animal veterinarian conduct the consultation. This consultation needs to be performed prior to IACUC review of a protocol. The veterinary consult may take the form of a face-to-face meeting, or a written review of a draft form by the VMO or VMC. No protocol may be given final approval until a veterinary consult by the VMO or VMC has been performed.

NOTE: *The review of a protocol by the VMO or VMC during an IACUC meeting does not satisfy this requirement.*

(c) The use of the designated review system may be used. VA policy stipulates that all IACUC members receive complete copies of all protocol forms to aid them in deciding whether

or not to request full committee review. **NOTE:** *See the USDA AWAR (9 C.F.R. §2.32[c][2]) and PHS Policy (see Sec. IV.C.2).*

(d) The research office must provide packets to IACUC members no later than 3 business days before the IACUC meeting. This packet must include an agenda with all business items listed, including reviewer assignments for all new protocols.

1. All IACUC members must have copies of all protocol forms.

2. Each new protocol must be assigned to at least two voting committee members. These members serve as the primary and secondary reviewers, and are expected to lead a discussion of the protocol. **NOTE:** *Experience has shown that the most effective reviews occur when the actual application, as well as the animal protocol form, is available for review by committee members.*

(e) Responses to all ACORP review items found in Appendix D must be provided in the given sequence when applications selected for ORD funding include an ACORP. Affiliate animal protocol forms may be used in all other cases, as long as the forms meet all Federal regulations and guidelines for IACUC review.

(f) Guidance for Completing Merit Award Forms. When appropriate, the “yes” checkbox for animal use on VA Form 10-1312-1 (Merit Review Application) needs to be checked, and an ACORP must be submitted for just-in-time review upon request if any of the following apply:

1. Animals are requested in the application budget for use in proposed experiments, whether housed on or off-site.

2. 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.

3. 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.

(g) Additional Guidance for Completing Merit Award Forms. The “no” checkbox for animal use on VA Form 10-1312-1, should be checked if animal use is limited to one or all of the following circumstances:

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. Although an ACORP is not required for submission, local IACUC approval for such use is required.

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 euthanatized animals, and those animals would be euthanatized 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 (see USDA-APHIS Policy Manual, Policy #10).

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 (see question 2, "Frequently Asked Questions about the Public Health Service Policy on Humane Care and Use of Laboratory Animals", Laboratory Animal 24 (9):24-26, 1995).

(h) Use of Parliamentary Procedures During IACUC Meetings. Consistent parliamentary procedures must be used to conduct 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. 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.

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

e. Annual Review of Proposals. The IACUC must review the conduct of all animal protocols annually.

(1) **First and Second Annual Review of Protocols**. The IACUC must review the conduct of all animal protocols annually. At the first and second anniversaries, the IACUC may review a standard form giving current basic information, such as IACUC approval number, IACUC approval date, title of project, and species used. The investigator then notes that either no changes have taken place, or describes any changes that have occurred. Responses are reviewed by the IACUC, or an IACUC-designee, for assessment of the changes reported. Any changes to the approved activity which are deemed of sufficient magnitude to merit further consideration may then be presented to the IACUC. **NOTE:** *All of these dispositions need to be documented as official IACUC actions.*

(2) **Third Annual Review.** Prior to the third anniversary, the IACUC must conduct a complete re-review of the protocol. This may be accomplished by asking the investigator to submit a new protocol utilizing the latest version of the protocol forms, or by re-reviewing a revision of the old form. If an old form is re-reviewed, any and all considerations added to the review items in Appendix D must be addressed, as must any changes in review resulting from changes in Federal regulations or guidelines. Because re-review of old protocol items according to new standards can be very challenging, it is a best practice to require that the protocol be reviewed by soliciting responses to each of the review items found in the most recent version of Appendix D, or that the most recent version of the affiliate's form be used for each triennial review, as is appropriate.

(3) The funding period of a project has no bearing on the need for annual reviews and triennial reviews.

f. **Recording and Reporting Requirements**

(1) **Preparation of IACUC Minutes.** IACUC minutes must be written and published within 3 weeks of the meeting date. VA medical centers with their own IACUCs must format their minutes to comply with following subparagraphs 8f(1)(a) through 8f(1)(j). For VA projects under consideration, the minutes of joint or affiliate IACUCs need to contain the same information somewhere in the document.

(a) At the top of the first page, on separate lines in a large typeface, place the bolded name of the facility and facility number, the official address, the official committee name, and the date of the meeting. Abbreviations are not acceptable. Subsequent pages are to be numbered.

(b) List all voting members present and absent (non-voting members may be listed separately). For each voting member, note the voting member's appointed role on the committee to establish that the IACUC is properly constituted (see subpar. 8a (1) for required voting members). Use the term "ex-officio" only when the member's office or legal role (such as the institutional veterinarian) dictates a member's presence on the committee.

(c) Indicate if a quorum is present. A quorum is defined as a majority (more than 50 percent) of voting members.

(d) Arrange the minutes into at least three sections: review of previous minutes, old business, and new business. At each meeting, a review of semi-annual review schedules for correction needs to be conducted to monitor progress toward completing corrections of deficiencies previously identified.

(e) Business items need to be retained under old business in subsequent minutes until either 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.

(f) For each project under consideration, list the first and last name of the principal investigator, and the complete name of the project.

(g) For each new project, the motion passed by the committee (approved, approved pending clarification, deferred, disapproved) must be recorded with the exact vote, which must include the number voting for the motion, the number voting against, and the number abstaining.

(h) Committee deliberations on each project must be reflected in the minutes so that an outside observer can understand the issues discussed, and recognize the specific revisions and clarifications requested for each protocol under consideration. Experience has shown that if IACUC members are asked to provide written or electronic copies of their reviews, their comments can be used to document deliberations and greatly streamline the process of writing the minutes as well as communicating IACUC decisions in writing to investigators.

(i) The minutes must note which members recused themselves for which project(s) to prevent conflicts of interest.

(j) 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.

(2) Once IACUC minutes are approved at the following meeting, the IACUC Chairperson needs to sign and date them at the bottom. No local official may alter the IACUC minutes once signed by the IACUC Chairperson, and no local official may exert pressure on any IACUC member to change the wording in the minutes to language more favorable to the institution. If requested by the CVMO or other VA Central Office official, complete copies of the signed minutes need to be sent through the ACOS for R&D and the medical center Director. The R&D Committee needs to review a copy of the signed minutes as an item of business, but R&D Committee approval is not necessary prior to sending minutes to ORD for review, i.e., if ORD requests a copy for review.

g. **Mandated Reporting of Deficiencies.** As a condition of extending the privilege of conducting animal research to individual medical centers, VA Central Office expects that the IACUC and institutional administrators will avoid any appearance of hiding or suppressing deficiencies. *NOTE: This goal is best achieved by prompt reporting of deficiencies before others outside of the program do so. Consistent with NIH Notice NOT-OD-05-034 dated 2/24/05, "Guidance on Prompt Reporting to OLAW under the PHS Policy on Humane Care and Use of Laboratory Animals," facilities should notify appropriate agencies by phone immediately that a full, written account of a reportable deficiency is forthcoming.*

(1) The main categories of deficiencies that must be reported to outside authorities and the elements needed in the report are as follows:

(a) Any serious or continuing non-compliance with 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. The report needs to include:

1. When and how the IACUC became aware of the problem.
2. When the investigation was performed to determine facts and detail the circumstances that led to the non-compliance.
3. The results of that investigation, and
4. What corrective actions the IACUC approved to stop the noncompliant activity and prevent future recurrences.

(b) Suspensions of protocols previously approved or suspensions of procedures or studies never given approval (see subpar. 8h). The report needs to include:

1. When and how the IACUC became aware of the problem.
2. When the investigation was performed to determine facts and detail circumstances that lead to the non-compliance,.
3. The results of that investigation.
4. When the IACUC convened a quorum to suspend the activity.
5. What corrective actions the IACUC approved to prevent recurrences.

(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.

(2) The report needs to include:

- (a) The date when the IACUC identified the deficiency.
- (b) The timetable and plan approved for correction.
- (c) Why the correction(s) could not be completed according to the timetable,.
- (d) The revised timetable.
- (e) The plan to finish the correction(s).

(3) The USDA AWAR (see 9 C.F.R. §2.31[c][3]) states that the failure to correct a significant deficiency must be reported in writing within 15-business days of the self-imposed deadline by the IACUC, through the Institutional Official, to USDA and any Federal agency funding that activity. This required 15-business day reporting period is extended to cover all categories of reportable deficiencies. **NOTE:** *Consistent with NIH Notice NOT-OD-05-034 dated 2/24/05, "Guidance on Prompt Reporting to OLAW under the PHS Policy on Humane Care and Use of Laboratory Animals," facilities should notify appropriate agencies by phone immediately that a full, written account of a reportable deficiency is forthcoming.*

(4) Although an ORD veterinary hold (see subpar. 4d) is not considered an IACUC suspension, it must be reported to other Federal agencies if the IACUC and IO find that information in the ACORP represents a reportable deficiency as defined in subparagraph 8g(1).

(5) Deficiencies meeting any of the criteria in subparagraph 8g(1) must be reported in writing within 15 business days through the ACOS for R&D and the medical center Director to the following agencies and offices:

(a) ORD (by contacting the CVMO's office).

(b) OLAW, as required by PHS Policy.

(c) 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.

(d) AAALAC, as required by AAALAC rules of accreditation.

(e) 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.

(f) The VA ORO, as required by ORO policy.

(g) Any Federal agency (other than the VA) funding an activity that has been suspended.

h. **Suspension of Projects.** The IACUC may suspend an activity that it previously approved if it determines that the activity is not being conducted in accordance with the description of that activity provided by the Principal Investigator (PI) and approved by the IACUC. It may also suspend any animal procedures not approved by the IACUC. 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.

i. **Investigation of Allegations of Improper Animal Care or Use.** All internal and external allegations of improper animal care and use at a medical center must be reviewed promptly by the IACUC, and investigated if warranted. A written report of the review or investigation needs to be approved by a majority of a convened IACUC quorum and sent to the medical center Director through the ACOS for R&D.

(1) If preliminary findings suggest that an allegation does indeed represent a reportable deficiency as defined in subparagraph 8g, the agencies and/or groups listed in subparagraph 8g(5) must be contacted as indicated in paragraph 8g(4).

(2) **Contact with CVMO.** If local efforts to correct deficiencies have proven inadequate, individuals may contact the CVMO directly to discuss concerns, solicit guidance, or seek information without requesting or receiving local permission to do so (see subpar. 6d).

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

(1) **USDA Annual Report of Research Facility.** This report (required by the USDA Animal Welfare Act Regulations and Standards, see Sec. 2.36) must be completed and submitted to ORD by November 15 each year as a component of Part II of the Research and Development Information System (RDIS). The forms are collected by ORD and sent to the appropriate USDA sector office. A copy of each form is also sent to the CVMO's office by ORD. Species not covered by the definition of an "animal" by USDA AWAR should not be included on this form. Instead, such animals should be reported on the VMU Annual Report (see subpar. 8j[4]).

(2) **AAALAC Reports.** Every third year a comprehensive AAALAC Program Description must be completed prior to the scheduled triennial AAALAC site visit (see Sec. 4, par. B), and annually, an abbreviated report also must be submitted to AAALAC (see Sec. 1, par. f).

(a) The triennial Program Description should not be submitted to ORD or the CVMO, unless a copy is requested.

(b) A copy of each annual report and all correspondence to and from AAALAC (minus the triennial Program Description) must be submitted to the CVMO and ORO no later than 30 days after submission to AAALAC, or receipt from AAALAC.

(3) **IACUC Semi-Annual Self-Assessment Reviews.** Semi-annual Self-assessment Reviews must be prepared by the IACUC as described in subparagraph 8d(1). No later than 60 days after the self-assessment review date, a copy of the approved report signed by a majority of IACUC members and the medical center Director must be forwarded to the CVMO's office through the ACOS for R&D and the medical center Director.

(4) **Annual VA 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. In contrast to the USDA Annual Report of Research Facility described in preceding subparagraph 8j(1), all animal species used must be included in the Annual VMU Report. Instructions for properly completing this report can be obtained from the CVMO.

(5) **PHS Assurances and Annual Assurance Updates**

(a) A PHS Assurance to conduct animal studies is required.

(b) New PHS Assurances and annual updates must be forwarded to the CVMO's office within 30 days of submission to PHS.

(6) **Correspondence.** 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.

k. **Mandatory Training.** Through IACUC oversight, each VA medical center must ensure that all personnel involved with animal research receive training to competently and humanely perform their duties related to animal research. This mandate extends to IACUC members, veterinarians, veterinary technicians, husbandry staff, research technicians, investigators, and all others that perform procedures or manipulations on laboratory animals. ***NOTE: It includes investigators responsible for supervising animal research that they themselves do not perform.***

(1) Prior to approving any protocol, the IACUC must ensure that all staff listed on the protocol have been adequately trained (see: USDA AWAR, 9 C.F.R. §2.32(a); Principle 8, U.S. Government Principles For The Utilization And Care Of Vertebrate Animals Used In Testing, Research, And Training). As a minimum, the training utilized must cover all topics listed in USDA AWAR, §2.32(c). IACUC members must be trained on topics pertinent to their committee tasks.

(2) The Office of Research and Development (ORD) has developed free web-based training that helps meet mandatory training requirements for both research staff and IACUC members (see App. A). ORD web-based training must be utilized on an annual basis to demonstrate compliance with Federal animal research training mandates, unless alternate and equivalent annual training approved by the CVMO has been adopted (see subpar. 8k[4]). Education goals for web-based training will be considered met when personnel are able to pass an exam that covers important topics in the training. The exam must be of sufficient difficulty to provide some assurance that important concepts have been learned.

(a) Investigators and research staff who utilize laboratory animals must pass the exam covering the "Working with the VA IACUC" web course plus the exam for any species-specific web course that covers the species proposed for use (can be found at: www.researchtraining.org).

(b) IACUC members must pass the exam covering the "Essentials for IACUC Members" web course (can be found at: www.researchtraining.org).

(3) Husbandry staff may access web-based training developed for them by the American Association for Laboratory Animal Science (AALAS) at: <http://www.aalaslearninglibrary.org/> ***NOTE: As part of a licensing agreement, some free registrations for this site can be obtained through the CVMO's office.*** Requirements for husbandry staff training need to be set by the local IACUC in consultation with the attending veterinarian and VMU supervisor.

(4) Stations wishing to utilize alternate web-based, didactic, or other types of training in place of ORD web-based training must document in writing to the CVMO that the alternate training covers all areas required by USDA Animal Welfare Act Regulations on an annual basis. If documentation is not deemed adequate, ORD web-based training, or more stringent alternative training must be adopted as approved by the CVMO.

9. VISITS TO VA ANIMAL FACILITIES BY NON-VA FEDERAL REGULATORS

If a medical center houses animals purchased with PHS funds, then OLAW, or other administrative units of the PHS, are authorized to conduct any investigation of VA facilities or

programs needed to meet their regulatory mandates. Likewise, if a medical center houses animal species purchased with any non-VA funds and those species are covered by the Animal Welfare Act Regulations, then any administrative unit of USDA is authorized to conduct any investigation of VA facilities or programs to meet their regulatory mandates. Copies of any correspondence received from non-VA federal agencies and any medical center replies must be forwarded to the CVMO and ORO through the ACOS for R&D and the medical center Director within 15 business days of receipt or submission (see subpar. 8g).

10. OCCUPATIONAL HEALTH AND SAFETY

a. **Personal Hygiene.** Each VA medical center must develop guidelines concerning personal hygiene for personnel engaged in the care and use of experimental animals. The guidelines must include instructions about:

- (1) Wearing and cleaning of protective clothing.
- (2) Smoking.
- (3) Eating and drinking practices in research laboratories and animal care areas.
- (4) Hand washing following contact with animals or animal tissues.

***NOTE:** Personnel subject to this directive must be made aware of its provisions (see App. C).*

b. **Uniforms for Animal Care Staff.** As a matter of personal hygiene, the medical center must provide clean uniforms and laundry service for personnel engaged in the care and use of laboratory animals.

c. **Facility Occupational Health and Safety Program.** Each VA medical center with a program of research in which laboratory animals are used must develop a written policy establishing a program of occupational health and safety for personnel engaged in the care and use of experimental animals consistent with the recommendations contained in Appendix C.

(1) VA employees, without compensation (WOC) personnel, VA research and education corporation employees, and students with significant animal contact must be given the opportunity to participate equally in the Occupational Health and Safety Program, unless the IACUC determines that such personnel are enrolled in an alternate program (e.g., affiliate's program) that complies with PHS policy. ***NOTE:** Consistent with PHS policy, OLAW will be the final arbiter if questions regarding the suitability of an alternate program are raised.*

(2) Employees whose duties require significant contact with dogs, cats, bats, or wild carnivores must be provided the opportunity of receiving pre-exposure rabies immunization in accordance with current CDC recommendations. The medical center must procure and administer the vaccine at no cost to employees requesting immunization.

(3) Transporting animals into or through areas used by patients or visitors must be avoided whenever possible. When essential to do so, all reasonable means of minimizing health risks to

patients and visitors posed by animal body fluids, waste, and aerosols need to be adopted. All animals transported through human patient care areas must be covered and caged such that patients and other non-research staff are not readily aware of their presence.

11. REFERENCES

The following regulations, guidelines, and documents are cited in this Handbook. In all cases, the most current version of each document replaces any outdated ones. The full text of these references can be obtained from the internet web site established at:
<http://www.researchtraining.org> .

- a. Animal Welfare Act, Public Law 89-544 as amended; codified at 7 U.S.C. 2131-2159.
- b. USDA Animal Welfare Act Regulations and Standards, 9 CFR Parts 1, 2, 3, and 4.
- c. The Health Research Extension Act of 1985, Public Law 99-158, as amended, "Animals in Research," codified at 42 U.S.C. Section 289d.
- d. PHS Policy on Humane Care and Use of Laboratory Animals. NIH, Office of the Director. Revised September, 1986, and reprinted October, 2000.
- e. 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.
- f. Guide for the Care and Use of Laboratory Animals. National Research Council, 1996 (or most recent edition).
- g. Report of the AVMA Panel on Euthanasia. Journal of the American Veterinary Medical Association, Volume 218(5): 671-696, 2001.
- h. Biosafety in Microbiological and Biomedical Laboratories. CDC and NIH. 4th edition (or most recent revision)
- i. NIH Guidelines for Research Involving Recombinant DNA Molecules. NIH, 1994, and as subsequently amended.
- j. CDC, Title 42 Code of Federal Regulations (CFR) 73, Possession, Use, and Transfer of Select Agents and Toxins.
- k. AALAC, International. "Rules of Accreditation," revised January 2001.
- l. Nuremberg Code of 1947.
- m. VHA Handbook 1108.1, Controlled Substances.

- n. VA Handbook 0730, Security and Law Enforcement.
- o. Title 38 United States Code, Part V, Chapter 73, Section 3707, Functions of Veterans Health Administration: Research Programs.
- p. National Research Council. National Need and Priorities for Veterinarians in Biomedical Research. 2004.
- q. Potkay S, NL Garnett, JG Miller, CL Pond, DJ Doyle. "Frequently Asked Questions about the Public Health Service Policy on Humane Care and Use of Laboratory Animals," Laboratory Animal 24:24-26, 1995.
- r. USDA Animal and Plant Health Inspection Service, Animal Care Section. Animal Care Policy Manual, Policy #10: Licensing and Registration of Producers of Antibodies, Sera and/or Other Animal Parts and Pregnant Mare Urine (PMU). April 14, 1997.
- s. Potkay S, NL Garnett, JG Miller, CL Pond, DJ Doyle. "Frequently Asked Questions about the Public Health Service Policy on Humane Care and Use of Laboratory Animals," Contemporary Topics 36:47-50, 1997.
- t. Baker DG. "Natural Pathogens of Laboratory Mice, Rats, and Rabbits and Their Effects on Research," Clinical Microbiology Reviews. 11: 231-266. 1998.
- u. VHA Handbook 1108.2, Inspection of Controlled Substances.
- v. M-2, Part VII, Pharmacy Services.
- w. VA Handbook 5005, Staffing, Part II, Appendix F32.
- x. VHA Handbook 1200.6, Control of Hazardous Agents in VA Research Laboratories.
- y. VHA Handbook 1200.8, Safety of Personnel Engaged in Research.
- z. VHA Directive 1105.1, Procedures for Management of Radioactive Materials.

CVMO CONTACT INFORMATION

1. Inquiries for the Chief Veterinary Medical Officer (CVMO) need to be directed to:

Chief Officer, Research and Development (12)
Phone: (404) 728-7644
Fax: (404) 327-4964

2. Information forwarded by mail needs to be addressed to:

Chief Veterinary Medical Officer
Chief Officer, Research and Development (12)
Department of Veterans Affairs
810 Vermont Avenue, NW
Washington, DC 20420

<http://www.researchtraining.org>

SPECIAL AGED RODENT PROCUREMENT

1. PROCUREMENT OF AGED RODENTS FOR GERIATRIC RESEARCH. An interagency agreement has been negotiated with the National Institute on Aging (NIA) to provide selected species, stock, strains, and age groups of animals, i.e., aged rodents, subject to the availability of the particular animal(s) requested and the eligibility of investigators to receive animals under terms of the interagency agreement. ***NOTE:** These procurement activities must be conducted pursuant to existing VA policy when applicable (e.g. VA Directive and Handbook 7126.2, "Procurement Sources and Programs")*

2. ELIGIBILITY. Department of Veterans Affairs (VA) investigators are eligible to receive animals under this interagency agreement provided that they are receiving funding for Merit Review, Career Development, or other projects approved by the Veterans Health Administration (VHA) Central Office as the Principal Investigator (PI), and aged rodents are required to complete scientific objectives. To receive consideration to receive aged rodents, submit a memorandum to the Chief Veterinary Medical Officer (CVMO) including the following information:

- a. Name of PI.
- b. Address of PI.
- c. Title(s) of VA project(s) in which aged rodents are to be used.
- d. Budget pages for the projects in which aged rodents are to be used.
- e. A justification for using aged rodents based upon specific aims in current projects funded by VHA Central Office.
- f. Approximate yearly need for aged mice and rats by age and strain.

3. REVIEW. The CVMO will review the preceding information and submit a recommendation to the Chief Research and Development Officer (CRADO), or designee. If approved, upon verification, NIA will be notified of the PI's eligibility to receive aged rodents for the current fiscal year.

4. CONTINUING USE OF NIA RODENTS. By September 1 of each year, each investigator wishing to continue to receive NIA animals must submit a memorandum to the CVMO requesting continued eligibility in the program. The memorandum must include the information specified in preceding paragraph 2. Investigators are notified by October 1 if their eligibility has been extended through the next fiscal year.

5. INITIATING PURCHASE REQUESTS. To initiate a purchase request through the local research office, an investigator must use the following procedure:

a. The investigator must submit a completed VA Form 10-4786, Request Form to Procure Special Animals for Aging Studies, and a VA Form 90-2237, Request, Turn-In, and Receipt for Property or Services, to the local Supply Service.

b. The local Supply Service must prepare and submit a VA Form 90-2138, Purchase Order, with VA Form 10-4786 to the NIA.

6. RODENT BIOLOGICAL DATA AND COST INFORMATION. Information regarding the source and cost of animals needed for preparation of a purchase order is obtained from the Office of Resources and Resource Development, NIA; telephone number (301) 496-6402. VA Forms 90-2138 are payable directly to the NIA contractor from whom animals are delivered.

OCCUPATIONAL HEALTH AND SAFETY FOR RESEARCH PERSONNEL WITH ANIMAL CONTACT

1. PURPOSE. This Appendix provides guidelines designed to facilitate the provision of a safe workplace and safe work practices for personnel working in an animal research setting. They provide a basis for meeting accepted occupational safety requirements for this work environment.

2. BACKGROUND. An occupational health program is essential for personnel who work in laboratory animal facilities, or who through their work have contact with animals. These types of animal contacts potentially expose personnel to physical demands, allergens, and hazardous agents, including infectious diseases, radioactive materials, and toxic substances. Infectious diseases may be experimental in origin, or naturally occurring zoonotic diseases that are peculiar to a given animal species. Human allergies to animals are common and may become serious enough to constitute an important health consideration, or a reason to discontinue work with a particular species of animal.

3. RESPONSIBILITY OF FACILITY DIRECTOR. Each Department of Veterans Affairs (VA) medical center Director, with a program of animal research, is responsible for developing and implementing a program for personal hygiene, protective safety measures, safe use of hazardous materials, and preventive medicine for personnel engaged in the care and use of research animals. *NOTE: This program needs to be tailored to the size and needs of the animal research program.*

4. PERSONNEL

a. **Preventive Medicine.** The following personnel considerations are essential components of a Preventive Medicine Program (PMP). All employees that meet the criteria provided in subparagraph 10c(1) of the Handbook must either participate in PMP, participate in a similar PMP provided by an affiliate or other institution, or sign a waiver declining to participate. The waiver is to make it clear that non-participation in PMP could result in adverse health effects. Regardless, employees may not opt out of immunizations or tests mandated by the Director or Chief of Staff for hospital staff, nor opt out of testing that is necessary to protect the health and well-being of laboratory animals (e.g., Tuberculosis [TB] testing of personnel with primate contact).

(1) **Scope.** Personnel must participate in PMP if they have to handle animals or handle unfixed animal tissues. Personnel exposed to airborne or other animal allergens on more than an occasional basis should also participate. The Institutional Animal Care and Use Committees (IACUC), with input from health care professionals, must decide the level of PMP services needed for each person or group based upon a risk assessment. *Note: A pamphlet explaining basic components of VA PMPs is available through the CVMO's office.*

(2) **Basic Program Content.** Key elements of a PMP for employees with animal contact or

exposure to animal allergens are as follows:

(a) **Pre-Employment Medical Evaluation.** A pre-employment physical exam needs to be conducted to ensure that a prospective new employee is capable of the physical demands of the position, and that pre-existing medical conditions do not place the employee or others at risk.

(b) **Medical Follow-up.** At least annually after employment begins, an occupational health and safety physician, or other qualified medical professional, needs to review each employee's medical history. Particular attention is to be paid to immunizations needed for the prevention and development of allergies that could place the employee in jeopardy while in the presence or in contact with animals. ***NOTE:** This review may take the form of a questionnaire review performed as part of an interview between the employee and a health care professional, or it may take the form of a physical exam (see par. 5).*

(c) **Access to Animals and IACUC Approvals.** Because VA must ensure that a safe workplace is provided, all employees covered in subparagraph 4a(1) must provide proof to the IACUC that they have enrolled in PMP before they enter the animal research facility and before they begin work with animals. The IACUC may wish to require proof of enrollment, or waiver, by all personnel before protocols are approved, and/or before personnel are issued access cards to animal use areas.

(d) **Occupational Safety Training.** Personnel who have contact with experimental animals need to receive training in the proper handling of the animals with which they will work. Most animal inflicted injuries occur because of inadequate training and experience, or because of carelessness. Personnel need to be instructed to avoid unnecessary risk when working with animals, and to seek expert assistance when in doubt. Training needs to include the use of appropriate protective clothing, equipment, and hygiene practices. Personnel whose work responsibilities require that they lift heavy objects and/or perform tasks requiring repetitive motions need to be trained in the ergonomics of their tasks.

b. **Reporting Injuries and Illness.** Injuries, animal bites, animal scratches, and cuts sustained in the animal research facility or research laboratory must be reported promptly to the employee's supervisor. The employee needs to then be referred to the Employee Health Physician, and VA Form 2162, Report of Accident, needs to be completed. ***NOTE:** Illness needs to routinely be reported to the employee's supervisor.*

c. **Personal Hygiene.** An important factor in protecting the health of personnel engaged in animal care or research is personal hygiene. All employees need to understand the importance of personal hygiene and the specific measures that routinely are to be taken to protect themselves against zoonotic agents found naturally in experimental animals, as well as hazardous agents used experimentally in approved biomedical studies using animals.

(1) **Hand Washing.** Hand washing is a crucial safety measure for safeguarding personnel in the animal research facility. Although the proper use of disposable gloves provides an effective means of preventing hand contamination, hands can easily become contaminated during the removal of contaminated gloves.

(a) Frequency. Hands need to be washed with soap and water whenever they touch contaminated or potentially contaminated surfaces, liquids, or body fluids. Hands need to be routinely washed before eating, drinking, applying cosmetics, touching contact lenses, and leaving the facility.

(b) Facilities Provided. All sinks in the animal research facility need to have soap and paper towels located conveniently near the sink. Electronically controlled or knee-operated faucets are preferable to hand operated faucet handles, particularly in biohazard areas.

(2) **Showers.** Showers, an excellent adjunct to personal hygiene, may be required after working with some hazardous agents. Showers need to be available to all employees with animal contact. ***NOTE:** Employees need to be encouraged to shower at the end of the workday.*

5. MEDICAL FOLLOW-UP QUESTIONNAIRE

An annual review of a medical questionnaire in the form of an interview by a qualified medical professional can substitute for a physical exam in PMP. The following information needs to be considered when developing a questionnaire for a PMP. ***NOTE:** Information collected is considered to be privileged medical information and subject to Federal regulations that govern the collection and use of personal information.*

a. Information such as name, social security number, date of birth, gender, pregnancy status, hospital service, job title, and contact information.

b. The species of laboratory animals encountered.

c. The amount of contact time per week (to include contact time with animal tissues, waste, body fluids, carcasses, or animal housing areas).

d. Does the employee's work involve human or animal pathogens, and if so, which pathogens.

e. Does the employee's work involve contact with non-human primates, and if so, has the employee ever been diagnosed with TB. If TB has been diagnosed or exposure documented, then the following information may be valuable:

(1) A list of medication taken, duration of therapy, and how long ago.

(2) Whether Bacille Calmette Guerin (BCG) vaccination has occurred, and if so, when.

(3) History of any positive tuberculosis (Tine, Purified Protein Dervative [PPD], Mantoux) tests.

f. Has the employee received immunosuppressive therapy that could increase the risk of zoonotic disease.

g. How often (never, rarely, sometimes, always) does the employee wear disposable gloves, a gown, a mask, a cap, or protective eyewear as part of assigned duties.

h. Does the employee smoke, eat, or drink in animal holding or procedure areas.

i. How often (never, rarely, sometimes, always) does the employee wash hands, change clothing (if soiled), or shower after handling animals during the day.

j. Is there any history of asthma, hay fever, allergic skin problems, eczema, sinusitis, chronic respiratory infections, or disease. **NOTE:** *A history of the same among blood relatives would be important to establish.*

k. Do any allergic symptoms occur during, or after, contact with a laboratory animal species (sneezing spells, runny or stuffy nose, watery or "itchy" eyes, coughing, wheezing, or shortness of breath, skin rashes or hives, difficulty swallowing), and if so, which species is involved, and how frequently does each symptom occurs (monthly, weekly, daily).

l. Does the employee have any house pets that could be responsible for allergic symptoms, or that could represent a disease transmission hazard to the employee or to animals in the research facility.

m. Has the employee ever suffered from an inguinal or similar hernia, from back pain or trouble, or from joint problems or arthritis. If so, the severity and corrective measure(s) such as surgery or rehabilitative therapy need to be described.

n. Does the employee work with chemicals in the workplace, and does the employee have any symptoms associated with such exposure.

o. Note any other significant health history that might be affected by exposure to workplace hazards.

p. Note the immunization and testing history to include the date, side effect(s), or other relevant information for each of the following: tetanus, rabies (initial and booster, immune globulin), hepatitis B, tuberculin (including chest radiograph for known reactors), and other immunizations or tests as would be appropriate for the employees work.

q. Note the printed name, signature, and date of the employee and interviewer.

6. PROTECTION

a. **Protective Clothing and Disposable Items.** Protective clothing must be provided to employees at no cost. Uniforms and laboratory coats must be laundered so that clean protective clothing is available whenever needed. Animal husbandry and research staff might have to change into clean uniforms or coats multiple times daily, and enough clean inventory must be on hand to meet these needs. Disposable protective items such as gloves, masks, head and foot

covers, gowns or other body cover must also be provided when use of these items is required by the IACUC or Subcommittee on Research Safety (SRS). Soiled protective clothing must not be taken away from the work site, and soiled outer garments must not be worn outside the animal research facility.

b. **Animal Care Personnel**

(1) **Uniforms.** Upon arrival at the duty site, animal care personnel need to change out of street clothing and into clean uniforms. Uniforms are to be changed whenever they become soiled. At the end of the workday, uniforms need to be placed in a hamper or disposable laundry bag designated for soiled clothing. All uniforms must be provided and laundered by VA.

(2) **Lifting.** Back injuries are a common hazard for animal research facility employees because of lifting requirements. Employees need to always practice safe lifting techniques. Back braces need to be available to employees who perform lifting tasks on a daily basis, and tasks should be made as ergonomically efficient as possible. Whenever possible, hydraulic or electric lifting equipment should be used.

(3) **Foot Injuries.** Employees who are at risk of crushing foot injuries from heavy objects must be provided steel-toed footwear.

(4) **Soiled Clothing.** Soiled clothing is not to be worn outside the animal research facility, and never worn or carried home. Soiled clothing laundry receptacles should be available in locker or change room facilities.

c. **Research and Other Personnel with Animal Contact.** The type of protective clothing needed depends on the procedures that will be performed, but as a minimum, clean lab coats and gloves should be worn by all personnel while handling animals or animal tissues. For those with allergies to animals, additional protection in the form of Powered Air Purifying Respirators (PAPR) or Racal hoods, N95 disposable dust and/or mist respirators, or fitted respirators with appropriate cartridges may be worn. Some respiratory protection devices may require employee evaluation through a formal respirator use program (contact the local medical center Industrial Hygienist or Safety Officer). Reassignment to duties that prevent exposure is recommended if possible.

7. GENERAL PERSONAL SAFETY CONSIDERATIONS

a. **Disposable Gloves.** The type of polymer needed for disposable gloves used in research depends upon the presence or absence of allergies and the potential for exposure to organic solvents and infections agents. **NOTE:** *Hospital safety personnel need to be consulted for appropriate choice of glove material.*

(1) Disposable gloves are useful in preventing the transmission of diseases between animal rooms, and in limiting the possibility of disease transmission between animals and humans. They limit staff exposure to contact allergens, and need to be available for caretakers and research personnel who contact animals, animal tissues, or soiled animal cages.

(2) Disposable gloves need to be discarded when they are visibly soiled, torn, punctured, or otherwise damaged such that their ability to act as a barrier is compromised. Prior to leaving an animal room or anteroom, personnel need to discard their gloves and wash their hands. Care is needed to prevent contamination of door knobs, faucet handles, paper towel dispensers, refuse container lids, and similar objects by personnel with contaminated gloves. Some personnel may develop contact dermatitis allergy to the absorbent material that is used to lubricate disposable gloves; however, alternative lubricants or lubricant-free gloves are available. Personnel must be informed of possible latex allergies.

b. **Hearing Protection.** The noise level in animal research facility areas may reach potentially damaging levels, particularly in cage washing areas and dog housing rooms. Ear protection needs to be provided whenever noise levels exceed those permissible levels established by the Occupation Safety and Health Administration (OSHA) regulations, or whenever requested by an employee. If protective headset-style protectors are too bulky or uncomfortable, inexpensive disposable foam ear plugs may be used. The animal research facility supervisor needs to assume responsibility for ensuring the appropriate use of ear protection.

c. **Eye Protection.** Protective eye ware needs to be used by employees who handle nonhuman primates or corrosive or otherwise dangerous liquids or vapors. Goggles or other devices that completely shield the eyes need to be provided by the medical center when appropriate. ***NOTE:** The medical center Industrial Hygienist or Safety Officer needs to be consulted for the type of protective eyewear needed for specific tasks that are potentially hazardous.*

d. **Other Precautions.** Personnel need to be trained to avoid hand contact with their eyes, face, mouth, or other body surfaces with contaminated gloves or hands.

e. **Special Circumstances.** Special equipment and clothing may be required when personnel are engaged in studies that involve hazardous agents. The specific measures needed are to be appropriate for the agents used, as determined by the Safety Officer in consultation with the investigator, the SRS, and the veterinarian.

f. **Smoking, Eating, Drinking, and Cosmetic Application.** Smoking, eating, applying cosmetics, installing contact lenses, and similar procedures are prohibited within the animal research facility or in animal study areas except in designated areas that are free of potentially contaminated materials.

(1) **Food and Beverage Storage.** Employee food and beverages are to be stored only in refrigerators and/or freezers designated exclusively for such use.

(2) **Smoking.** Smoking is now prohibited within all VA medical facilities, and is to be conducted outside, usually in specifically designated areas. Personnel who smoke need to wash their hands prior to smoking.

8. WORK WITH HAZARDOUS AGENTS

a. **Scope.** Safety in VA research laboratories is the primary responsibility of the VA SRS. These responsibilities include inspections, training, investigation, documentation, and safety program review (see VHA Handbook 1200.8, Safety of Personnel Engaged in Research, and VHA Handbook 1200.6, Control of Hazardous Agents in VA Research Laboratories). The SRS and the IACUC must interact effectively to ensure that adequate safety measures are mandated to protect personnel who work in the animal research facility when biological, chemical, or radiological agents are in use. The specific measures needed are dependent on the risk to human and animal health represented by the agent, and the difficulty involved in containing the agent.

b. **Primary Objective.** The primary objective is to prevent exposure of the animal care staff and other animal workers to hazardous agents present in animal tissues, animal secretions, soiled bedding, and elsewhere in the animal environment. The key elements to safety when working with hazardous agents are:

(1) Trained, knowledgeable personnel to perform the study, and

(2) Prior review and approval of the proposed use of hazardous agents by qualified personnel.

c. **Procedures**

(1) Before experimental animals are treated with any hazardous agent, the project must have been approved by the Research and Development (R&D) Committee, and the procedures must have been approved by IACUC and SRS.

(2) An appropriate Standard Operating Procedure (SOP) written for the husbandry staff and other personnel who will work with the animals must be prepared for each hazardous agent planned for use in animals. The SOP should be prepared with input from the Veterinary Medical Unit (VMU) supervisor, the veterinarian, the Safety and/or Biosafety Officer, and the responsible investigator(s). ***NOTE:** The most recent edition of the Center for Disease Control and prevention (CDC)-National Institutes of Health (NIH) publication entitled Biosafety in the Microbiology and Biomedical Laboratory needs to be consulted for guidelines on safely performing animal studies with infectious agents, based upon the animal and laboratory biosafety level precautions appropriate for the level of the agent.*

(3) **Prior** to the initiation of any study, personnel who work with animals exposed to hazardous agents (or who clean their cages) must be trained in proper procedures for working with the animals and in the proper procedures relating to waste and equipment.

d. **Special Xenozyoonosis Considerations.** Immunologically compromised rodents such as the nude mouse and the severe combined immuno-deficient (SCID) mouse, that receive human xenografts, body fluids, blood, or human infectious agents and related materials, present a potentially unique and poorly understood (xenozyoonosis) risk. These rodents may develop

persistent infections while remaining otherwise healthy. For this reason, such animals injected with these materials need to be handled with caution, following Biosafety Level 2 or 3 practices, in accordance with the recommendations of the Safety Officer.

e. **Universal (Standard) Precautions.** Universal or "Standard" Precautions are a set of safe practices in which all human blood and certain human body fluids are treated as if known to be infectious for Human Immunodeficiency Virus (HIV), Herpes B Virus (HBV), and other blood borne pathogens. Intended primarily for personnel working directly with human blood components, other body fluids and excreta, and unfixed tissues, such practices are relevant to all personnel working with potentially infectious materials in animal studies. Personnel working with animals treated with such materials must receive annual training to comply with the Bloodborne Pathogen Standards.

f. **Chemical Agents and the Material Safety Data Sheet**

(1) Although all chemicals and drugs are potentially dangerous, special concern is necessary when working with known carcinogens, mutagens, immunosuppressive agents, toxic drugs, potent steroids, agents of unknown pharmacological activity, and other chemicals listed as hazardous waste by the Environmental Protection Agency (EPA).

(2) All chemical agents purchased commercially are to have a Material Safety Data Sheet (MSDS) that accompanies the shipment of the chemical, or available online as allowed by law. Purchasing offices should forward the MSDS immediately to the Research Office from where it should be distributed to the using investigator and the animal research facility. The animal research facility must maintain an MSDS logbook for chemicals such as detergents, cleaners, and alcohols used (VHA Handbook 1200.8, Safety of Personnel Engaged in Research, para. 3a[2]).

g. **Radioactive Agents.** The safety principles for work with radionuclides are similar to those for work with other hazardous agents with some important additions:

(1) The Radiation Safety Officer must review and approve, or require specific procedures that are to be followed when using radionuclides in animals.

(2) Personnel working with radionuclides must be trained specifically for work with these materials (see VHA Handbook 1105.1, "Procedures for Management of Radioactive Materials").

(3) All acquisition and disposition of radionuclides must be in accordance with the Nuclear Regulatory Commission (NRC) regulations covering these materials.

h. **Procedures for the Animal Care Staff**

(1) **Warning Signs and Safety Protocol for Animal Rooms that Contain Hazardous Agents.** A complete copy of the safety protocol for the hazardous agents found in an animal room (with biosafety class, if applicable) needs to be posted near the entrance of the animal room. The safety protocol must contain all relevant information necessary to identify the personnel, procedures, safety precautions, waste disposal, carcass disposal, and related

information about the hazardous study.

(2) **Disclosure.** The following information needs to be posted on the animal room door, the cubicle, or other area dividers:

(a) Large biohazard, chemical hazard, or radiation hazard sign, as appropriate, and a limited access warning sign.

(b) The name of the agent, and the name and telephone number of the individual to contact in event of an emergency involving the agent.

(c) The personal protective equipment (PPE) required to safely enter the room.

(3) **Separation of Animals Treated with Hazardous Agents.** Animals receiving hazardous agents need to be housed separately from other animals to prevent cross contamination and simplify isolation of contaminated wastes. ***NOTE:** The use of negative-pressure ventilated racks, biosafety cabinets, and other similar high efficiency particulate air (HEPA)-filtered devices are helpful in isolating small animals exposed to hazardous agents. Properly managed cubicles may be suitable for containing experiments with hazardous agents to small areas.* A biohazard or other appropriate warning sign and the name of the hazardous agent needs to appear on the cage cards of animals treated with a hazardous agent.

(4) **Cleaning, Feeding, and Watering Animals Treated with Hazardous Agents.** If both treated and untreated animals are housed in the same room, the untreated animals need to be cleaned, fed, and watered first to reduce the possibility of accidental contamination of untreated animals.

(a) Rooms housing treated animals need to be cleaned last and animals in these rooms fed, watered, and manipulated after these procedures have been completed in other rooms.

(b) Upon completion of a study involving use of infectious or other hazardous material, the room housing animals exposed to such agents needs to be decontaminated before introduction of new animals.

***NOTE:** The Research Safety Officer (or hospital equivalent) needs to be consulted to determine the best method to decontaminate the room. This will vary with the hazardous agent in use, and cannot be generalized. It is important that personnel performing the decontamination be informed about their task, and provided with PPE.*

(5) **Use of a Bedding Change Station or Biocontainment Hood to Change Bedding**

(a) A device that draws aerosols away from the caretaker, such as an air filtered change station, needs to be used when soiled, contaminated bedding is removed from animal cages. Whenever possible, the exhaust from such containment devices needs to enter the exhaust system of the building directly, in such a manner that the concentration of dander and pollutants is minimized in the room.

(b) The caretaker needs to wear PPE, including a mask and gloves when removing soiled bedding from cages. Soiled bedding should be removed from cages in the cage wash room rather than in the animal rooms unless bedding changes in the room are approved by the IACUC and biosafety committee as part of a SOP for containing hazardous agents.

i. **Waste Disposal**

(1) **Bedding.** Bedding contaminated with hazardous agents may present one of the most difficult management problems. Contamination with infectious agents may require that bedding be sterilized before being transported to the cage wash room for dumping. If soiled bedding containing hazardous material cannot be rendered harmless prior to transporting to the cage wash room, it may be necessary to bag, or double bag the bedding for direct transportation to an incinerator, or other disposal system. Regardless of the nature of the contamination, the methods of disposal need to be determined by the Safety Officer in consultation with the veterinarian, and comply with NRC, EPA, and CDC-NIH requirements.

(2) **Carcass Disposal.** Contaminated carcass disposal is often similar to disposal methods for other contaminated materials, but in this case needs to reflect the nature of the hazardous agent in use. Upon completion of the necessary work with the carcass, it must be bagged, labeled, and disposed of in accordance with applicable regulations. Holding, when necessary, must be accomplished in a refrigerator or freezer reserved for carcass disposal.

9. MISCELLANEOUS SAFETY PROCEDURES FOR ALL PERSONNEL

a. **Needle and Syringe Disposal.** Employees must follow VA policy on the proper use and disposal of syringes and needles. Needles are not to be recapped. Instead, syringes with attached uncapped needles should be dropped into puncture proof containers for disposal. Such containers must be located in every room in which sharps are used. **NOTE:** *In some instances, neutralization of a hazardous agent prior to syringe and needle disposal may be necessary.*

b. **Adequate Animal Restraint.** The chance of accidental needle sticks is reduced if animals are anesthetized or chemically restrained before being injected with hazardous agents. Manually restrained, unanesthetized animals are often capable of jarring needles and redirecting their path, or causing spills during struggles against restraint.

c. **Prevention of Aerosol Formation.** Whenever possible, hazardous agents need to be prepared or purchased in rubber-topped vials so that the aerosols associated with open tube manipulations can be minimized. Solutions containing hazardous agents are never to be expressed through a needle into disposal containers or disinfectant pans because of the aerosols produced; rather the syringe with solution must be discarded directly into an appropriate puncture proof sharps container.

(1) When infectious agents are used, the sharps container needs to be sterilized before disposal.

(2) When hazardous agents require disposal by incineration immediately after use, the sharps container must be processed in the same fashion.

d. **Use of Hoods.** Hazardous agents need to be injected or otherwise administered within an appropriate biocontainment or chemical hood. When technical considerations make such a practice impossible, exceptions are to be justified and approved by the local SRS.

e. **Manipulating Animals.** The fewer manipulations of an animal that a single individual performs when handling hazardous agents, the better. Should an accident occur, it is much safer to have a second person available to assist in decontamination procedures, and to audit the accident.

f. **Reduce Distractions.** When hazardous agents are being manipulated in the animal research facility, distraction needs to be minimized.

(1) Research personnel need to schedule with the animal care staff a time for manipulations so that routine cleaning and husbandry procedures can be avoided, postponed, or rescheduled.

(2) Loud noises need to be minimized.

10. SPECIAL CONSIDERATIONS

a. **Special Health Considerations for Female Employees.** A review of occupational hazards that could be detrimental to pregnant women and the unborn child should be conducted. Women who are pregnant and work with animals should make their physician and VA employee health officials aware of the pregnancy as early as possible so that the employee can be made aware of potential risks in consultation with the Occupational Health Physician, and/or the medical center Safety Officer, and Radiation Safety Officer (see subpar. 10c[2][b]).

b. **Selected Primate Zoonotic Diseases.** A number of primate zoonotic diseases may pose a risk for animal workers and research staff in the typical animal research facility. Work with primates requires special attention to occupational health and safety requirements. Protective clothing plus masks, gloves, head and face shield or goggles always need to be worn when personnel are in primate housing rooms or when working with primates. ***NOTE: Guidance on protecting personnel from primate zoonotic diseases can be found in the 2003 NRC publication entitled Occupational Health and Safety in the Care and Use of Nonhuman Primates.***

(1) **Cercopithecine herpesvirus infection (*Herpesvirus simiae*, CHV1, Herpes B virus).** This is a latent herpesvirus that naturally infects macaque monkeys such as rhesus and cynomolgous monkeys. Human infection is acquired by the bite of an infected animal during periods of reactivated infection, or by exposure of naked skin or mucous membrane to infected saliva or monkey excreta. Wounds from contaminated cages and scratches by infected animals are also possible means of infection. Although many macaques have antibody to the agent, indicating latent or active infection, and primate bites are not uncommon, few human cases have occurred. When the agent is transmitted, it causes an ascending encephalomyelitis in humans

that is often fatal. Immediate and thorough cleaning of the wound and prompt medical attention are essential after actual or potential exposure. **NOTE:** *Guidelines in the most recent edition of the CDC-NIH publication entitled Biosafety in Microbiological and Biomedical Laboratories need to be followed whenever a potential exposure with this virus occurs. The most recent recommendations for prevention and treatment of B-virus in potentially exposed persons need to be consulted before work with macaque species begins. Whenever possible, primates known to be free of this virus should be used in research.*

(2) **Tuberculosis (TB).** TB may infect many primate species, but Old World primates are much more susceptible than New World species. The disease is usually transmitted from humans to primates and possibly from primates to humans, although documentation of the latter is rare. Not all species of Mycobacteria cause tuberculosis, but generally, those that cause TB in man also cause it in monkeys. TB spreads rapidly through Old World primate colonies; therefore, infected primates are almost always euthanized to prevent further transmission of the disease. The intradermal tuberculin skin test, which uses Old Tuberculin in animals, detects most infected animals; however, some infected animals go undetected. The tests are to be administered and read carefully by qualified personnel for best results. Humans and primates must be tested routinely to protect both populations.

(a) Primates need to be tested at the time of arrival at the medical center and at 2-week intervals thereafter through at least six consecutive negative tests. Because of their lower sensitivity to Mycobacterial antigens, monkey colonies need to be tested every 3 to 6 months.

(b) Personnel working with primates need to be tested at the time of employment and at least annually thereafter. **NOTE:** *The latest CDC guidelines for tuberculin testing of primates need to be followed.*

(3) **Simian Immunodeficiency Virus (SIV).** The human health risk posed by monkeys infected with Simian Immunodeficiency Virus (SIV) is uncertain at this time; however, several instances of human seroconversion to SIV have been observed in animal workers. Monkeys infected with SIV must be handled as though SIV is infectious for humans.

c. **Other Selected Zoonotic Hazards**

(1) **Q Fever.** Ruminants are the primary host for this rickettsial disease. Although any ruminant could potentially be infected and shed the organism, sheep have been the most frequent source of infection in the research setting.

(a) The causative organism, *Coxiella burnetti*, is spread by aerosol or direct transmission from ruminant tissues (particularly placental tissues and birth fluids), soiled bedding, or blood and other body fluids. Although most human infections pass asymptotically, it may appear as an acute febrile disease resembling influenza, with a low fatality rate in treated cases. Because most sheep flocks in the United States are enzootically infected, quarantine and testing may be of little practical value as preventive measures.

(b) Occupational health needs to be focused on preventing exposure of human workers to the infection. Protective clothing, including gloves, masks, and other protective items need to be worn by those having contact with birth tissues or fluids, where titers of the agent are likely to be highest. All personnel who normally work with these materials must be advised accordingly. Effective measures need to be taken to prevent direct and indirect contact between small ruminants and hospital patients or visitors.

(2) **Toxoplasmosis**

(a) Cats and other felines are the definitive host of this protozoal infection which they acquire mainly from eating infected mammals (especially rodents), which act as intermediate hosts. The parasite, *Toxoplasma gondii*, is harbored in the intestinal tract of cats, and is usually asymptomatic.

(b) While the actual risk to humans from exposure to cats tends to be exaggerated, the potential for human infection should not be disregarded. Many humans are exposed to the agent without noticeable effect. Of primary concern are immunodeficient individuals and females, just prior to or during pregnancy. Infection during pregnancy can produce abortions or congenital malformations in the fetus, with the risk greatest during the first trimester. Unless they are known to have antibodies to *T. gondii*, pregnant women need to avoid cleaning litter pans or contact with cats that have an unknown diet history. As a precautionary measure, consideration may be given to assignment of pregnant women to duties that do not include contact with cats.

(c) All employees are to thoroughly wash their hands after contact with surfaces potentially contaminated by cat feces. Cat feces and soiled litter need to be disposed of daily before sporocysts become infective. **NOTE:** *This is usually after a 2 to 3 day incubation period.*

(3) **Rabies.** While human rabies is now a rare disease in the United States, it is almost invariably fatal and thus needs to be considered when working with animals that pose a potential threat to workers. Rabies is usually transmitted only when the virus is introduced into open cuts or wounds in skin or mucous membranes. Exposure may be from bites by an infected animal or much less frequently through scratches, abrasions, open wounds, or mucous membranes contaminated with saliva or other infectious material.

(a) Vaccination is the most valuable preventive measure with local wound treatment and vaccination following potential exposure next. Historically, dogs are the most common vector of rabies infection to humans. The incidence of rabies in dogs in the United States is now very low; while rabies in wild animals, especially skunks, raccoons, and bats, is much more commonly recognized. Personnel who have contact with dogs, cats, other carnivores, wild mammals, and susceptible species of bats (or their tissues) must be advised to receive pre-exposure immunization against rabies.

(b) Pre-exposure immunization does not eliminate the need for prompt post-exposure prophylaxis. **NOTE:** *The most recent CDC guidelines on post-exposure immunization need to be followed.*

(4) **Cat Scratch Disease.** Cat Scratch Disease is caused by the rickettsia *Bartonella henselae*. The disease is characterized by lymphadenopathy and signs of systemic infection, including a mild and short-lasting fever. The history of recent exposure to a cat scratch or bite, or trauma from inanimate object potentially contaminated by cats, combined with the symptoms described, is sufficient to consider Cat Scratch Disease in the differential diagnosis. Typically the disease begins as a cutaneous lesion which develops within 3 to 10 days at the site of injury and may be followed in about 2 weeks by regional lymphadenopathy and systemic signs. The primary means of prevention is thorough cleaning of cat scratches and bites. Usually, the disease is relatively benign and the patient recovers without complication, although in a small proportion of cases bacteremia and serious sequelae such as encephalitis have occurred, particularly among immunocompromized individuals.

(5) **Rat Bite Fever.** Two bacterial etiologies are recognized: *Streptobacillus moniliformis* and *Spirillum minus*. The disease is usually associated with wild rodent bites, rarely with laboratory bred rodents. In humans, the disease is characterized by an abrupt onset of chills and fever, headache and muscle pain, followed shortly by a maculopapular or sometimes petechial rash. The primary wound usually heals promptly, but after an incubation period of about 10 days, systemic signs appear. **NOTE:** A 7 to 10-day course of penicillin or tetracycline is recommended for treatment of the disease.

(6) **Dermatomycoses.** The most common causes of dermatomycosis in humans acquired from animals are *Trichophyton* spp., and *Microsporum canis*. Cats, rats, cattle, and guinea pigs are the most common sources, and may not exhibit clinical signs of disease. Personnel who develop circumscribed, intensely itching lesions that are non-responsive to ordinary household remedies on exposed parts of their bodies, need to be examined for dermatophytes.

(7) **Other Zoonotic Diseases.** Other zoonotic diseases to which animal workers may be exposed are potentially endless, but include:

(a) Bacterial diseases such as tularemia, salmonellosis, shigellosis, brucellosis, campylobacteriosis, helicobacter infection, and many others.

(b) Viral diseases. Viral diseases that occasionally infect animal workers include hantavirus (wild rodents), hepatitis A (some primates and great apes), lymphocytic choriomeningitis (hamsters, rats and possibly mice), and contagious ecthyma (sheep).

(c) Miscellaneous other zoonotic diseases. These should not be overlooked include psittacosis, amoebiasis, cryptosporidiosis, and tapeworm, roundworm, and/or hookworm infection.

NOTE: Consideration to these possibilities should be given to animal workers with vague or otherwise poorly defined infectious disease.

11. INFECTIOUS DISEASE RISK TABLE.

Specific procedures required for the Occupational Safety and Health Program for the animal research facility are dependent upon the degree and type of exposure to laboratory animals as well as the nature of the work being done. The following table summarizes suggested procedures for four risk categories. Additional risk categories may be added by the medical center:

Risk Category	Definition	Pre-Employment Physical	Annual Questionnaire	TB Skin Test or Chest Radiograph	Rabies Vaccine or Serology	Tetanus Toxoid	Pre-Employment and Annual Serum Banking	Toxoplasma Serology	Rubeola Vaccine	Q Fever Vaccine
1	Exposure to rodents or rabbits	++	++	o	o	++	o	o	o	o
2	Exposure to Carnivores (dog, cat, ferret)	++	++	o	+++	++	o	F + M o	o	o
3	Exposure to ruminants	++	++	o	+	++	o	o	o	+
4	Exposure to Primates	++	+++	+++	+	++	+	o	+	o

Key: o: Not ordinarily required.
 +: May be advisable in some circumstances.
 ++: Usual practice.
 +++: Essential component of an effective program.

M: Male
 F: Female

NOTE: The occupational health program outlined in Table 5 of NIH Publication No. 92-3415 entitled "Institutional Animal Care and Use Committee Guidebook" may be a useful reference.

12. REFERENCES

- a. Barkley, W.E. and J.H. Richardson, "Control of Biohazards Associated with the Use of Experimental Animals," Laboratory Animal Medicine, J.G. Fox, B.J. Cohen, and F.W. Loew, editors, 595 - 602. (New York: Academic Press, 1984).
- b. Benenson, A. S., Control of Communicable Diseases in Man, 15th edition. (Washington, DC: American Public Health Association, 1990).
- c. Biosafety in Microbiological and Biomedical Laboratories, 4th edition (or latest).
- d. Title 10 Code of Federal Regulations (CFR) Chapter 1, Parts 0-171, Nuclear Regulatory

Commission. **NOTE:** *See Part 20, Standards for Protection Against Radiation.*

e. Guide for the Care and Use of Laboratory Animals, U.S. Department of Health and Human Services, Public Health Service (most recent version).

f. Title 29 CFR Parts 1900-1910, Occupational Safety and Health Administration.

g. Occupational Health, Institutional Animal Care and Use Committee Guidebook. U.S. Department of Health and Human Services, Public Health Service, (Washington, DC: NIH Publication No. 92-3415, 1992).

h. Title 40 CFR Part 261 Subpart D, Lists of Hazardous Wastes. Environmental Protection Agency.

i. Occupational Health and Safety in the Care and Use Nonhuman Primates. National Research Council, ILAR, 2003.

j. VA Manual MP-3, Part III, Safety, Occupational Health and Fire Protection (or superseding document).

ANIMAL COMPONENT OF RESEARCH PROTOCOL (ACORP)

If a medical center chooses to apply for Department of Veterans Affairs (VA) funding for a project involving animal research, they are strongly urged to use the following sample format for providing the required information. **NOTE:** *All abbreviations must be spelled out the first time they are used.*

1. REQUIRED ELEMENTS.**a. Background Information**

- (1) Name of Principal Investigator(s).
- (2) VA facility name and number.
- (3) Proposal title.
- (4) Animal species covered by this Animal Component of Research Protocol (ACORP) (only one). **NOTE:** *A separate list of responses should be provided for each species.*
- (5) The source of funding. Indicate the source(s) of funds that will be used to perform these animal procedures once approved by the VA Institutional Animal Care and Use Committees (IACUC):
 - (a) VA.
 - (b) United States (U.S.) Public Health Service (e.g., National Institutes of Health (NIH)).
 - (c) Private or charitable foundation (if so, identify).
 - (d) University Departmental Funds (if so, identify).
 - (e) Private company (if so, identify).
 - (f) Other (if so, identify).

b. ACORP Status

- (1) If this ACORP does not describe a new project, indicate that the information is for a revised ACORP with a new funding source, a revised ACORP that reflects changes, additional, or new studies, an ACORP submitted as a 3-year renewal, or some other circumstance (specify).
 - (a) Provide the previous ACORP title.
 - (b) Provide the previous IACUC approval number (VA and affiliate, if applicable).

(c) If this is a 3-year renewal, provide a progress report describing work accomplished during the last approval period. Include the number of animals used, the objectives that were met and how the work proposed in this renewal extends the previous study(ies).

(2) Indicate if the animal procedures described will be performed even if VA or extramural Public Health Service (PHS), National Science Foundation (NSF) or other external funding is not received.

(3) Indicate if the type of animal use will be research, teaching or training, testing, sentinel animal use, breeding and colony management only (no experimental procedures), or other (specify).

c. **Lay Description.** Using non-technical (lay) language that a senior high school student would understand, briefly describe how this project involving animals might improve the health of people and/or other animals. **NOTE:** *A scientific abstract from a grant proposal is not acceptable.*

d. **Experimental Design**

(1) Using non-technical (lay) language that a senior high school student would understand, describe the experimental design in no more than one or two paragraphs.

(2) In language scientific colleagues outside of your discipline would understand, describe the experimental design for the animal experiments planned, and the sequence of events to reveal what happens to the animals. Include all procedures and manipulations, and explain why they must be performed. Give the best estimate of how many animals will undergo the procedures or manipulations described. For complicated experimental designs, a flow chart, diagram, or table is strongly recommended to help the IACUC understand what is proposed. Do not describe the details of surgical procedures, monoclonal antibody production, or behavioral training. **NOTE:** *Such details are requested later as attachments.*

(3) Describe the characteristics of the selected species, strain, stock, mutant, or breed that justify its use in the proposed study. Consider such characteristics as body size, species, strain, breed, availability, data from previous studies, and unique anatomic or physiologic features.

e. **Personnel**

(1) Give the names of all research staff expected to work with the animals in this study. For each person, describe the individual's education, training, and experience with experimental animals in general and describe the individual's experience performing the exact procedures in the species described in this ACORP. This description must help IACUC members determine if all animal manipulations, including surgery, testing, and blood collection, are performed by individuals who are qualified to accomplish the procedures skillfully and humanely. **NOTE:** *A listing of academic degrees alone is not an adequate response. Qualifications to perform euthanasia is requested in subparagraph 1u(3) and need not be given here.*

(2) If personnel do not have experience with the exact procedures described in this ACORP, how will they be trained, who will train them, and what are the training experiences or qualifications of the person(s) doing the training? If not applicable, so indicate.

f. **Occupational Safety and Health**

(1) Indicate if all personnel listed in subparagraph 1e have been enrolled in the Occupational Health and Safety Program for those with laboratory animal contact. If not, indicate if personnel have declined to participate, are enrolled in another equivalent program, or will enroll before studies commence.

(2) Indicate if there are any non-routine measures such as special vaccines or additional health screening techniques that would potentially benefit research, husbandry, or veterinary staff participating in or supporting this project. Routine measures included in the Occupational Health and Safety Program (typical vaccinations and Tuberculosis [TB] screening) need not be mentioned.

g. **Animal Use Information.** For the species proposed for use, provide the strain, stock, mutant, or breed designation, the gender, the age or size, the source (vendor), and the health status. For rodents and rabbits, indicate if the animals are specific-pathogen-free (SPF), gnotobiotic (germ-free or defined flora), conventional, feral, or some other description. For dogs, cats, pigs, and other “large animals,” indicate if the animals are SPF, conditioned, conventional, feral, or some other description. For non-human primates, indicate the viral status (e.g., Herpes B, Simian Immunodeficiency Virus [SIV], etc.) and TB status. Also indicate if the animals will be surgically altered by the vendor (e.g., ovariectomized rats).

h. **Pain and/or Distress Categories.** Assign all requested animals by breed, strain, and/or mutant and by proposed year of use to a United States Department of Agriculture (USDA) category of pain and/or distress, then total by proposed year of use. If there is difficulty in determining the appropriate category, contact the attending veterinarian or IACUC Chairperson for assistance. The same animal cannot be assigned to more than one USDA category. If several different procedures are planned, the animal needs to be placed in a category based on the most painful or distressful procedure. VA policy requires that the planned procedures for the 4th and 5th years of a submitted VA grant be described, even though, under PHS policy, the IACUC must perform a new review 3 years after the initial approval date.

(1) **USDA Category B.** List by year the number of animals that will be bred or purchased for breeding, but not used for experiments. This includes breeders, young that cannot be used because of improper genotype or gender, and any other animals that will not have any research procedures performed on them or will not participate in research studies. If numbers cannot be determined exactly, estimate as closely as possible. **NOTE:** *If tail snips are necessary for genotyping, this category is not appropriate.*

(2) **USDA Category C.** List by year the number of animals that will undergo procedures that involve no, or only very brief, pain or distress, with no need for or use of pain relieving

drugs. Examples include: observational studies, most intravenous and parenteral injections of non-irritating agents, most blood collections from peripheral vessels, and the collection of cells and/or tissues from animals after euthanasia has been performed.

(3) **USDA Category D.** List by year the number of animals that will undergo procedures involving potential pain or distress that is relieved by appropriate anesthetics, sedatives, or analgesics. Examples include:

(a) Major and minor surgery performed under anesthesia (survival or non-survival), tissue or organ collections prior to euthanasia, painful procedures performed under anesthesia (such as retro-orbital blood collection in rodents),

(b) Prolonged restraint accompanied by tranquilizers or sedatives, and

(c) Experiments involving infectious or other hazardous materials in animals that have provisions for immediate euthanasia if they become sick to effectively prevent pain and/or suffering.

NOTE: *If an endpoint is used that involves significant pain or distress, consideration needs to be given to putting animals into USDA Category E.*

(4) **USDA Category E.** List by year the number of animals that will undergo procedures in which pain or stress is not relieved with the use of anesthetics, analgesics, tranquilizers, or by euthanasia. Examples include:

(a) Studies in which animals are allowed to die without intervention (e.g., LD₅₀, mortality as an end-point).

(b) Studies that allow endpoints that are painful or stressful.

(c) Addictive drug withdrawals without treatment.

(d) Pain research.

(e) Studies involving noxious stimuli or conditioning.

i. **Description of USDA Category D and E Procedures.** If any USDA Category D or E studies are planned, provide the information in following subparagraphs 1i(1) and/or 1i(2), as is applicable.

(1) For each USDA Category D procedure, describe the procedure, provide the frequency of monitoring after the procedure and how long animals will be monitored, the person(s) who will perform the monitoring, and the analgesic, sedative, or anesthetic used, (plus dose, route, and duration. For any surgical procedures described in Attachment 5, enter only a brief description in the "Procedure" column, and then enter "See Attachment 5 for details."

(2) Each year a report describing and justifying all USDA Category E procedures must be submitted by each facility to the USDA and the VA. Describe each USDA Category E procedure, justify completely why pain or distress relief cannot be provided. If the species is covered by USDA regulations, your description will be used in the USDA Annual Report. If animals will be allowed to experience natural death as a result of experimental procedures (e.g., infectious disease or oncology studies), or an endpoint is used that allows the animals to experience significant pain or distress, you must justify why an alternate endpoint (such as weight loss, clinical signs, tumor size, etc.) prior to death or pain or distress can not be used.

j. **Justification for Number of Animals Requested and Group Sizes.** Describe how the estimated number of animals needed for the experiments was determined. When appropriate, provide the number and type of experimental and control groups in each experiment, the number of experiments planned, and the number of animals in each group. The Institute for Laboratory Animal Research (ILAR) Guide for the Care and Use of Laboratory Animals states that whenever possible, the number of animals requested should be justified statistically. A power analysis is strongly encouraged to justify group sizes when appropriate. *NOTE: An Office of Research and Development (ORD) web-based power calculator at www.researchtraining.org will be available in 2005.*

k. **Laboratory Animal Veterinary Support**

(1) Give the name of the laboratory animal veterinarian responsible for providing adequate care to the animals that will be used, with the individual's institutional affiliation.

(2) VA Policy requires that a laboratory animal veterinarian be consulted during the planning stages of any procedure involving laboratory animals, before IACUC review. Give the name of the laboratory animal veterinarian consulted during the planning of procedures involving animals. *NOTE: As an alternative to an actual meeting, the veterinarian may perform a pre-review of the ACORP and provide comments to the principal investigator so that the ACORP can be revised prior to IACUC review.*

(3) Give the date of the veterinary consultation (meeting date, or date written comments were provided by the veterinarian to the principal investigator).

l. **Husbandry**

(1) **Caging Needs.** To allow the animal care staff to plan for caging needs, indicate the type of caging that will be needed: gnotobiotic (germ-free and defined flora) isolators, biohazard or other special hazard containment caging, sterile rodent microisolator caging with filtered cage top, non-sterile rodent microisolator caging with filtered cage top, standard rodent shoebox caging with no filter top, standard non-rodent caging appropriate for species, or other (describe).

(2) The ILAR Guide for the Care and Use of Laboratory Animals states that consideration should be given to housing social animals in groups whenever possible. Indicate if social animals (such as most mice and rats) will be housed socially or not, or if the species is not considered a social animal.

(3) If social species will not be housed socially, provide a justification for housing them singly.

(4) The ILAR Guide for the Care and Use of Laboratory Animals recommends the use of contact bedding (i.e., shoebox or microisolator cages) instead of wire mesh floors for housing rodents. If rodents will be used, indicate if they will be housed on suspended wire mesh floors or other flooring in which the animals do not rest on bedding.

(5) If rodents will not be housed on contact bedding, provide a justification for not doing so.

(6) The IACUC must ensure that special consideration is given to dogs, primates, and genetically modified animals.

(a) If dogs are proposed for use, is there any scientific justification for excluding the dogs in this study from the institutional dog exercise plan required by USDA?

(b) If primates are proposed for use, is there any scientific justification for excluding the primates from the institutional primate psychological enrichment plan required by USDA?

(c) If genetically engineered or modified animals are proposed for use, do they exhibit any characteristic clinical signs or abnormal behavior related to their genotype or phenotype?

(7) If any cannulae, acrylic implants, venous catheters, or other similar medical devices will be implanted into an animal such that the device extends chronically through the skin, explain what implantation and wound management measures will be taken to minimize the chances of chronic infections around the device(s) where they penetrate the skin.

m. **Housing Sites**

(1) If all animals purchased with VA or VA foundation funds will be housed only in VA facilities, provide the housing locations.

(2) If all animals purchased with VA or VA foundation funds will not be housed only in VA facilities, provide the housing locations off-site, and provide information requested in paragraph 2 of this Appendix.

n. **Antibody Production.** If animals will be used to produce monoclonal or polyclonal antibodies, or if existing hybridoma cell lines will be injected into animals, provide the information requested in paragraph 3 of this Appendix.

o. **Test Substances.** If test substances will be administered to animals, provide the information requested in paragraph 4 of this Appendix. Test substances are defined as materials administered to animals. This includes, but is not limited to: radioisotopes, toxins, antigen, pharmacological agents, infectious agents, carcinogens or mutagens, biomaterials, prosthetic devices, and cells, tissues, or body fluids. ***NOTE:** The following substances do not need to be addressed in paragraph 4 of this Appendix, unless they are hazardous: routine pre- or post-operative drugs described in paragraph 6 of this Appendix, antigens, adjuvants, or hybridomas*

described in paragraph 3 of this Appendix, and euthanasia agents entered in subparagraph 1u, Special Procedures.

p. **Location of Procedures.** The IACUC must be aware of the location of all surgical procedures, as well as the location of all procedures performed outside of the animal research facility.

(1) Indicate the location where all non-surgical procedures will be performed outside the animal research facility. Be sure to include the sites of procedures such as radiography, fluoroscopy, computed axial tomography (CAT), or magnetic resonance imaging (MRI) that may be performed outside the animal research facility.

(2) Indicate the method of transport (if required) through non-research areas to procedure locations outside the animal research facility. Such transport must be discreet so that hospital staff and patients are not aware of the transport, and are not exposed to allergens and/or body fluids from the transported animal(s).

q. **Body Fluid, Tissue, and Device Collection**

(1) Indicate if any body fluids, tissues, or implanted devices or materials will be collected from animals after euthanasia.

(2) Indicate if any body fluids, tissues, or implanted devices or materials will be collected from animals before euthanasia.

(a) If collection in live animals is not limited to blood collection associated with antibody production, complete paragraph 5 of this Appendix. If the body fluid, tissues, implanted devices, or materials are collected as part of a surgical procedure, be sure to describe these collections as part of the surgical protocol in paragraph 6 of this Appendix.

(b) If blood collection associated with antibody collection is already described in paragraph 3 of this Appendix, do not complete paragraph 5 of this Appendix.

r. **Surgery.** If survival or non-survival surgery will be performed, provide the information requested in paragraph 6 of this Appendix.

s. **Endpoint Criteria.** Provide specific endpoint criteria that will be used for determining when sick animals, both on and off study, will be euthanatized or otherwise removed from a study. Examples of appropriate criteria that need to be considered include: a weight loss limit as a percentage of initial or expected body weight, allowable durations of anorexia, allowable tumor size or total tumor burden expressed as a percentage of body weight, the presence of health problems refractory to medical intervention, and severe psychological disturbances. ***NOTE:*** *Other criteria appropriate for the species under consideration should also be considered.*

t. **Euthanasia.** If animals will be euthanatized as part of the planned studies, provide the following information:

(1) Describe the exact method of euthanasia for each animal used. Include the agents used, dose (as applicable), and route of administration.

(2) Indicate if all euthanasia methods proposed are acceptable according to the latest report of the American veterinary Medical Association (AVMA) Panel on Euthanasia. If unsure how to answer, contact the veterinarian or IACUC for guidance. If not, justify any method that is not considered “acceptable” by the latest “Report of the AVMA Panel on Euthanasia.”

(3) List the personnel who will perform euthanasia and indicate their training and experience with the method of euthanasia and the species involved. If personnel are not yet trained, explain how they will be trained before performing euthanasia themselves.

(4) If the animal care staff find an animal dead, describe how the carcass must be handled (e.g., refrigerated or frozen), and indicate if a staff member needs to be contacted immediately.

u. **Special Procedures.** Indicate if any experimental procedures or special husbandry procedures planned that are not described in the local standard operating procedures (SOP) manual or elsewhere in this ACORP. Special procedures can include: special restraint practices (including non-human primate chairing), special animal health monitoring, special diets, caging, environmental control, exercise, environmental enrichment, means of identification, use of noxious stimuli, forced exercise, or behavioral manipulation. If so, complete paragraph 7 of this Appendix.

v. **Consideration of Alternatives and the Prevention of Unnecessary Duplication.**

Complete the following items and retain copies of computer database search results to demonstrate compliance with the law, if regulatory authorities or the IACUC choose to audit the project.

(1) Investigators must consider less painful or less stressful alternatives to procedures, and provide assurance that proposed research does not unnecessarily duplicate previous work. Perform one or more database searches to meet these mandates unless compelling justifications can be made without doing so. In tabular form using a separate row for each database search conducted, provide the following information and indicate for which of the following paragraph(s) the search is relevant (complete information must be provided to comply with USDA Policy #12): name of the database(s), date the search was performed, the period of time covered by each search, and the key words or search strategy used.

(a) Indicate if any of the animal procedures described in this ACORP be replaced by computer models or in vitro techniques? State if such replacement is or is not possible, and provide a narrative on how you came to your conclusion.

(b) Indicate if a smaller, less sentient mammalian species or a non-mammalian species (e.g., fish, invertebrates) can be used to substitute for the mammals in any of the experiments planned. State if such substitution is or is not possible and provide a narrative on how the conclusion was reached.

(c) Indicate if a different animal model or different animal procedure that involves: less distress, pain, or suffering; or fewer animals substitute for any proposed animal model or animal procedure planned. State if such replacement is or is not possible, and provide a narrative on how the conclusion was reached.

(d) State whether the proposed research unnecessarily duplicates previous work. Provide a narrative on how the conclusion was reached.

w. **Other Regulatory Considerations**

(1) **Controlled Drugs.** All drugs used in animals and classified as controlled substances by the Drug Enforcement Agency (DEA) must be stored in a double-locked cabinet, and must be accessible only to authorized personnel in accordance with VHA policy.

(2) List the controlled substances that will be used in animals for this project, and include the building and room number where they will be stored.

(3) To comply with VA pharmacy policies, all controlled substances used on VA property must be ordered through, and received by, the local VA pharmacy prior to issue for research use. Indicate if the use of all controlled substances will comply with these VA pharmacy policies.

(4) If any human patient procedural areas will be used for these animal studies, complete paragraph 8 of this Appendix.

(5) If an explosive anesthetic or other explosive agent will be used in any portion of these animal studies, complete paragraph 9 of this Appendix.

x. **Paragraphs Completed.** To aid reviewers, indicate which of paragraphs 2 through 10 of this Appendix are completed and attached. Do not attach blank Sections which are not applicable to this ACORP. Check with the local IACUC to see if an optional paragraph 10 of this Appendix is required.

y. **Certifications.** If this ACORP will be submitted to VA Central Office for Just-In-Time approval prior to receiving VA funding, the signatures of the Principal Investigator(s), IACUC Chairperson and veterinarian must appear (see subpar. 1z). ***NOTE: The requirement for an Research and development (R&D) Committee Chairperson's signature and the requirement that signatures be less than 1 year old have been dropped.***

z. **Certifications by Principal Investigator(s)**

(1) Provide a dated signature that certifies that:

(a) No personnel will perform any animal procedures until they have been approved by the IACUC.

(b) When new or additional personnel become involved in these studies, their qualifications, training, and experience will be submitted to the IACUC and IACUC approval must be granted before they are involved in animal studies.

(c) All personnel must be enrolled in the institutional Occupational Health and Safety Program prior to their contact with animals, or the personnel must have declined in writing to participate (if allowed by local policy).

(d) After-hours telephone numbers must be provided to the animal care staff in case of emergency.

(e) The information provided in this ACORP must be complete and accurate.

(f) IACUC approval is valid for 1 year only, and that approval must be renewed annually. Every third year the IACUC must perform a new review of the protocol, and a newer version of the ACORP might be required to provide additional information at the time of the triennial review.

(g) IACUC approval must be obtained before:

1. Additional animal species are used, additional animals not approved by the IACUC are used, or there is an increase in the number of procedures performed on individual animals.

2. There is a change in procedures in any way 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. Additional procedures not described in this ACORP are performed.

4. Other investigators are allowed to use animals on this protocol for other protocols, or the animals approved on this protocol are used on another of your IACUC-approved protocols.

(2) **Minority Opinions (For IACUC Use).** IACUC members must be given the opportunity to submit minority opinions. Enter the full text of any minority opinions in this item.

(3) **Approval Signatures.** The Attending Veterinarian and IACUC must provide a dated signature to verify that they have:

(a) Evaluated the care and use of the animals described in the ACORP in accordance with the provisions of the USDA Animal Welfare Act Regulations and Standards, PHS Policy, the Guide for the Care and Use of Laboratory Animals, and VA Policy, and

(b) Found the use of animals described in the ACORP to be appropriate.

2. USE OF A NON-VA FACILITY TO HOUSE ANIMALS PURCHASED WITH VA OR VA RESEARCH AND EDUCATION CORPORATION FUNDS

a. **Location of Housing.** Indicate which non-VA institution will house animals purchased with VA or VA Research and Education Corporation funds for this project, and give the current Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International accreditation status for each (see subpar. 7f in Handbook 1200.7 for policy on AAALAC accreditation). Be sure to consider affiliated institutions and contract facilities that purchase and house animals on your behalf to make custom antibodies or other biological products. Consult with the veterinarian or IACUC to determine which institutions must be entered.

b. **Facility and Room(s).** Give the facility name and room numbers where the animals will be housed.

3. ANTIBODY PRODUCTION

a. **Monoclonal Antibody Production.** Indicate if monoclonal antibodies need be produced in animals or harvested from hybridoma cell lines.

(1) Indicate if antibody harvest is limited to existing hybridoma cell lines with no further immunizations or lymphocyte fusions planned.

(2) If new hybridomas will be produced, provide the following information in tabular form, using a separate row in the table for each immunization day: injection day (e.g., day 0, 7, 30, etc.), antigen, total amount in milligrams (mg) and volume in milliliters (ml) of antigen injected, identity and ml of adjuvant injected, total injection volume per animal (antigen plus adjuvant; ml), number of injections, injection route, and location of injections on body. Also, list possible adverse effects in animals that might be seen from the proposed antigen or adjuvant injections and what measures will be taken should these adverse effects occur.

(3) If feeder cells for supporting hybridoma colony growth will be collected from animals, describe the exact procedures that will be used to collect the feeder cells and the number of animals needed for this purpose.

b. **Consideration of Alternates to Animal Use for Collection of Antibody from Ascites.** If animals will be used to expand hybridoma cell lines, alternate research methods that can replace the use of animals must be considered.

(1) Explain why *in vitro* cell culture systems for harvesting monoclonal antibodies are not adequate to meet the research objectives.

(2) Provide the following information in tabular form:

(a) Hybridoma cell line designation.

(b) Number of animals used for ascites production.

- (c) Priming agent and volume.
- (d) Number and timing of priming injections.
- (e) Volume of injected hybridoma cells.
- (f) Number of abdominal taps before euthanasia.

(3) Indicate what criteria will be used to determine if animals should be euthanatized prior to the last planned abdominal tap.

c. **Blood Collection as Part of Monoclonal Antibody Production.** Indicate if survival blood collections will be obtained from animals following immunization or as a “pre-bleed” prior to immunization.

(1) Provide the following table, including any “pre-bleeds” prior to immunizations:

- (a) Site of blood collection.
- (b) Amount of blood collected expressed as volume (ml) and percentage of body weight (assume 1 ml weighs 1 gram).
- (c) Number of blood collections.
- (d) Interval between collections.

(2) Indicate if anesthetics, tranquilizers, or analgesics will be used prior to blood collection. If none will be used, justify the omission of these agents. Otherwise, provide the agent(s) including dose (mg per kilogram [kg]), volume (ml), route, and frequency and duration.

d. **Polyclonal Antibody Production.** Indicate if polyclonal antibodies will be produced as part of this project.

(1) If so, provide the following information in tabular form, using a separate row for each immunization day, i.e., injection day (e.g., day 0, 7, 30, etc.):

- (a) Antigen.
- (b) Total amount (mg) and volume (ml) of antigen injected.
- (c) Identity.
- (d) Concentration and volume (ml) of adjuvant injected.
- (e) Total injection volume per animal (antigen plus adjuvant; ml).

(f) Number of injections per animal.

(g) Injection route.

(h) Location of injections on body.

(2) In an appropriate format, list the possible adverse effects in animals that might be seen from the proposed antigen or adjuvant injections and what measures will be taken should these adverse effects occur.

e. **Blood Collection as Part of Polyclonal Antibody Production.** Indicate if the survival blood collections are to be obtained from animals following immunization, or as a “pre-bleed” prior to immunization.

(1) Provide the following table, including any “pre-bleeds” prior to immunizations:

(a) Site of blood collection,

(b) Amount of blood collected expressed as volume (ml) and percentage of body weight (assume 1 ml weighs 1 gram).

(c) Number of blood collections.

(d) Interval between collections.

(2) Indicate if anesthetics, tranquilizers, or analgesics will be used prior to blood collection. If none will be used, justify the omission of these agents. Otherwise, provide the agent(s) including dose (mg per kg), volume (ml), route, and frequency and duration.

f. **Terminal Blood Collection.** Indicate if animals used for monoclonal or polyclonal antibody production will be exsanguinated as a method of euthanasia. If so, describe the method of exsanguination. If anesthetics, tranquilizers, or analgesics will not be used prior to exsanguinations, justify the omission of pain-relieving agents. If such agents will be used, describe the administration of pain-relieving agents including dose (mg per kg), volume (ml), route, and frequency and duration. Indicate how the death of animals will be verified following blood withdrawal.

g. **Screening of Antigens.** Indicate how antigens or cell lines will be screened to make sure they do not harbor infectious agents that could infect other laboratory animals or people after injection.

4. TEST SUBSTANCES

a. **Toxic Agents.** Indicate if toxic chemicals, toxic pharmacologic agents, known or suspected mutagens, carcinogens, teratogens, Deoxyribonucleic Acid (DNA)-binding, or other similar agents will be used in animals.

(1) In tabular form, provide the following information, listing each agent in a separate row:

- (a) Agent.
- (b) Diluent.
- (c) Route of administration.
- (d) Dose (e.g., mg per kg) and volume (ml).
- (e) Frequency and duration of administration.
- (f) Reason for administration.
- (g) Expected effects.

(2) Indicate which of the agents, if any, are known or suspected mutagens, carcinogens, or teratogens.

(3) Indicate if any of the agents are on the Centers for Disease Control and Prevention (CDC)-USDA list of “select agents” that might have bioterrorism uses. If so, ask the facility research office to contact the VA Central Office Biosafety Officer for further instructions as soon as possible. A CDC license and VA Central Office approval must be obtained before beginning any study(ies) with this agent.

(4) Indicate if the animals are to be anesthetized or sedated when these agents are administered. If so, detail the method of anesthetic, sedative, or tranquilizer administration including agent, dose and volume, and route.

b. **Infectious Agents.** Indicate if bacterial, viral, rickettsial, fungal, protozoal, or other infectious agents are to be used in animals. If the agent will have a radioactive label added, also provide the information requested in subparagraph 4d when prompted. Likewise, if the infectious agent contains recombinant nucleic acid, fill out item in subparagraph 4f.

(1) Provide the following data in tabular format, with each agent on its own row:

- (a) Agent and strain or construct.
- (b) CDC biosafety level (BSL) of agent (BSL1, 2, 3, 4).
- (c) Route of administration.

(d) Dose (e.g., CFU, PFU) and volume administered (ml).

(e) Frequency of administration.

(2) Indicate if an antibiogram, anti-viral drug sensitivity screen, or other appropriate drug sensitivity panel has been determined for the agent(s) listed in order to assist physicians in selecting proper therapy if an inadvertent human infection occurs.

(3) Indicate if the animals are to be anesthetized or sedated when these agents are administered. If so, detail the method of anesthetic, sedative, or tranquilizer administration including agent, dose and volume, and route.

(4) Indicate if any of the agents on the CDC-USDA list of “select agents” that have bioterrorism uses. If so, ask the facility research office to contact the VA Central Office Biosafety Officer for further instructions as soon as possible. A CDC license and VA Central Office approval must be obtained before beginning any study(ies) with this agent.

c. **Biological Materials.** Indicate if serum, cell lines, tissue, nucleic acid or other biological materials will be administered to animals. If any of the agents are radioactive or will have a radioactive label added, describe the agent in subparagraph 4d.

(1) Provide the following information in tabular form with each agent on its own row:

(a) Material (e.g., fluid, cells, tissues).

(b) Diluent.

(c) Source (e.g., vendor, other animals, colleague).

(d) Route of administration;

(e) Dose (e.g., ml per kg, mg per kg, cells per kg) and volume (ml).

(f) Frequency and duration of administration.

(g) Reason for administration.

(h) Expected effects.

(2) Indicate if the animals will be anesthetized or sedated when these agents are administered. If so, detail the method of anesthetic, sedative, or tranquilizer administration including agent, dose and volume, and route.

(3) Indicate how these materials will be screened to make sure they do not harbor infectious agents that could infect other laboratory animals or people.

d. **Radioactive Agents.** Indicate if radioactive compounds or agents will be administered to animals.

(1) Provide the following information in tabular form, each agent in its own row:

- (a) Radioactive agent (include isotope).
- (b) Diluent.
- (c) Agent dose (mg per kg) and volume (ml).
- (d) Activity (e.g., mCi/kg).
- (e) Route of administration.
- (f) Frequency and duration of administration.
- (g) Reason for administration.
- (h) Expected effects.

(2) Indicate which investigator has been given permission by the Radiation Safety Committee, or equivalent committee, to utilize the isotope(s).

(3) Indicate if the animals are to be anesthetized or sedated when these agents are administered. If so, detail the method of anesthetic, sedative, or tranquilizer administration including agent, dose and volume, and route.

e. **Other Agents.** Indicate if other substances not listed previously will be administered to animals. Do not include anesthetics, analgesics, and/or sedatives that are described elsewhere as part of surgery and post-operative care.

(1) Provide the following information in tabular form with each agent on its own row:

- (a) Substance.
- (b) Diluent.
- (c) Dose and volume,
- (d) Route of administration,.
- (e) Frequency and duration of administration.
- (f) Reason for administration.

(g) Expected effects.

(2) Indicate if the animals will be anesthetized or sedated when these agents are administered. If so, detail the method of anesthetic, sedative, or tranquilizer administration including agent, dose and volume, and route.

f. **Recombinant Nucleic Acid and Recombinant Infectious Agents.** If any of the substances described in paragraph 4 of this Appendix are recombinant constructs not exempt from the animal research guidelines included in the latest version of the NIH Guidelines for Research Involving Recombinant DNA Molecules, consult with the facility Biosafety Committee and veterinarian to make sure you comply.

g. **Pain or Distress.** If animals will potentially experience pain and/or distress as a result of the administration of agents listed in this paragraph, describe the nature of the pain and/or distress that animals might experience and describe measures that will be taken to alleviate any pain and/or distress.

h. **Hazardous or Toxic Agents.** If any of the agents listed are hazardous or toxic to humans or animals, or covered by the NIH Guidelines for Research Involving Recombinant DNA Molecules, provide the name of the agent, the safety, biosafety, or radiation safety committee that has approved the use of this hazardous agent, and whether the committee was a VA or affiliate committee, and a list all animal research facility staff who will come in contact with animals given these agents or with contaminated bedding, cages, or other items.

(1) Discuss how the animal research facility staff listed have been (or will be) informed of the possible risks of exposure, and have been (or will be) trained to avoid exposure to these agents.

(2) **Signatures and Certifications.** If any hazardous agents will be used in animals, provide evidence of approvals by the Principal Investigator(s), Attending Veterinarian, Biosafety Officer or Chairperson, Research Safety or Biosafety Committee, Radiation Safety Officer, or Chairperson, Radiation Safety or Isotope Committee, and IACUC Chairperson by their signatures such that the following certifications are provided:

(a) Before any animal experiments involving any hazardous agents are performed, SOPs designed to protect all animal research facility staff as well as non-study animals must be developed and approved by the appropriate VA or affiliated university safety committee and the IACUC.

(b) All staff that might be exposed to these agents must be informed of possible risks and must be properly trained to follow the SOPs to minimize the risk of exposure.

5. ANTEMORTEM SPECIMEN COLLECTION

a. **Blood Collection.** If blood will be collected from animals, provide the following information in tabular form with each procedure on a separate row: site and method of blood

collection, amount of blood collected, expressed as volume (ml) and percentage of body weight (assume 1 ml of blood weighs 1 gram), number of blood collections, and interval between collections.

b. **Use of Anesthetics, Tranquilizers, or Analgesics for Blood Collection.** If anesthetics, tranquilizers, or analgesics will not be used to prevent pain or stress during collection of blood, justify their omission (either scientifically or because the collection method involves no or momentary pain) and completely describe the physical restraint that will be used during collection. Otherwise, provide the following data in tabular format: anesthetic, tranquilizer, or analgesic agent, dose (mg per kg) and volume (ml), route, and frequency.

c. **Other Tissue Collection.** If other body fluids (e.g., cerebrospinal fluid, peritoneal fluid, urine) or tissues will be collected from live animals (awake or anesthetized), provide the following information in tabular format, each tissue or fluid in a different row:

- (1) Tissue or fluid collected.
- (2) Site.
- (3) Method of collection.
- (4) Amount (gram) or volume (ml).
- (6) Interval between collections.

d. **Use of Anesthetics, Tranquilizers, or Analgesics for Collection of Fluids or Tissues.** If anesthetics, tranquilizers, or analgesics will not be used to prevent pain or stress during collection of body fluids or tissues, justify the omission of pain-relieving agents (either scientifically or because the collection method involves no or momentary pain) and completely describe the physical restraint that will be used during collection. Otherwise, provide the following in tabular form with each agent in a separate row:

- (1) Anesthetic, tranquilizer, or analgesic agent.
- (2) Dose (mg per kg) and volume (ml).
- (3) Route.
- (4) Frequency.

6. SURGERY

a. **Major Survival Surgery.** The Guide for the Care and Use of Laboratory Animals defines a major survival surgery as a surgery in which a major body cavity is penetrated and exposed or surgery in which substantial impairment of physical or physiological functions is produced. Examples of such surgeries provided in the Guide for the Care and Use of Laboratory

Animals include: laparotomy, thoracotomy, craniotomy, joint replacement, and limb amputation. Indicate if more than one major survival surgery will be performed and if so, provide a complete scientific justification for performing more than one major survival surgery on individual animals, and give the interval(s) between the multiple surgeries, and the rationale for choosing the interval(s).

b. **Description of Procedure(s)**. Describe the surgical procedure(s) in enough detail so that the IACUC reviewers can determine what procedure(s) are actually being performed. If several different surgeries are being performed, be sure to describe each one.

c. **Personnel**. Provide the names of the personnel who will perform the surgery, and note that the surgical experience of each person involved in the surgery.

d. **Anesthetist**. Provide the names of the personnel who will perform the anesthetic induction and monitor the animal during surgery.

e. **Location of Surgeries**. Provide the building and room number(s) where the surgical procedure(s) will be performed. A dedicated surgical facility must be used for major survival surgeries on non-rodent species (see subpar. 6a). If allowed by local policy, non-survival surgery on non-rodent species and survival surgery on rodent species may be performed in a procedure room or laboratory.

f. **Pre-Operative Procedures**. Pre-operative procedures need to include all preparations of the animal(s) for surgery.

(1) Indicate which of the following procedures will be performed: fasting (rarely used in rodents or rabbits; provide the length of the fasting period), withhold water (provide the length of time that water will be withheld), catheter placement (location).

(2) Describe any additional pre-operative procedures.

g. **Pre-Operative Medications**. Provide the following information in tabular form, including any antibiotics, sedatives, or tranquilizers, and the anesthetic agent(s) that will be used to induce anesthesia prior to surgical site preparation, with each agent in a separate row:

(1) Agent.

(2) Dose (mg per kg) and volume (ml).

(3) Route.

(4) Frequency (e.g., times per day).

(5) Duration (e.g., days).

h. **Preparation of the Surgical Site.** Describe how the surgical site(s) will be prepared prior to surgery. Include details of hair-clipping, skin disinfection, and the use of surgical drapes.

i. **Intraoperative Medications.** Provide the following information in a tabular format, one row per agent, including any anesthetic agents, paralyzing agents, fluids, or other pharmaceuticals that will be administered to the animal during surgery (include experimental pharmaceuticals):

- (1) Agent.
- (2) Dose (mg per kg) and volume (ml).
- (3) Route.
- (4) Frequency (e.g., times per day).

j. **Paralyzing Agents.** Federal regulations prohibit the use of paralytics (neuromuscular blocking agents) for surgery, unless other appropriate anesthetic agents are used to induce a surgical plane of anesthesia. Paralytics do not provide any pain relief; therefore, animals are unable to respond physically to pain because motor reflexes are paralyzed. If such agents will be used, justify the use of these agents and indicate how the animals will be monitored to ensure that the depth of anesthesia is sufficient to prevent pain.

k. **Physical Support.** Indicate any physical methods used to support the animal during surgery (e.g., heating pads, blankets, etc.).

l. **Intra-Operative Monitoring.** Describe the method(s) to be used to monitor the state of anesthesia and general well-being of the animal during surgery.

m. **Survival Surgery Considerations and Post-Operative Care.** If survival surgery will be performed, indicate how long will the animal survive after surgery.

(1) Indicate which of the following procedures will be used to maintain a sterile field during surgery:

- (a) Sterile instruments.
- (b) Surgeon cap.
- (c) Sterile gloves.
- (d) Surgeon scrub.
- (e) Sterile drapes.

(f) Sterile gown.

(g) Face mask.

(2) Describe any other procedures not listed.

(3) List any physical methods used to support the animals in the immediate post-operative period (e.g., heating pads, blankets, fluids, etc.).

(4) Unless scientifically or otherwise justified to the IACUC's satisfaction, one is obligated to routinely provide post-operative pain relief for all vertebrate animals undergoing survival surgery. Indicate if the use of analgesics is planned to provide post-operative pain relief to the animal following surgery. If not, provide a justification for not using postoperative analgesics. If so, provide the following in tabular format, each agent on its own row:

(a) Agent.

(b) Dose (mg per kg) and volume (ml).

(c) Route.

(d) Frequency (e.g., times per day).

(e) Duration (e.g., days).

(5) Complete the following table for other medications (such as fluids, antibiotics, anti-coagulants, and other pharmacological agents) that will be administered post-operatively, using a separate row for each agent:

(a) Agent.

(b) Dose (mg per kg) and volume (ml).

(c) Route.

(d) Frequency (e.g., times per day).

(e) Duration(e.g., days).

n. **Frequency and Responsibility for Post-operative Care.** The names and after-hours telephone (or other contact) numbers of the personnel listed in following subparagraphs n(2) and n(3) must be provided to the Veterinary Medical Unit (VMU) staff in case of an emergency.

(1) Give the frequency of postoperative monitoring and how long the monitoring will continue.

(2) Indicate who will be responsible for post-operative care until the animal can ambulate without danger to itself.

(3) Indicate who will be responsible for post-operative care thereafter (including after-hours, weekends, and holidays).

o. **Post-operative Complications**

(1) Describe any possible or expected post-operative complications and what will be done if these complications arise.

(2) Provide criteria by which a decision to euthanize a surgical animal post-operatively will be made.

(3) In case there is an emergency medical situation and appropriate staff cannot be reached, identify drugs or classes of drugs that should not be used as part of the treatment plan.

(4) In the event that emergency euthanasia must be performed, or an animal is unexpectedly found dead, indicate how the carcass should be handled.

p. **Responsibility for Maintaining Animal Post-surgical Medical Records.** Indicate who will be responsible for maintaining accurate, daily, post-surgical written medical records.

q. **Certifications.** With a signature, the principal investigator(s) must certify that each animal under observation or treatment will be identified such that care for individual animals can be documented:

(1) That daily postoperative medical records of the animal must be maintained, including an evaluation of overall health, a description of any complications noted, treatment provided, and the removal of sutures, staples, wound clips, or other such devices;

(2) That records will document administration of all medications and treatments given to animals, including those given to reduce pain or stress;

(3) That daily records will cover the post-operative period as defined by local policy;

(4) That each entry in the records will include a signature or the initials of the person making the observation or treatment;

(5) All records will be readily available to the veterinary staff or the IACUC for review; and

(6) That the names and contact numbers of persons to notify or consult in case of emergencies will be provided to the facility manager and veterinarian.

7. SPECIAL HUSBANDRY AND PROCEDURES

a. **Special Husbandry.** Indicate if special husbandry practices not described in the local SOP manual will be required for this protocol. Examples of special husbandry practices could include temperature extremes, food or water deprivation, dietary manipulations, calorie restrictions, special housing and/or caging, modified light cycle, special health monitoring, and unusual means of identification.

(1) Provide a complete description of all non-standard practices or procedures, including the frequency and duration of these practices or procedures.

(2) Justify the use of these non-standard practices or procedures.

b. **Other Procedures.** Indicate if other procedures such as prolonged physical restraint, use of noxious stimuli, forced exercise, behavioral manipulations, total or partial body irradiation, radiography or other imaging studies are planned but not described elsewhere. Describe each procedure and the expected outcome(s) in detail, to include the frequency, duration, and interval between repeated manipulations, if appropriate.

c. **Personnel.** Indicate who will perform the procedures and practices described in subparagraphs 7a and 7b, and indicate who is responsible for monitoring the condition of these animals. After-hours telephone (or other contact) numbers of the personnel listed must be provided to the veterinary staff in case of an emergency. For all personnel, provide the following information:

(1) Role (performing procedure and/or monitoring).

(2) Office phone.

(3) Pager or cell phone number.

(4) After-hours contact number.

(5) E-mail address.

d. Indicate if these practices or procedures have the potential to cause more than momentary pain and/or discomfort. If so, describe the potential pain and/or discomfort.

(1) Indicate if pain or stress-relieving agents will be administered to the animals that experience pain and/or discomfort. If not, provide a scientific justification for not using pain or stress relieving agents. If so, provide the following data in tabular form, one row per agent:

(a) Agent.

(b) Dose (mg per kg) and volume (ml).

(c) Route.

(d) Frequency (e.g., times per day).

(e) Duration(e.g., days).

(2) Describe the methods used to monitor the condition of the animals during and after the procedures and the criteria that will be used to remove individual animals from these procedures should pain or suffering be present.

8. REQUEST TO USE PATIENT CARE PROCEDURAL AREAS FOR ANIMAL STUDIES

a. Provide the name of Principal Investigator(s).

b. Provide a concise statement of the potential benefit to VA patients if a patient care area is used for research involving animals.

c. Explain why the animal research facility or a laboratory area cannot be utilized for the proposed procedures.

d. Identify the species and number of animals to be used.

e. Discuss the potential pain and/or distress to animal subjects during the procedures to be conducted in a patient procedural area, and interventions planned for the prevention or alleviation of such pain and/or distress.

f. Identify the equipment and location (building and room numbers) of the patient care area(s) to be used.

g. List the date(s) and time of day that the procedure(s) will be performed.

h. Discuss the method of transporting the animals to and from the procedural area. Include a description of the transport containers, any vehicles used, and the precautions to be taken to avoid contact with patients, visitors, and other non-research personnel.

i. Provide a complete description of the measures to be taken to prevent the transmission of zoonotic pathogens from animals to patients and patient care personnel.

j. Provide a complete description of the measures to be taken to prevent disturbances (e.g., noise, odors) to patients and patient care personnel.

k. Provide a complete description of methods to be employed to prevent contamination of equipment and room surfaces by animal feces, urine, saliva, blood, or other body fluids.

l. Provide details of the procedures to be followed in cleaning and disinfecting equipment and room surfaces following use.

m. Obtain approval in the form of signatures from the attending veterinarian and the IACUC Chairperson, responsible medical administrators in charge of the area and/or equipment, and the facility Director.

9. REQUEST TO USE EXPLOSIVE AGENT IN ANIMAL RESEARCH FACILITY OR IN ANIMALS

- a. Provide the name(s) of the Principal Investigator(s).
- b. Give the name(s), title(s), and prior pertinent training and experience of individuals who will administer the explosive agent.
- c. Provide the name of the explosive agent(s), and the Material Safety Data Sheet number(s).
- d. Explain why a non-explosive agent or agents cannot be used instead.
- e. Give the beginning and ending dates during which the explosive agent(s) will be used.
- f. Give a brief description of the studies for which the use of an explosive agent is proposed.
- g. Give the species, weight, and approximate number of animal subjects that will be administered the explosive agent(s).
- h. Give the building and room number in which agent(s) will be used.
- i. Give a detailed description of the procedure(s) involving the explosive agent(s) including assurance that:
 - (1) Procedures are performed within a properly operating, ventilated safety hood.
 - (2) All electrical equipment used with the agent are placed and powered outside the hood.
 - (3) Once the seal is broken on containers of ether or other explosive anesthetic agents, they will be placed into a safety hood throughout use, stored in an explosion proof refrigerator, or safety hood, and discarded properly once used up.
 - (4) That proper disposal procedures for items (including carcasses) containing traces of the agent will be safe and appropriate.
- j. Obtain the following signatures for approval:
 - (1) IACUC Chairperson.
 - (2) Attending Veterinarian.

(3) Facility Safety Officer.

(4) ACOS for R&D.

(5) VISN Safety Officer.

10. LOCAL INFORMATION. Provide any further information required by the local VA IACUC.

**DEPARTMENT OF VETERANS AFFAIRS (VA) INSTITUTIONAL ANIMAL CARE
AND USE COMMITTEES (IACUCS) SEMI-ANNUAL SELF-REVIEW ITEMS**

1. IDENTIFICATION OF MEDICAL CENTER. In large type, provide the name and number of the medical center, the official address of the medical center, and the date(s) of the Department of Veterans Affairs (VA) animal care and research use program review.

2. CHECKLIST FOR PROGRAM REVIEW. For each following review item, indicate if the item is not applicable, if compliance is acceptable, if a deficiency is classified as a minor deficiency, or if a deficiency is classified as significant.

a. Institutional Animal Care and Use Committee (IACUC) Policies and Responsibilities

(1) The IACUC consist of at least five members, appointed by the Institutional Official (IO) for renewable terms.

(2) The members include an Attending Veterinarian, a VA scientist with animal research experience, and other lay and non-affiliated members.

(3) The Chairperson is appointed by the medical center Director for 1 year renewable term.

(4) The IACUC reports to the Research and Development (R&D) Committee and the IO when appropriate.

(5) The IACUC is responsible for oversight and evaluation of the institution's program.

(6) The IACUC conducts semi-annual evaluations of the animal care and research use program at the VA medical center.

(7) The IACUC either:

(a) Conducts oversight and evaluation of the animal care and research use program (facilities) at all other institutions that house VA animals, or

(b) Reviews and evaluates the semi-annual review of another IACUC in lieu of its own review of those programs (facilities).

(8) The IACUC conducts semi-annual inspections of all VA animal facilities, laboratory and other procedure areas, and rooms that hold animals more than 12 hours.

(9) IACUC semi-annual review includes all areas where animals are housed more than 12 hours, and all areas where procedures on animals are performed.

(10) The IACUC ensures that a veterinary consult is provided prior to IACUC review of protocols.

(11) The IACUC ensures that a VA Animal Component of Research Protocol (ACORP) is used for review when applications are to be submitted for VA funding.

(12) The IACUC ensures that procedures are in place for review and approval of all VA-funded research regardless of performance location.

(13) The IACUC ensures that procedures are in place for review and approval of all animal research performed at VA regardless of funding source.

(14) The IACUC ensures that procedures are in place for review and approval of significant changes to all protocols prior to initiation of changes.

(15) The IACUC ensures that policies are in place for special procedures (e.g., multiple surgeries, restraint).

(16) The IACUC ensures that program and procedures are in place for use of hazardous agents in animal research.

(17) The IACUC has procedures in place to review and investigate internal or external concerns or allegations about animal care or use.

(18) The IACUC has procedures in place to prevent reprisals against whistle blowers who report potential deficiencies in the animal care and research use program, and to protect anonymity to the extent required by law.

(19) The IACUC has procedures in place for suspension of animal activities if warranted by findings and after majority vote of quorum.

b. IACUC Reporting Requirements

(1) IACUC minutes meet formatting requirements in VA Handbook 1200.7, subparagraph 8f(1).

(2) IACUC minutes are submitted for review by the VA R&D Committee, then, if requested, are sent to the Chief Veterinary Medical Officer (CVMO) at VA Central Office,

(3) Semi-annual reports are reviewed and signed by medical center Director after IACUC approval.

(4) IACUC and Associate Chief of Staff (ACOS) meet with the facility Director to discuss semi-annual report.

(5) Semi-annual Reports are submitted to CVMO within 60 days of review.

(6) Minority IACUC opinions are included in semi-annual reports and minutes.

(7) Departures from The Guide for the Care and Use of Laboratory Animals or Public Health Service (PHS) Policy are detailed, and reasons for departure are given.

(8) Significant deficiencies are distinguished from minor deficiencies in the semi-annual report.

(9) The IACUC and IO notify the CVMO, the United States Department of Agriculture (USDA), Office of Laboratory Animal Welfare (OLAW), the funding agency, Association for Assessment and Accreditation of Laboratory Animal Care, International (AAALAC), and the Office of Research Oversight (ORO) within 15 business days of instances of serious non-compliance.

(10) The IACUC and IO notify CVMO, USDA, OLAW, the funding agency, AAALAC, and ORO within 15 business days of suspensions of protocols.

(11) The IACUC and IO notify CVMO, USDA, OLAW, AAALAC, and ORO within 15 business days of failure to correct major deficiencies.

(12) USDA Annual Report is submitted to USDA as part of the VA Research and Development Information System (RDIS) Part II Report.

(13) Animal species not covered by the USDA Animal Welfare Act (AWA) Regulations are included in the Veterinary Medical Unit (VMU) Annual Report.

(14) The AAALAC Program Description is submitted triennially, and the AAALAC Annual Report is submitted annually to AAALAC.

(15) The AAALAC Annual Report and other correspondence to and from AAALAC are sent to CVMO and ORO.

(16) Annual VA VMU report is sent to CVMO.

(17) PHS Assurance, annual updates, and correspondence to and from OLAW are sent to CVMO and ORO within 15 business days of receipt or mailing.

c. **IACUC Records Requirements**

(1) Minutes of IACUC meetings and semi-annual reports are kept for 3 years.

(2) IACUC documents are kept for 3 years after end of study.

(3) The IACUC randomly reviews IACUC records representing at least 5 percent of the total active projects (no fewer than 5) to determine if appropriate documentation is present in records (see VHA Handbook 1200.7).

(4) All PHS, USDA, ORO, AAALAC, and other reports and correspondence related to the animal care and research use program are maintained for at least 3 years.

d. Personnel Qualifications And Training

(1) IACUC ensures that all personnel on a protocol have been properly trained before IACUC approval is given.

(2) IACUC has established and implemented a web-based annual training program compliant with Handbook 1200.7, or an alternative training program approved by the CVMO.

(3) The training program includes professional, management, supervisory personnel, and:

(a) Animal care personnel.

(b) Investigators, instructors, technicians, trainees, and students.

(c) Humane practices of animal care (e.g., housing, husbandry, handling).

(d) Humane practices of animal use (e.g., procedures, anesthesia, surgery).

(e) Research methods that minimize animal numbers.

(f) Research methods that minimize animal pain or distress.

(g) Use of hazardous agents and access to Occupational Safety and Health Administration (OSHA) hazard notices.

e. Occupational Health and Safety (OHS) of Personnel. The OHS Program is established and compliant with Appendix C of VA Handbook 1200.7 and covers all personnel listed in par. 10c(1) who work in laboratory animal facilities.

(1) The facility provides laundry service, uniforms, and all personal protective equipment needed free of charge to employees.

(2) The OHS Program is based upon hazard identification and risk assessment.

(3) The personnel training provided is appropriate for species used, and hazardous agents used (e.g., zoonoses, hazards, special precautions).

(4) Husbandry and technical staff understand and use proper personal hygiene procedures during work (e.g., work clothing, laboratory policies).

(5) Procedures are in place for proper use, storage, and disposal of hazardous materials.

(6) Procedures are in place to provide appropriate personnel necessary protective equipment such as masks, respirators, gowns, eye protection equipment, boots, etc.

(7) A program is in place for medical evaluation and/or preventive medicine based upon risk.

(8) A pre-employment evaluation is offered to employees to make sure the workplace does not pose unnecessary risks.

(9) Immunizations offered are appropriate (e.g. rabies, tetanus).

(10) Zoonosis surveillance is appropriate for species housed (e.g., Q-fever, LCMV, parasites).

(11) Procedures are in place for reporting and treating injuries, including bites, etc.

(12) Special precautions are in place for personnel who work with primates.

(a) Tuberculosis screening includes all potentially exposed personnel.

(b) Training and implementation of procedures are in place for bites and scratches, including procedures and supplies to immediately treat human exposure to *Cercopithecine herpesvirus 1* (Herpes B).

(13) Education is provided regarding *Cercopithecine herpesvirus 1* (Herpes B) infections when susceptible primates are housed.

f. **Veterinary Medical Care**

(1) Institutional arrangement is present with a veterinarian with appropriate laboratory animal qualifications.

(2) Back-up veterinary care has been arranged when primary veterinarian is not available.

(3) Veterinarian can access all animals and animal procedure areas as needed.

(4) Emergency, weekend, and holiday veterinary care of animals has been arranged.

(5) Veterinarian oversees:

(a) Daily care of animals.

(b) Disease prevention and control.

(c) The quarantine program.

(6) Veterinarian provides oversight and guidance for:

(a) Treatment of disease.

(b) Surgery programs.

(c) Pre- and post-surgical care.

(d) Anesthesia, analgesia, and euthanasia procedures.

(7) Intra- and post-operative surgical records must be maintained on larger non-rodent species in accordance with accepted veterinary practice.

(8) Controlled substances are handled in accordance with paragraph 7 in VA Handbook 1200.7.

(9) All visits by part-time veterinarians are documented.

3. CHECKLIST FOR FACILITIES REVIEW. For each review item listed below, indicate if the item is not applicable, if compliance is acceptable, if a deficiency is classified as a minor deficiency, or if a deficiency is classified as significant.

a. **Policies And Responsibilities**

(1) Animal procurement is from authorized vendors only.

(2) Primary enclosures, cage, or shelters are appropriate for species housed.

(3) Social environment, i.e., appropriate for the species housed.

(4) A compliant primate enrichment program exists.

(5) Exercise for dogs is provided when mandated by AWA Regulations.

(6) Special procedure policies (e.g., diet restriction, prolonged restraint) are conducted per IACUC approval.

(7) Use of specialized housing (e.g., barrier, isolation when appropriate, etc.) is utilized just as it was approved by the IACUC.

(8) Food, water, and bedding is appropriate for species housed.

(9) Animal handling is appropriate for the species housed.

(10) Cage or room sanitation is appropriate for the species housed.

- (11) Waste disposal meets facility, municipal, and Federal policies and regulations.
- (12) Animal identification is appropriate for the species housed.
- (13) Medical/surgical records are accessible and appropriate for species housed.
- (14) Genetics, i.e., the nomenclature of species is accurate on protocol forms and on cage cards.
- (15) Animal transportation inside facility is discreet and compliant with institutional policy.
- (16) Animal transportation between facilities is in climate-controlled vehicles, when appropriate, and compliant with institutional policy.
- (17) Emergency, holiday/and weekend husbandry care of animals is provided.

b. Physical Facilities

- (1) Procedural laboratories that house animals longer than 12 hours, must meet animal housing standards.
- (2) All rooms and laboratories in which animal procedures occur are visited by the IACUC as part of the facility review.
- (3) Specialized space (e.g., barrier, surgery, quarantine, necropsy) is maintained properly and safely utilized.
- (4) Support facilities (cold storage, restrooms) are properly maintained and safely utilized.
- (5) Facility maintenance problems are reported and corrected in a timely fashion.
- (6) Ventilation is monitored to ensure adequate air changes and proper directional air flow.
- (7) HVAC motors, belts, and equipment are on a regular preventive maintenance program to prevent HVAC failures.
- (8) Emergency power is available to power HVAC equipment in the animal research facility in the event of an electrical outage, or an effective plan exists to provide supplemental cooling or other measures to maintain temperatures within the ranges dictated by the Guide for the Care and Use of Laboratory Animals.
- (9) Reheat coils in animal rooms fail in the off position to prevent catastrophic overheating of animals.
- (10) Air changes per hour in animal rooms meet standards in the Guide for the Care and Use of Laboratory Animals.

- (11) Directional air flow is proper to ensure a safe working environment and control of infectious agents.
- (12) Air is flowing into the animal research facility from outside areas to reduce allergen and pathogen exposure outside the facility.
- (13) Wall, ceiling and floor finishes allow for appropriate sanitation.
- (14) Paint on the animal housing services is intact and not chipped or cracked.
- (15) Ceiling tiles and plaster ceilings that experience water damage must be replaced in a timely fashion to prevent mold growth.
- (16) Requests for emergency facility repairs are addressed in a timely fashion by institutional personnel to prevent distress to animals and personnel.
- (17) Temperature and humidity in animal rooms are monitored to ensure that they stay within acceptable ranges.
- (18) Temperature and humidity in animal rooms stay within normal ranges.
- (19) Noise levels are controlled to prevent distress to animals and personnel.
- (20) Facility cage, equipment, and sanitation methods meet standards in the Guide for the Care and Use of Laboratory Animals.
- (21) Cage wash and autoclave temperatures are monitored to meet applicable standards in the Guide for the Care and Use of Laboratory Animals.
- (22) Room care records document that husbandry staff observe animals on a daily basis and clean and water animals as is appropriate.
- (23) Soiled bedding disposal procedures are appropriate.
- (24) Infectious waste generated by animal experiments is handled appropriately.
- (25) Vermin control measures are adequate, and do not unnecessarily compromise animal and human health or scientific studies.
- (26) Security measures meet requirements in subparagraph 7k of VHA Handbook 1200.7.
- (27) The ability of facilities management personnel to properly detect and respond to elevations in animal room temperatures is tested and retested as required by subparagraph 7b(2)(c) in VHA Handbook 1200.7.

4. LIST OF INVESTIGATOR LABORATORIES, HOLDING AREAS, AND PROCEDURE AREAS OUTSIDE THE ANIMAL RESEARCH FACILITY WHERE ANIMALS ARE UTILIZED, MANIPULATED, OR HOUSED

Provide the location, investigator(s), species utilized, and a brief description of procedures performed. Note any deficiencies.

5. IMPORTANT REGULATORY NOTES

a. **Scope of the Semi-annual IACUC Self-assessment**. The semi-annual self-assessment must include all VA facilities and investigator areas where laboratory animals are used in procedures or housed for more than 12 hours. It must include all facilities and programs that house animals purchased with VA funds (see subpar. 3c in VHA Handbook 1200.7). If the animals are housed in a satellite or an affiliate facility, a formal arrangement may be made between the VA IACUC and the facility in order that the VA IACUC may review that facility's semi-annual self-assessment as an IACUC business item instead of sending a VA IACUC team to inspect that facility and program. If the VA IACUC does not set up this type of agreement, the facility and its animal care and research use program must be evaluated as part of the VA IACUC semi-annual self-assessment report.

b. **Definition of a Significant Deficiency**. Nearly identical definitions of a significant deficiency are found in the USDA AWA Regulations and PHS Policy. The two definitions follow:

(1) **USDA Animal Welfare Act Regulations, 9 C.F.R. §2.31(c)(3)**, "A significant deficiency is one which, with reference to Subchapter A, and, in the judgment of the IACUC and the Institutional Official, is or may be a threat to the health or safety of the animals."

(2) **Public Health Service Policy on Humane Care and Use of Laboratory Animals, IV. Implementation by Institutions, paragraph B.3**, "...a significant deficiency is one which, consistent with this Policy, and, in the judgment of the IACUC and the Institutional Official, is or may be a threat to the health or safety of the animals. If program or facility deficiencies are noted, the reports must contain a reasonable and specific plan and schedule for correcting each deficiency..."

6. TABLE OF PROGRAM AND FACILITIES DEFICIENCIES

For each deficiency noted in paragraphs 1-4 in this appendix, provide in tabular form the location of the deficiency (if applicable), a description of the deficiency, the reason(s) for the deficiency, a plan for correction, whether the deficiency is classified as minor or significant, the timetable for correction, and (when appropriate) the date corrections are complete.

7. POST-REVIEW DOCUMENTATION

a. **Documentation of Review Team.** In tabular format, provide the typed name, role on IACUC (Chairperson, veterinarian, scientist, lay member, non-affiliated member), and note participation in the program review and/or the facility review.

b. **Documentation of Minority Opinion(s).** Any member who wishes to provide a minority opinion **MUST** be allowed to do so. Provide the text of any minority opinion.

c. **Documentation of Review and Approval By IACUC Members.** A majority of all voting members (not a majority of a quorum) must approve and sign the review. The review must be completed within 1 month of the self-assessment for IACUC review. In tabular format, for each member, provide the typed name, role on the IACUC, signature, and date to certify that members:

(1) Have reviewed and approved all items in Appendix E,

(2) Have read any minority opinions appearing in this report, and

(3) Hereby authorize IACUC representatives to review this report with the medical center Director.

d. **Statement of AAALAC Accreditation.** *NOTE: See PHS Policy on Humane Care and Use of Animals, par. IV.B.3. Indicate if all facilities and programs covered by this review are accredited by AAALAC.*

e. **Communication with the Medical Center Director.** VHA Handbook 1200.7 stipulates that a majority of all voting IACUC members must approve the report and indicate their approval by signatures next to their typed names and roles on the committee. The VMO and/or VMC, the IACUC Chairperson, and the ACOS for R&D must discuss the report in a face to face meeting with the medical center Director (other IACUC members may also attend); then the medical center Director must sign the report indicating that the Director has reviewed the report during a face to face meeting with the IACUC representatives. *NOTE: The Director's signature does not imply that the Director agrees with the report, but once approved by the IACUC, it may not be altered by any official. A discussion of disputed items may be provided in a cover memo. The Director's signature acknowledges receipt of the report, and verifies that the Director has personally discussed its contents with the IACUC. No other official may sign for the facility Director.*

f. **Final Processing.** A signed copy of the complete report must be sent through the ACOS for R&D and the medical center Director to the CVMO within 60 days of the self-assessment date. The R&D Committee needs to review the approved report as an item of business, but R&D approval is not required before submission of the final document to the CVMO. Send a photocopy with all signatures to the CVMO. The original must be retained for at least 3 years.