The University of Vermont
Institutional Animal Care and Use Committee
Serving The University of Vermont
http://www.uvm.edu/iacuc/

MANUAL FOR VERTEBRATE ANIMAL RESEARCH

Research Protections Office
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Summary of Changes Since February 2016 version

7.A.4. Veterinary Verification and Certification (NEW)

This section was added to reflect a new review type, in accordance with OLAW Guidance #NOT-OD-14-126, allowing the veterinarian alone to review and administratively approve certain procedures, changes to drugs/anesthetics, changes in housing location and euthanasia methods within AVMA guidelines.

7.D. 3. Six Year Renewal (new content)

This section was updated to incorporate the new procedures for submitting protocols for 6-year renewal. Section is now titled “Continuing Review and 6-Year Renewal”

Attachment C. Animal Use Protocol Amendment Algorithm

Updated to reflect Veterinary Verification and Certification (VVC) process

Attachment D & E: Performance of Repeat Procedures and Formulary for Rodents

These attachments describe actions that the Veterinarian alone can approve administratively through the Veterinary Verification Consultation review type.

RESEARCH MANUAL FOR VERTEBRATE ANIMAL RESEARCH:

[Click here for a printer friendly PDF version.]

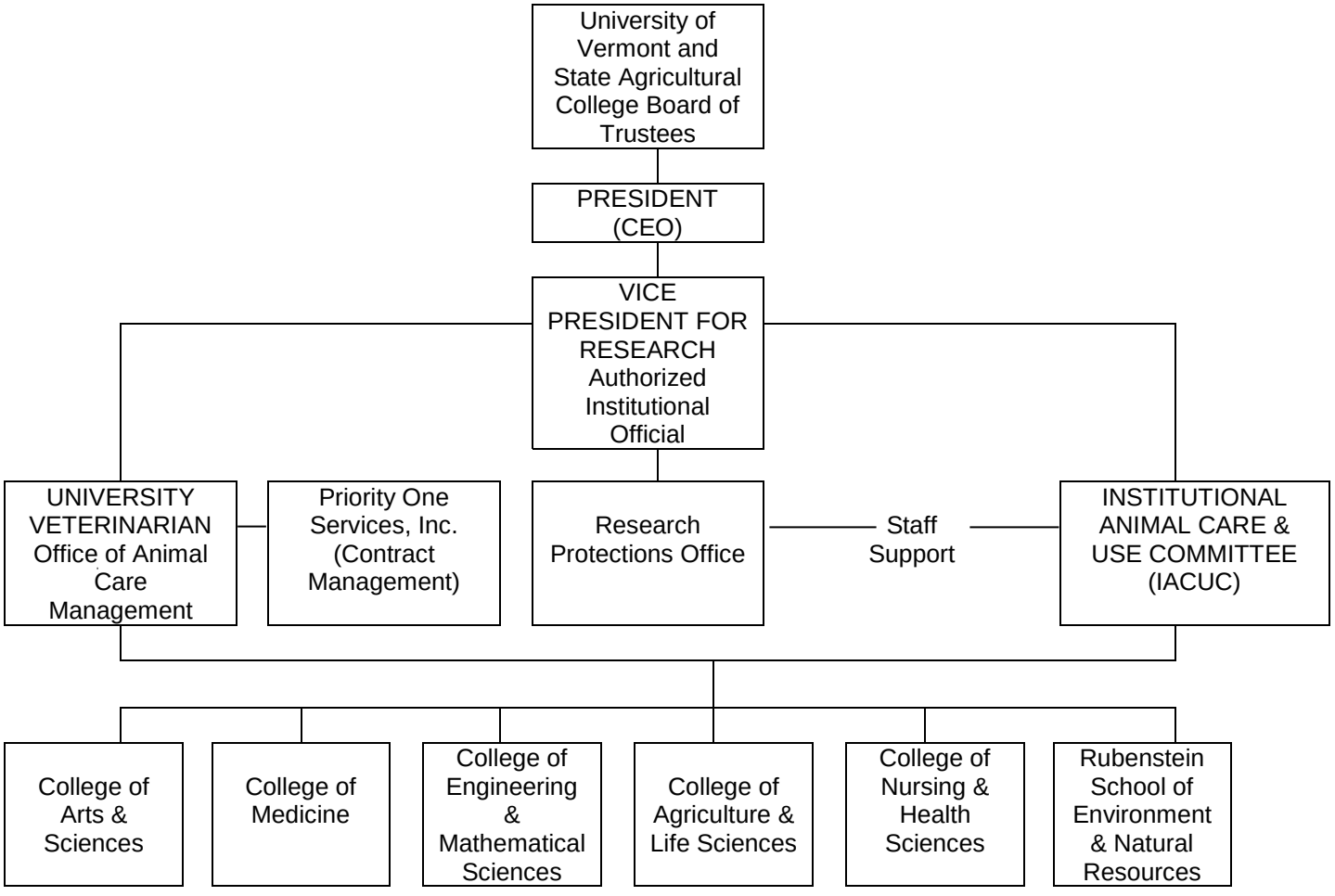
Attachments

1. COMMITTEE'S MISSION

The University of Vermont is committed to the humane care and use of animals in activities related to research, testing and teaching. The University has adopted the animal care principles in accordance with the Guide for the Care and Use of Laboratory Animals ("the *Guide"*), and in compliance with applicable federal, state, and local laws and regulations, such as the federal Animal Welfare Act, and Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS).

The University of Vermont Institutional Animal Care and Use Committee (IACUC) has an Assurance on file with the Office of Laboratory Animal Welfare in accordance with the PHS Policy. The Committee is regulated by the USDA under the Animal Welfare Act as documented in the Code of Federal Regulation Title 9, Subchapter A Parts 1, 2 and 3. The University's Animal Care and Use Program is fully accredited by AAALAC International.

Assuring laboratory animal welfare necessitates a partnership among the Institutional Official (IO), the IACUC, the University Veterinarian and the investigators. Ultimately, accountability for assuring humane care and use of the animals resides with the institution, but this may only be achieved when all the constituents contribute to this shared goal. The following organizational chart clearly outlines the direct lines of responsibility and corresponding authority.



In order to accomplish the objectives inherent in these regulations and principles, there are primarily two organizational components designated to ensure their implementation in the overall animal care and use program.

1. The Institutional Animal Care and Use Committee (IACUC) is the University's central review body for matters relating to the care, use and treatment of animals in these areas. The IACUC office is located within the Office of Sponsored Programs.

2. The Office of Animal Care Management is responsible for oversight of all animal care and use and for ensuring compliance with federal, state and local regulations. The University Veterinarian is the Director of this office.

3. Priority One Services, Inc. is the contract manager for the Animal Resources Center.

2. COMMITTEE'S RESPONSIBILITIES/AUTHORITY/COMPOSITION

The IACUC was established in accordance with the Animal Welfare Act and the Health Research Extension Act under the authority of the Vice President for Research and Dean of the Graduate College to ensure the humane care and use of animals for research and education at the University under optimum conditions, which, at a minimum, comply with all pertinent laws.

The Office of Animal Care Management (OACM)/Animal Resources Center (ARC) is administered by the University Veterinarian/Priority One Services, Inc. and is charged with the veterinary care and husbandry of the animals, the occupational health and safety of personnel, and ensuring the appropriate training of personnel working with animals in accordance with all relevant regulations and guidelines governing the humane care and use of animals. The University Veterinarian and the OACM are under the authority of the Vice President for Research and Dean of the Graduate College.

2.A. Responsibilities and Authority

1. Review and report at least once every six months, on the evaluation of the research facility's program for the humane care and use of animals.

2. Inspect, evaluate and report to the Institutional Official, at least once every six months, inspection findings of the institution's animal facilities, including satellite facilities and animal study areas.

3. Review and investigate legitimate concerns involving the care and use of animals at the institution.

4. Make written recommendations to the Institutional Official regarding any aspect of the research, animal program, facilities or personnel training.

5. Review and have authority to approve, require modifications in (to secure approval), withhold approval of those sections of applications or proposals related to the care and use of animals.

6. Review and have authority to approve, require modifications in (to secure approval) or withhold approval of proposed significant changes regarding the use of animals in ongoing activities.

7. Notify investigators and the institution in writing of its decision to approve or withhold approval of those activities related to the care and use of animals, or of modifications required to secure IACUC approval as set forth in the PHS Policy at IV.C.4.

8. Conduct continuing review of each previously approved, ongoing activity covered by PHS Policy at appropriate intervals as determined by the IACUC, including a complete

review in accordance with the PHS Policy at IV.C. 1-4. at least once every three years.

9. Be authorized to suspend an activity involving animals as set forth in the PHS Policy at IV.C.6.

2.B. Composition

Committee membership is comprised of members with varying professional and personal backgrounds and who have demonstrated a genuine interest in and commitment to the purpose of the Committee. Membership includes one Doctor of Veterinary Medicine, one practicing scientist, one member whose primary concerns are in a nonscientific area, one individual who is not affiliated with the institution in any way other than as a member of the IACUC.

3. CONTACTS

The administrative office of the Committees on Human Research is located in 213 Waterman Bldg, 85 South Prospect St, Burlington, VT 05405, (802) 656-5040. The RPO staff as well as a list of the current Committee Chairs and the Veterinarian is located under contacts on our website.

4. OFFICE OF ANIMAL CARE MANAGEMENT (OACM)

As stated above, the University Veterinarian administers the Office of Animal Care Management (OACM), which is charged with the veterinary care and husbandry of the animals, the occupational health and safety of personnel, and ensuring the appropriate training of personnel working with animals in accordance with all relevant regulations and guidelines governing the humane care and use of animals.

Further information is available at web site http://www.uvm.edu/~oacm/
The main OACM office is located in 116 Hills Building. Administrative personnel are as follows:

Dr. Ruth Blauwiekel, University Veterinarian 656-0459 drruth@uvm.edu

John Lovelette, Business Manager 656-2206

Project Manager, Priority One Services, Inc., 656-1006 facmgr@med.uvm.edu

5. TRAINING REQUIREMENTS AND OCCUPATIONAL HEALTH

Initial training is web-based and includes:

- General training (IACUC procedures, the principles of the Three R's, methods for minimizing animal pain and distress, facility access and logistics, use of PPE, basic animal observation and restraint, reporting animal welfare concerns). A supplemental training on statistical design and justification of animal numbers is provided online.
- Surgery and anesthesia module (surgical planning and preparation, aseptic technique, choices of anesthetics, administration and monitoring, intra- and post-operative support, documentation, analgesia)
- Euthanasia (humane methods, operation of euthanasia chambers, considerations for fetal and neonatal rodents, confirming death, disposal of carcasses)
- Controlled substances use (procurement, storage, record-keeping, disposal)

Personnel having completed any training module take an on-line learning assessment which is logged in the Blackboard web-based instructional system. IACUC staff members have access to this system and confirm that a person has completed the relevant modules prior to addition to the protocol roster. Additional on-line resources are available pertaining to justification of animal numbers (biostatistics), rodent analgesia and animal census procedures. "Hands-on" biomethods training is offered on an as needed basis by the Veterinary Technicians, who keep a roster of those who have been trained. When the University Veterinarian participates in training (such as for surgical procedures or confirming competence in conditionally-acceptable methods of euthanasia), this training is documented.

Training of Animal Care staff includes review of relevant SOP's, one-on-one training by the Facility Manager, and "shadowing" of more experienced personnel. In addition, Animal Care staff all review the IACUC and the RM&S on-line training and complete the learning-assessment tools.
Other opportunities for training include staff and animal user meetings and seminars, a quarterly Animal Care newsletter, and postings to the Animal Care list-serve.

Appropriate level training must be complete for all key personnel prior to protocol or amendment approval release. The various training requirements are listed below

5.A. General Training

A formal program for training and education about the use of animals in research is established along the guidelines of the Guide, OLAW Assurance, USDA Regulations & the “Education and Training in the Care and Use of Laboratory Animals” National Research Council publication. General training is required for all persons working with animals prior to using animals.

A web-based program referred to as “General” training course for all individuals has been developed. The program includes a short on-line exam. Participation in the “General” training program is required and is documented.

Persons identified as requiring further training by the veterinarians are encouraged to enroll in a hands-on research rodent training session which is given by the veterinary technicians. This practicum focuses on restraint, biology of mice and rats, colony management, sample collection, injection techniques and other methods.

The general course discusses occupational health risks of dealing with animals. In addition, basic precautions to avoid exposure to animal pathogens and allergens are emphasized in the training session with the veterinarian. See Section 5.E. for additional information regarding the Occupational Health and Safety Program.

Didactic training is provided on a regular basis, covering topics such as record-keeping, anesthesia, surgical techniques, post-operative analgesia, and euthanasia.

5.B. Specific Training

5.B.1.a. Working With Hazardous Agents in Animals

Those involved with the use of hazardous agents/organisms are primarily trained for working with those agents/organisms in their research laboratories by the PI. The Office of Environmental Safety (OES) monitors the use of chemical and biohazardous agents and the Radiation Safety Office (RSO) monitors radiation exposure.

NOTE: All projects proposing to utilize recombinant DNA or infectious agents require review and approval from The Institutional Biosafety Committee (IBC) prior to IACUC

submission. The IBC is charged with reviewing all research projects and activities involving recombinant DNA (as outlined in the "Guidelines for Research Involving Recombinant DNA Molecules") to assure that specific practices for constructing and handling (i) recombinant DNA molecules and (ii) organisms and viruses containing recombinant DNA molecules are followed. The IBC is also charged with responsibility for reviewing the use of infectious agents in research at UVM. A representative of the Office of Environmental Safety serves on the IBC, as does the Director of the Department of Risk Management, the University Veterinarian, the Radiation Safety Director, and faculty of the College of Medicine with particular expertise in infectious agents. For more information go to http://www.uvm.edu/ibc/ and http://www.uvm.edu/~radsafe/.

The OES offers Chemical Safety Training which covers general laboratory safety and an overview of regulations, OSHA laboratory standards and the UVM Chemical Hygiene plan. Training may also be provided by the person's laboratory supervisor, provided that training is adequately documented. Chemical labeling and storage requirements and a copy of the UVM Laboratory Safety Audit are available on the OES website http://esf.uvm.edu/

The RSO requires that a person complete Radiation Safety Training prior to using radioisotopes or radiography in the laboratory. A certification exam is required at the completion of the course. The Radiation Safety Handbook is available online.

All animal caretakers are instructed and trained by the ARC Facility Manager in the husbandry, sanitation procedures and precautions to be followed when working in any biohazard area. Each protocol utilizing hazardous agents requires an instruction sheet which is reviewed by the Facility Manager with the caretakers and is posted on the animal room door. The instructions on the sheet include animal and personnel safety.

Refer also to the "Biohazardous Materials" policy.

5.B.1.b. Personnel Performing Surgery

There is a web-based surgery training course that must be completed. After completing the web portion and submitting the test to ARC, the researcher wishing to perform surgery must meet with one of the veterinarians to review the protocol surgical procedures in detail.

Protocol procedures include drug usage, anesthesia procedures, pre-surgical care, surgical procedures, and post-surgical care. Discussions include proper animal preparation, preparation and use of instruments and other surgical materials. Also included are requirements for gowning and gloving, proper sterile technique when operating on animals, locations for performing the surgery, and tissue handling during surgery.

5.B.1.c. Personnel Performing Anesthesia

Anesthetic agents are discussed in the surgery web-based training (above). Anesthetic monitoring, recovery and record-keeping are discussed in the one-on-one surgical training given by the veterinarians. Personnel who do not have prior experience with rodent procedures are also encouraged to enroll in a biomethods training offered by the veterinary technicians, in which each participant anesthetizes their own animal using injectable agents.

5.B.1.d. Personnel Carrying Out Euthanasia Procedures

Again, web-based training is required for personnel performing euthanasia, in addition to

a meeting with one of the veterinarians. For protocols utilizing a conditional form of euthanasia, personnel must be observed by a member of the veterinary staff while performing the procedure to certify that the person is proficient in the technique.

5.C. Continuing Training

Ongoing “hands-on” training for present and incoming research personnel is provided by the veterinary staff. Regularly scheduled small group sessions cover restraint, injection and sampling techniques, recognition of common health problems, aseptic technique, anesthesia and euthanasia. This training is provided to individuals on an as-needed basis following consultation with the University Veterinarian.

5.D. Other Resources

Workshops, guest speakers and/or consultation on various relevant topics such as research models and mouse colony management are provided to the research community.

Library support for searches for alternatives to animal use and/or procedures which cause more than momentary or slight pain and distress to animals is available through the University Library Services. The Office of Animal Care Management and the Research Protections Office have numerous reference materials available.

Information on the following topics is also available: Levels of discomfort/distress in animal experimentation; anesthetic and analgesic drug formulary for different species; AVMA Guidelines for Euthanasia.

Self-study materials on handling and basic manipulative procedures for commonly used laboratory animals are available.

Video tapes are available on ethics, animal uses, handling techniques, and surgery both in the library and the OACM office. The Northern Mountain Branch of AALAS meets three times a year and is open to all involved in the use of animals.

5.E. Occupational Health and Safety Program

The University's Department of Risk Management & Safety (RM&S) has contracted with an occupational health provider, Champlain Medical, to provide occupational health monitoring for University personnel who work with animals. A written risk assessment survey must be completed by each person listed on an active IACUC protocol. This survey is routed through the Research Protections Office (RPO) and logged before being forwarded to Champlain Medical. Access to the animal facilities is not granted to personnel until they have completed and returned the survey. For Animal Care workers, the medical evaluation includes a physical exam, pulmonary function test and review of immunization status. Animal Care employees are required to have a current tetanus immunization; tetanus vaccination is offered and encouraged for other personnel. For University employees and students, the risk assessment is used to determine who should receive additional follow-up and remediation (which may include pulmonary function test, use of an N95 mask, appropriate immunizations, or other precautionary measures). An annual reassessment is required for all personnel and students who continue to work with animals.

Zoonotic agents, animal allergies and other hazards are described in the on-line IACUC training for personnel and assessment of these risks is addressed in the risk assessment form that is submitted to Champlain Medical. The annual re-assessment form addresses

changes in health status such as pregnancy or immunocompromise. Animal Care staff members must read and sign off on a written SOP before performing any activity that may be hazardous and in addition are personally trained by the Facility Manager. All research personnel who work with infectious agents sign an informed consent document acknowledging that they are aware of the hazards and have read the relevant SOPs. In the case of infectious agents, personnel who are immunocompromised or women who are pregnant are informed of the risk and advised to notify their supervisors. Minor injuries (such as animal bites, sprains, etc.) are treated at Champlain Medical or at the University of Vermont Medical Center. University of Vermont Medical Center emergency services are readily accessible for more serious injuries should they occur.

Risk Management & Safety (RM&S) manages laboratory safety and hazardous chemical waste and the use of radioisotopes on campus. RM&S oversees the use of chemical and biological agents to ensure that they are used safely and in accordance with all applicable government regulations and University policies and procedures. RM&S also conducts training in the handling of hazardous chemicals, biohazardous agents and blood-borne pathogens. RM&S staff members conduct regular audits of each laboratory as described in UVM's Environmental Management Plan (http://esf.uvm.edu/uvmemp/).

The University of Vermont has an Institutional Biosafety Committee (IBC) in accordance with the NIH "Guidelines for Research Involving Recombinant DNA Molecules" and other relevant federal regulation. Investigators utilizing recombinant DNA and/or infectious agents must submit a protocol to the IBC for review and approval. The University Veterinarian may determine during pre-submission of an IACUC protocol that a concurrent IBC application should be prepared and submitted to the IBC. In addition, the Biosafety Officer or his designate reviews the Hazardous Materials section of any IACUC protocol utilizing hazardous chemicals, ionizing radiation, infectious agents or recombinant DNA, and conducts laboratory risk assessments as appropriate. This shared membership and communication between the IACUC and the IBC helps to ensure that risks are recognized and managed effectively.

Animals exposed to or treated with infectious agents are maintained in rooms with double barriers in filter-topped caging or in semi-rigid isolators. When appropriate, a Class II Biosafety cabinet (BSCll) is used for husbandry and other procedures. Laboratories using infectious agents in animals must submit information about the agent and an SOP for working with the animals to the Animal Facility Manager Containment practices and other information relative to the specific biological agent housed in a room then are posted on the animal room door. For chemical agents, animals' cages are marked with special cage cards and the bedding and caging are handled as appropriate to the agent. For biological agents, bedding and other animal wastes are either double-bagged in a BSCll and sealed/boxed for incineration or autoclaved prior to disposal in the regular trash. All BSCll are certified annually.

Personal Protective Equipment (PPE) appropriate to the room is indicated by signage on the door and discarded in the anteroom prior to exiting the area. PPE is provided by the animal facility for use by research personnel as well as animal care staff. This PPE may include isolation gowns and masks, gloves, shoe covers, bouffant head covers, N95 respirators, face shields and Tyvek coveralls, depending on the agent and procedures.

All research personnel who work with infectious agents must report any accident involving exposure to the agent to their supervisor immediately and visit the emergency room or consult with the Infectious Disease Physician on call. A plan of action is filed with the IBC and prophylactic antibiotics/vaccines may be inventoried in either the laboratory or the University of Vermont Medical Center pharmacy, depending on the risk assessment and plan for that specific agent. Serology may be done to detect changes in antibody titer and further follow-up is conducted as deemed appropriate by the Infectious Disease Physician.

There are no nonhuman primate species or small ruminants currently in use as models at UVM.

All animal care personnel are provided with work garments for daily routine wear (usually scrubs, occasionally coveralls), which are laundered by commercial arrangement (Unifirst). All animal care personnel are provided with rubber steel-toed boots or shoes, plastic aprons, heavy rubber gloves, ear protection, goggles, fit-tested respirators and other PPE when required. Hands are washed upon leaving an animal holding room; each room has a sink and antimicrobial soap available. When departing one building for another, caretakers are required to change to street clothes and change to clean scrubs when entering the next facility. No work-issued clothing is taken home or worn outside the animal care areas.

Animals traveling to any laboratory or procedural space outside of the animal facilities must be in filter-topped caging on a cart and covered by draping material, a box, or some other secondary container. Signage is posted in any elevators which are used for animal transport.

Exceptions: Undergraduate students whose exposure is limited to one hour per week per semester, research involving aquatic animals, or personnel who work only with animal products are not required to enroll in the program. Undergraduate students are made aware of the program and are provided with information about risks. Students in need of attention should contact the Student Health Center. While IACUC Board members are not required to take part in the program, they are strongly encouraged to participate if they attend semiannual inspections.

Any other exceptions to required program enrollment are considered on a case-by-case basis by the UVM veterinarian.

5.F. Animal Science Student Training

Department of Animal Science students, with assistance from faculty advisors, develop individualized programs that lead to rewarding careers in a wide variety of occupations. These programs apply to farm, laboratory, zoo, and companion animals; their interaction with human society; and the contribution of animal products, such as milk and meat, to the world food supply. For these classes a web-based training has been developed which can be found at http://asci.uvm.edu/animal_testing/index.html.

This training is appropriate for the required classes. If the role of the student, however, involves responsibilities not typically required of the class, such as husbandry or procedures with the animals, the student would be required to take additional training as appropriate. The University Veterinarian should be contacted by the instructors for guidance.

6. FELLOWS, RESIDENTS, POST-DOCTORAL FELLOWS, ASSOCIATES, TRAINEES, AND STUDENTS CONDUCTING VERTEBRATE ANIMAL RESEARCH

Fellows, residents, post-doctoral fellows, post-doctoral associates, post-doctoral trainees, and students (graduate or undergraduate) cannot conduct vertebrate animal research without having a faculty sponsor/instructor who is responsible for overseeing the research activities.

The faculty sponsor is responsible for:

a) reviewing the materials for submission to the IACUC for accuracy and completeness;
b) assisting and supporting the student in his/her interaction with the IACUC and for overseeing the resolution of any issues arising during the review process; and

c) oversight of the student's research to ensure that the protocol is followed as approved.

Students who are principal investigators have responsibilities as listed in Investigator Responsibilities.

7. COMMITTEE REVIEW AND SUBMISSION PROCESS

7.A. Types of Review

All projects (with or without internal or external funding) which involve the use of vertebrate animals must undergo IACUC review and receive approval prior to initiation. **Investigators are required to consult with the veterinarian and obtain her signature on the final protocol form prior to submitting the protocol form to the Committee.** There are three types of Committee review: full, designated or administrative. Determination of the type of review is usually based upon the expected level of animal pain or discomfort and types of procedures. For pain levels see policy "Determination of Levels of Pain & Distress."

NOTE: Any projects proposing to utilize recombinant DNA or infectious agents, requires review and approval from The Institutional Biosafety Committee (IBC) prior to IACUC submission. The IBC is charged with reviewing all research projects and activities involving recombinant DNA (as outlined in the "Guidelines for Research Involving Recombinant DNA Molecules") to assure that specific practices for constructing and handling (i) recombinant DNA molecules and (ii) organisms and viruses containing recombinant DNA molecules are followed. The IBC is also charged with responsibility for reviewing the use of infectious agents in research at UVM. A representative of the Office of Environmental Safety serves on the IBC, as does the Director of the Department of Risk Management, the University Veterinarian, the Radiation Safety Director, and faculty in the College of Medicine with particular expertise in infectious agents. For more information go to http://www.uvm.edu/ibc/ and http://www.uvm.edu/~radsafe/.

7.A.1. Full Committee Review

A full committee review is required for all protocols with pain levels of D or higher. The IACUC uses a primary/secondary reviewer method for full Committee reviews. The primary reviewer is always a scientific representative of the Committee and is responsible for presenting a summary of the protocol at a fully convened meeting along with any concerns or points requiring clarification and/or stipulations. A secondary reviewer is usually assigned by the IACUC Chair. The secondary reviewer adds any additional concerns. The University Veterinarian then outlines any additional issues and then the review is opened for discussion by the Committee. All Committee members are provided relevant materials and have access to all other documentation related to the study.

7.A.2. Designated Review

Protocols that meet the criteria for designated review are posted to allow all IACUC members an opportunity to review. If no member calls for a Full Committee review, the IACUC Chair will assign one Committee member and the University Veterinarian to complete the review. The reviewers' comments and clarifications and/or stipulations are resolved with the investigator. The Designated IACUC reviewer or the IACUC Chair may at any point call for a Full Committee Review.

7.A.3. Administrative Review

The chair alone (or his/her designee from the Committee) reviews and approves actions in this category. This category captures review of actions that do not require an actual Committee review, e.g., minor amendments, some continuing reviews, previously approved protocols that have been resubmitted or identical protocols submitted to different funding agencies, protocols with no direct animal use, or when funds will be used for salary support only on a previously approved protocol.

7.A.4. Veterinarian Verification and Certification

The Veterinarian alone reviews and approves actions in this category. The changes that can be handled administratively by the veterinarian alone include:

- Procedures outlined in Guidelines for the Performance of Repeat Procedures (Attachment D)
- VVC Formulary for Rodents (Attachment E)
- Changes in housing location
- Euthanasia methods within the AVMA guidelines for Euthanasia of Animals.

7.A.5. Projects in which Animal Use is Limited to Animal Products

Animal products is defined as material obtained from a USDA slaughterhouse, animal byproducts, or shared animal products from other investigators. These projects do not require IACUC review. For additional information see the Animal Tissue policy.

7.A.6. Projects in which Animal Use is Limited to Teaching Activities

Protocols in which animal use is limited to teaching activities may be submitted using the Teaching Protocol form in lieu of the Animal Use Protocol form. This form is primarily used for Animal Science projects that are primarily or solely used for teaching purposes when pain category is less than C, which do not include procedures that cause more than momentary pain or distress. Researchers are still required to submit teaching protocols to the University Veterinarian for review prior to submitting it to the Committee. Contact RPO staff for advice.

7.B. Criteria for Review

All proposed activities are reviewed to ensure that the following federal requirements for granting IACUC approval are met:

Activities -- All activities involving animals must be in accordance with USDA Regulations/PHS Policy.

Animal numbers and group sizes – The IACUC requires that the experimental design be described and animal numbers justified either with a power calculation or a reference to previously-published work of comparable scientific design. A biostatistician serves on the Committee and has the specific charge of evaluating the numbers justification section. An online biostatistics tutorial providing guidance for the investigators was launched in the spring of 2013.

Harm/benefit analysis – All protocols which entail more than momentary pain/distress (USDA category D or E) are reviewed in a convened meeting of the IACUC. During the discussion, the IACUC notes the responses of the investigator to the rationale for utilizing animals and the potential significance of the work. For protocols which entail more than momentary pain/distress without provision of analgesia, a specific scientific justification for withholding analgesia is required. If the Committee has further questions regarding the harm/benefit analysis, the investigator may be required to provide further clarification prior to approval of the protocol.

Search for alternatives – In the case of any protocol which entails more than momentary pain or distress to the animals, the investigator must perform a literature review seeking alternatives which could achieve the same scientific objectives with a lesser degree of pain/distress. The investigator must describe in a narrative what leads him/her to the conclusion that there are no alternatives to the proposed procedures.

Rationale and Methods -- All proposals must include:

- •Identification of the species and the approximate number of animals to be used;
- • A rationale for involving animals and for the appropriateness of the species and numbers of animals to be used;
- • A complete description of the proposed use of the animals;
- • A description of procedures designed to assure that discomfort and pain to animals will be limited to that which is unavoidable for the conduct of scientifically valuable research, including provision for the use of analgesic, anesthetic, and tranquilizing drugs where indicated and appropriate to minimize discomfort and pain to animals; and
- • A description of any euthanasia method to be used.

Note: Some investigators have requested to use videotaping as part of their protocol. Videotaping cannot be used as a substitute for protocol monitoring activities and there are strict criteria about controlling access, especially if it is being viewed externally. Contact the RPO for advice.

Duplication -- Assurance that activities do not unnecessarily duplicate previous efforts must be provided.

Surgery -- Requirements for sterile surgery and pre/postoperative care must be met. An animal may not be used for several major operative procedures from which it will recover, without meeting specified conditions.

Euthanasia--The euthanasia method must be consistent with the recommendations of the current AVMA Panel on Euthanasia (2000 edition or later).

Housing/Health -- Animal living conditions must be consistent with standards of housing, feeding and care directed by veterinarian or scientist with appropriate expertise. Medical care must be provided by qualified veterinarian.

Qualifications --Personnel must be appropriately trained and qualified. Completion of all the University of Vermont's Office of Animal Care Management training program is required for all individuals working with animals or identified on a protocol.

Deviation from Requirements --Must be justified for scientific reasons, in writing.

The Committee's review process always includes a check for compliance with all applicable IACUC or institutional policies and procedures.

7.C. Initial New Protocol Review and Submission Process

7.C.1. Initial New Protocol Review

Any project with USDA pain level D or above requires a “full committee” review. (see 7.A.1. above).

Any project with USDA pain level C or below may qualify for a “designated” review. (see 7.A.2. above)

IACUC review efforts focus on the appropriateness of animal numbers, procedures and adequacy of investigator skills. Normally scientific peer review is left to outside funding agencies. In lieu of outside review, IACUC requires the department of record to certify that the research project has scientific merit.

7.C.2. Initial New Protocol Submission

Meetings are routinely held on the fourth Monday of each month. The deadlines for submission of materials for full committee review are: the first Monday of the month to the Veterinarian and the second Monday of the month to the IACUC office. The decision as to the type of review a proposal receives (designated or full committee) is based on the expected level of animal discomfort and types of procedures. Protocols are placed on the agenda as they come in.

Step 1: Submission of the Protocol. After consultation with the University Veterinarian and obtaining the veterinarian's signature, an investigator submits a completed IACUC protocol to the IACUC Research Review Administrator.

Step 2: Initial Review. Following the receipt of a Protocol, the type of review a proposal will receive (full, designated or administrative) is determined based on the expected level of animal pain and distress and types of procedures proposed. This determination is usually made by the IACUC chair in consultation with IACUC staff. The veterinarian also may be consulted if there is a question about the type of review which is appropriate. Protocols designated USDA Pain level "D" or "E" are given full review at a convened IACUC meeting. Completeness of the protocol also is checked by the RPO staff at this time.

Step 3: Review (By Type). At convened monthly meetings, the IACUC considers new protocols requiring full committee review and reviews the Reports of Designated Reviews and Reports of Administrative Reviews. Possible outcomes of the Committee's review include unqualified Approval, Modifications Required to Secure Initial Approval or Withhold Approval.

7.C.3. Review of Grants

The IACUC is required to ensure that all research described in a grant application or proposal is entirely consistent with any corresponding protocol(s) reviewed and approved by the IACUC. Any discrepancies must be resolved prior to the start of the project. The IACUC works with Pre-Award Services to establish that an appropriate connection is made between the application and the protocol being reviewed.

7.C.3.i. New Competing or Competing Renewal Grant Applications

To meet the requirement listed above, any time you will be submitting a *new competing* grant or *a competing renewal application*, a new protocol must be submitted to the IACUC for review and approval. Pre-Award Services will not clear funds for release until there is an approved protocol. Continued approvals will be checked on an annual basis for the life of the grant.

Note: It is very important that the proposal and protocol be matched correctly for the reason mentioned above.

7.C.3.ii. When the Project is a New Competing or a Competing Renewal Application and the New Protocol is Identical or Substantially Similar to an Approved Protocol

Obtaining grant funding is extremely competitive. The same grant proposal may be submitted to multiple funding agencies at once or the same agency at different time points. If you obtain new funding, it is your responsibility to submit the corresponding grant and protocol for IACUC review and approval.

The IACUC treats identical protocols as new applications, however, a new committee review may not be required if the project is the same or substantially similar to the previously approved protocol.

If this is the case, you must submit the following:

1. One copy of your new grant application and the corresponding protocol.
2. A letter to the committee chair explaining that you are submitting a similar grant application to a different funding agency. State that this new protocol application is identical to the old one (provide IACUC file #) with regard to hypotheses, specific aims, and vertebrate animal involvement (or describe minor differences).

If this application is essentially the same as the previously approved application with only minor differences clearly described in a letter, the protocol will receive administrative review. If substantial changes are proposed, then a new committee review may be required.

7.C.3.iii. Competing Resubmissions or Supplements

Grant resubmissions require an amendment to a previously approved protocol if it is identical or substantially similar to that protocol and grant. The amendment form and a copy of the resubmitted grant application are to be submitted for review and approval. Administrative and competitive supplements also require an amendment to a previously approved protocol. The amendment form and a copy of the supplement are to be submitted for review and approval.

7.C.3.iv. Just-in-Time Provision for IACUC Submissions

What is "Just-in-Time" Review
The NIH just-in-time policy allows grant applications to be submitted to NIH for peer review without prior IACUC approval. This policy has been extended by the University to all UVM grant proposals where the granting agency does not require IACUC approval at the time the proposal is submitted. Researchers should check with the Pre-Award Services Office to determine the funding agency's IACUC approval requirements.

Process for "Just-in-Time" Review
If the sponsor accepts just-in-time vertebrate animal review, as soon as the researcher is notified that the proposal received a favorable priority ranking from the granting agency, the protocol should be submitted to the IACUC for review.

If the project is a new or competing renewal and *is identical or substantially similar* to a previously approved protocol, see section 7.C.3.ii., above, for further guidance. If the project is *not identical or substantially similar*, researchers should check the IACUC submission deadlines for the next available IACUC meeting as special requests for insertion onto an agenda after the scheduled deadline may not be possible. **NOTE: It is not necessary for the researcher to submit a protocol if the priority ranking is unfavorable.**

If the just-in-time request is for a resubmission, see section 7.C.3.iii. for submission guidance.

The delay in submission of a protocol for IACUC review approval may delay an award but should not affect the receipt of an award.

7.C.4. Interinstitutional Assurance Agreement

UVM researchers may arrange to carry out portions of research that involve the use of animals via an NIH-funded subcontract from an NIH-awardee (often a private company) that does not itself have an approved Animal Welfare Assurance on file with the NIH Office of Laboratory Animal Welfare (OLAW). In such situations, OLAW requires that the company apply for an "Interinstitutional Assurance," under which UVM assures that the research will be carried out under the terms of its own OLAW-approved Animal Welfare Assurance.

Interinstitutional Assurance Agreements require signatures from the private company, UVM Associate VP for Research and the IACUC Chair. If you are handling completion of this form, please contact the office at iacuc@uvm.edu or call Ms. Abbey Peterson at 6-5040. The office will assist in the accurate completion of the form and in obtaining institutional signatures.

A sample form may be downloaded at http://grants.nih.gov/grants/olaw/sampledoc/interinstitutional_assurance.htm.

7.D. Continuing Review and Six -Year Renewal

7.D.1. Requirements

There are requirements for continuing review in both the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals and the United States Department of Agriculture (USDA) Regulations on Animal Welfare**.** Animal welfare regulations require a continuing review at least annually for USDA-covered species and according to PHS Policy Section IV.C.5, “The IACUC shall conduct continuing review of each previously approved, ongoing activity covered by this Policy at appropriate intervals as determined by the IACUC, including a complete review in accordance with IV.C.1.-4. at least once every three years.” The IACUC developed the following processes to meet the requirements of both of the above. It is the policy of the IACUC to review all vertebrate animal research appropriate to the degree of pain involved, but not less than once per year. Each protocol continuing beyond every three-year point will receive complete de novo review (triennially).

If a protocol remains open beyond a second triennial review, that protocol will go through the 6-year renewal process which requires that the PI submit a new Animal Use Protocol form for that project. A new IACUC protocol number will be issued at that time and the previous protocol will be effectively closed.

The purpose of continuing review is to monitor:

1) the status of the protocol
2) verify that completed activities were conducted in accordance with the approved protocols,
3) solicit information about activities projected for the coming year, and;
4) reflect changes in key personnel and whether mandatory training is complete

7.D.2. Annual and Triennial Continuing Reviews

For the first and second year of the protocol, the Investigator will be forwarded a notice and continuing review form for completion and submission. The Investigator will complete only the relevant sections and submit the form for review and continued approval.

Prior to the end of the third year the Investigator will be forwarded the same continuing review form indicating that it is a triennial review and that all sections need to be completed. The additional triennial section of the form allows the Committee to do a "complete review" as required by PHS Policy. The Investigator will also be provided a copy of his/her currently approved protocol. They will be required to confirm in the continuing review form that that is the protocol they are using. This will verify that the Committee and the Investigator's records are in agreement.

For the fourth and fifth year of the protocol, the Investigator will be forwarded a notice of continuing review and a continuing review form for completion and submission. The Investigator will complete only the relevant sections and submit the form for review and continued approval. This is the same process used for the first and second year of the protocol.

Continuing reviews that are **not** on a triennial year will be reviewed administratively either by the IACUC Chair (non-USDA regulated species only) or through the Designated Review Process.

Continuing reviews that **are on** a triennial year will be reviewed by the designated review process to conduct a "complete review."

No new changes to the protocol are to be requested by the Investigator at the time of continuing review. Often, as part of the completion of the continuing review forms, it becomes apparent that a change in animal numbers will need to be made. If Investigators need to make a change in the currently approved protocol, they must submit a separate protocol amendment request for review. The same reviewer will be assigned the Continuing Review and any associated amendments whenever possible.

As part of the continuing review process, the Committee may require that the research be restricted, modified, reviewed more frequently or terminated/suspended. Alternatively, special precautions or Committee-imposed restrictions, or shortened review periods, may be modified if current data support such actions.

The most visible element of the continuing review process approval is the **Verification of Approval** (VOA) form. This form indicates an expiration date which can only be extended through the Continuing Review process.

Expired Approvals: Extensions beyond the expiration date cannot be granted. If the

expiration date has passed, or is in jeopardy of passing, the Committee must be notified as soon as possible.

a. If the Committee does not provide continued approval of the research by the specified expiration date, research activities are suspended and animals are moved to a holding protocol pending continued approval of the research by the Committee.
b. Researchers found to be conducting research activities without a current IACUC approval are in noncompliance with the regulations.

7.D.3. Six-Year Renewal (New)

As regulations change, the Animal Use protocol form is updated to ask questions that allow the IACUC to ascertain if new projects meet current regulatory requirements. For protocols requesting continued approval beyond six years, we are now requiring completion of the most current Animal Use protocol form for this same reason.

Protocols that are up for six-year renewal will be reviewed by the Committee using the same process that is used to review initial applications. The decision as to the type of review a proposal receives (designated or full) is based on the anticipated level of animal discomfort and types of procedures.

Veterinary consultation for the six-year renewal is required as is scientific merit review. Protocols requiring full review are placed on the agenda as they are received, so it is important to send your six-year renewal minimally **6-8 weeks** prior to the expiration date to allow processing time.

One year prior to the beginning of the sixth year of the project, researchers will be forwarded a specific renewal notification. PIs will also receive a 90, 60 and 30-day reminder prior to six-year expiration date. PIs must submit a current Animal Use Protocol form if they wish to extend the project.

7.D.4. Documentation

Once approved, the Committee will return a signed Verification of Approval form to the PI via interoffice mail. A copy of the approved protocol is available to the Office of Animal Care and Use Management through the InfoEd electronic system. A copy of the VOA should be kept by the PI as documentation of continuing review completion.

7.E. Request for Modification/Amendment to Previously Approved Protocol (Attachment C)

7.E.1. Requirements

Review of any changes to previously approved research is required by regulation and is an essential element of the ongoing review of research involving vertebrate animals. Regulations mandate that changes cannot occur until after review and approval.

The IACUC recognizes that research is a continuous process and that changes in the conduct of the research are necessary. However, no changes to an approved protocol should be implemented until the IACUC has reviewed and approved the changes.

An algorithm has been developed that categorizes amendments and shows the path of IACUC review that each category of amendment may take. The determination of whether a proposed amendment is "significant" vs. "minor" falls to the IACUC chair, in consultation with the University Veterinarian, as necessary.

7.E.2. When to Request

Requests for approval of modifications may be submitted at any time. Complete an Animal Use Protocol Amendment form. The changes must be approved before any changes can be implemented in the conduct of the protocol. NOTE: If the amendment involves a new use of hazardous materials or radiation, additional review by other committees is required prior to implementation.

7.E.3. How to Request an Amendment to Approved Protocol and Review Process

The Animal Use Protocol Amendment form is intended to capture all of the required elements for a significant review of proposed amendments. Complete the form and attach a revised version of the protocol.

Minor amendments will usually be reviewed administratively by the IACUC Chair and Significant Amendments will be reviewed through the Designated Review Process in accordance with the algorithm noted above.

Note: The Animal Use Protocol Amendment form is located in the forms section of the IACUC website and should be downloaded each time it is needed as forms are frequently updated.

Changes to protocol personnel require an amendment to the protocol. The Committee has a specific form, Request for Change in Personnel, to make these changes. Submit this completed form and your amended protocol. Note: Make sure any new personnel have completed the required training.

7.E.4. Documentation

Once approved, the IACUC will return a signed Animal Use Protocol Amendment form. Proof of the amendment approval must be kept by the PI (perhaps in a Research Regulatory Binder) as evidence that the IACUC has approved the change.

Note: A copy of the approval is available to the Office of Animal Care and Use within the InfoEd electronic system.

7.F. Notice of Termination

It is the responsibility of the investigator to notify the IACUC when a project is completed. Projects that have been completed, withdrawn or terminated are closed immediately upon notification. The Office of Animal Care Management is notified by the IACUC of all closures. All animal use on a specified protocol is stopped. No further purchase of animals can be made under the specified protocol number.

8. PRINCIPAL INVESTIGATOR RESPONSIBILITIES

8.A. Expectations of a Principal Investigator

There are certain expectations of a principal investigator (PI). When the principal investigator submits a research protocol to the IACUC, by signing the Protocol Form you agree to the expectations listed below:

I have provided an accurate description of the proposed animal care and use protocol and agree to the following conditions:

All experiments involving live animals will be performed under my supervision or that of other qualified individuals as indicated in the attached forms. The personnel involved have been or will be trained prior to any animal work in proper procedures of animal handling, administration of anesthetics and analgesics, and AVMA recommended methods of euthanasia to be used in this project. This includes: 1) each person working with animals in this protocol will take the UVM General Training course prior to working with animals; 2) each person working with animals in this protocol will be briefed by the PI on the hazards associated with the project prior to working with animals; 3) each person who will perform surgery in this protocol will take the required UVM Surgical Training Course prior to surgery: each person who will perform anesthesia will meet with the University Veterinarians, each person who will work with Agricultural Animals will receive Agricultural Training by the University Veterinarians

All research personnel who have substantial direct contact with animals over 8 hours/week will be referred to Office of Animal Care Management by me regarding the necessity for having an Occupational Health Physical.

All personnel will be informed of the requirement to report all animal bites and animal related accidents to Risk Management.

All personnel will be informed that any concerns for inhumane care and treatment of animals or unlawful acts involving animals should be reported to the Office of Animal Care Management or, alternately, to the Office of Sponsored Programs and that anyone reporting such concerns cannot be discriminated against or be subject to any reprisal for reporting their concerns.

I agree to abide by governmental regulations and University policies concerning the use of animals.

I will ensure that veterinary care is provided to animals showing evidence of pain or illness.

I agree to give consideration to tissue sharing and will do so whenever possible.

I certify that any animal use proposed in a grant or contract proposal to support this research corresponds to the information provided herein.

If the procedures concerning animal use in this research activity are to be revised or changed, I will so notify the IACUC of these changes before the change is implemented. I understand that failure to request an amendment for changes in animal use may place the University and myself in violation of Federal regulations and the Animal Welfare Act.

As required by Federal regulations, I assure that the activities described do not unnecessarily duplicate previous experiments and I assure the animal models proposed are the most appropriate for achieving the objectives of this project and have provided justification for each model used in the protocol (Animal Research Plan, (1) Rationale).

Other research personnel (technicians, graduate students and post-doctoral associates) have an equally important role in that they often conduct the day-to-day activities of the study.

8.B. Requirements of the Principal Investigator

As the principal investigator you must:

Ensure proper training and occupational health of the research team;
Ensure protocol adherence, and;
Provide reports on the progress of the study.

8.B.1. Ensure Proper Training of the Research Team

The principal investigator is responsible for ensuring that the research team has appropriate training prior to and during the conduct of the study as listed in Section 5.

8.B.2. Ensure Protocol Adherence

It is the principal investigator's responsibility to ensure that the IACUC-approved protocol is being followed at all times by the research team. This includes making sure that amendments are submitted for IACUC review in a timely fashion and then once approved implemented by the research team.

8.B.3. Provide Reports on the Progress of the Study

During the course of a research study, new information might become available. As new information becomes available, the principal investigator is obligated to report to the IACUC. Common items that need to be reported in a timely fashion to the IACUC are described in detail below.

a. Continuing review of approved studies

It is the responsibility of the principal investigator to submit the current status of active protocols at least annually. Some protocols require more frequent review based on pain level/risk. The IACUC makes this determination and notifies the principal investigator. Please refer to Section 7.D. for additional information on submission of continuing reviews.

Note: As part of the progress report, investigators are requested to breakdown how the animals have been used by pain level. Therefore accurate records of ongoing animal use must be kept.

b. Reporting incidents and animal deaths

Principal investigators and/or research staff are responsible for reporting animal welfare incidents to OACM and IACUC. Please refer to Section 9 and the Reporting Animal Death Policy for additional information.

c. Amendments to a previously approved protocol

Requests for changes (amendments) to approved studies may be submitted at any time but before the change is implemented, it must receive IACUC approval. Refer to Section 7.E. for further instructions on how to submit an amendment.

e. Change in personnel

It is required that the investigator notifies the IACUC office when there are any additions or deletions to research staff participating in a protocol. Refer to Section 7.E.3. for further instructions on how to submit this type of amendment.

Amendments to add personnel will not be approved until the new personnel have completed the required training. Refer to Section 5 to learn more about required training.

f. Premature termination/suspension

The IACUC should be notified when a protocol has been terminated or suspended prematurely and the reasons for the premature termination or suspension. To notify the IACUC, submit a memo or email.

g. Study closures

Notify the IACUC when a protocol has been closed permanently.

8.B.4. Coverage for PI (revised 5/5/15)

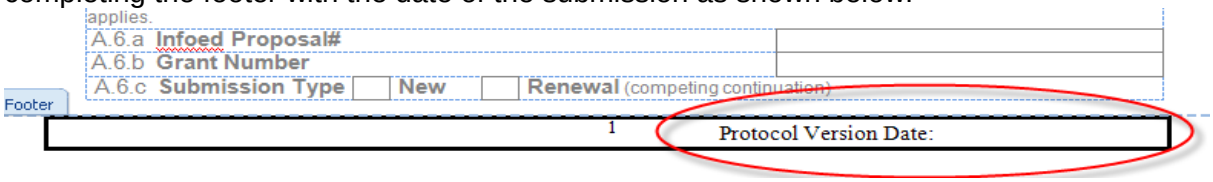
At the time of initial protocol submission, the PI must either designate a person to be in charge and fulfill all responsibilities for oversight of the protocol in their absence or provide a plan for coverage (one option is to cease activities during an absence – this requires IACUC notification). That person will be identified in the protocol as the designee. If a formal leave is planned, (e.g., sabbatical, medical, maternity or other official leave type) the IACUC needs to be notified, so that it may redirect protocol inquiries during that time. The responsible designee must understand the protocol and comply with the requirements as noted above.

8.C. Guidance for the Investigator

8.C.1. Communication with the IACUC

The IACUC requires investigators to submit all protocols and protocol-related submissions (e.g. amendments, key personnel changes) via email attachments. Investigators in turn can expect to receive their IACUC correspondence via email. This change is a giant step forward and should result in less paperwork for the investigators and the IACUC staff.

We continue to require protocol submissions to be signed by the vet, the PI and others (e.g. departmental reviews) as necessary. We have identified a potential pitfall with this new process to be confusion with document versions. We must all be vigilant about making sure we are always working with the currently approved version of the protocol and protocol roster. Please update your documents every time they are submitted by completing the footer with the date of the submission as shown below.



This date footer is not automatic, therefore you must change it each time you revise your protocol. You should not use the automatic date feature as this will add further confusion by changing your date every time you happen to open the document. Failure to update this protocol version date may delay review of the submission.

All submissions need to be sent to the IACUC@uvm.edu email box where new submissions will be monitored and processed in the order they are received.

When you are in communication with the office, whether in writing, by telephone, fax or e-mail, you should have the following information available.

- IACUC number, if assigned at the time of contact
- Principal investigator's name
- Protocol title
- Date and type of submission (if applicable)

We can more readily assist you with this information.

8.C.2. Written Communication of IACUC Decisions

Decisions made by the IACUC will be communicated to the principal investigator (or designee if provided) through a memorandum outlining the approval status and/or concerns, questions and/or comments of the IACUC. This correspondence will be forwarded via email to the principal investigator.

The IACUC notifies investigators and the institution of its decisions regarding protocol review through written memoranda and the minutes of IACUC meetings which are transmitted electronically. The decision to withhold approval is communicated to the investigator along with the reasons for withholding approval. There is no appeal process for the IACUC's decision to withhold approval, however, an investigator may address the IACUC's concerns by writing and submitting a new protocol.

The IACUC Chair will convey one of the following four decisions in writing to the investigator promptly after the meeting:

Approval

The principal investigator may begin the research study upon receipt of the Verification of Approval form.

Modifications Required for Initial or Continuing Approval

This decision is determined when the protocol is recommended for approval by the IACUC pending the investigator's response to IACUC-directed stipulations/questions and/or revisions. The principal investigator must provide, via email, a memorandum responding to the IACUC's recommendations. We ask that you indicate the IACUC number on this correspondence. If a revision to the protocol is necessary, attach a full revised protocol with changes indicated. Remember to update the protocol version date in the footer of the protocol.

Depending upon the issues that have been raised, the review of the response may occur through a Designated or Full process.

Withhold Approval

Questions regarding the scientific merit and use of animals are of such significance that the committee finds approval of the study to be unwarranted. The authority of the IACUC to withhold approval of a study may not be overridden.

NOTE: The IACUC has a 30, 60, 90 day reminder system for all pending protocol items. The investigator is reminded that the IACUC has requested something from them in regards to a protocol and is awaiting his/her response. At the 120 day mark the protocol is withdrawn from the Committee's consideration. This helps to ensure that changes to protocols are handled in a timely fashion.

8.C.3. Accessibility of Records

The investigator must make available all research records for direct access by the IACUC staff. A copy of completed medical records for animals of USDA-covered species must be sent to OACM in a timely manner. Depending upon the protocol sponsorship there may be others with access needs such as the FDA or other regulatory authorities.

9. Animal Welfare Incident Reporting

9.A. Policies

9.A.1. In accordance with the Animal Welfare Act, (9 CFR Ch.1), Part 2 – Subpart C), 2.32. Training and instruction of personnel include methods whereby deficiencies in animal care and treatment are reported, including deficiencies in animal care and treatment reported by any employee of the facility. No faculty employee, Committee members, or laboratory personnel shall be discriminated against or be subject to any reprisal for reporting violations or standards under the Act.

9.A.2. Local Policy: Priority One-UVM SOP #1.1.3 Reporting Animal Welfare Concerns

All procedures performed at the Priority One Services, Inc. facilities and contract staffing services locations must comply with all applicable regulations governing the care and use of animals. Non-compliance will result in corrective action for the person(s) involved. Any concern regarding animal welfare will be taken seriously and investigated. Corrective action, if indicated will be taken and the individual(s) expressing the concern will be informed.

9.B. Determining When and How to Report Incidents

The University has an online compliance reporting system "Ethics Point" (https://secure.ethicspoint.com/domain/media/en/gui/24544/index.html) which can be accessed through UVM's Compliance & Privacy Services. This system allows people to anonymously report an animal welfare incident and receive information about the followup without compromising their identity. For those who prefer, there are also paper Animal Welfare Incident reporting forms available in the central Animal Facilities and available in an electronic format at the Office of Animal Care Management's website (http://www.uvm.edu/~oacm/). The General Animal Care training outlines these methods of reporting animal welfare concerns; in addition, the AV gives many talks to students and staff throughout the academic year, describing the process of assuring that research animals are well cared for and the reporting process for animal welfare concerns.

10. OVERSIGHT AND MONITORING

10.A. Internal

Twice each year the IACUC conducts a complete review of the University of Vermont's Animal Care and Use Program and inspects facilities where animals are housed and/or used. The *NRC Guide for the Care and Use of Laboratory Animals* and *Animal Welfare Act and Animal Welfare Regulations* are the principal documents used by the IACUC in its evaluations. Researchers who house animals in their laboratories over 12 hours should expect visits by the subcommittee of the IACUC at approximately 6-month intervals. All survival and non-survival surgical sites are also visited. Researchers can expect a notice of inspection 1 month in advance.

Written reports of the program evaluation and inspection are prepared according to PHS policy criteria and are submitted to the full committee for discussion and modification, if necessary, prior to taking action. Final reports are then forwarded to the institutional official.

In addition to looking at the research facilities during the semiannual inspection, IACUC members will conduct protocol monitoring visits. For further information, see Monitoring Process/Protocol Followup policy.

10.B. External

Annually an Animal Welfare Officer from the USDA will inspect the animal facilities and may inspect individual labs. The inspector will meet with the University Veterinarian or a designee who will escort the Animal Welfare Officer through the facilities.

Attachment A:
Committee Policies

These are direct links to the individual policies that have been approved by the IACUC.

#	Policy	Date Reviewed	Date Originally Approved
1.	Agricultural Animal Use	12/16/15	01/12/01
2.	Animal Numbers: Initial and Continuing Review	inactive	inactive
3.	Animal Tissue Use	NA	12/17/07
4.	Antibody Production *(retired 11/20/12)*	inactive	04/28/03
5.	Autoclave Use and Sterilization *(5/3/11 refer questions to EHS)*	inactive	11/24/03
6.	Biohazardous Material	10/19/15	3/24/08
7.	Biological Agents *(included in Hazardous Material Policy)*	inactive	inactive
8.	Blood Collection	04/27/15	02/24/03
9.	Euthanasia Methods	01/11/16	10/23/06
10.	Death as An Endpoint	10/27/14	12/22/03
11.	Emergency Evacuations During Animal Surgery	10/27/14	02/28/05
12.	Emergency or Disaster	10/27/14	07/11/05
12.1	Enrichment and Social Housing for Laboratory Rodents	9/26/16	03/28/11
13.	Food or Fluid Restriction	04/27/15	05/28/03
14.	Frog Oocyte Harvest	01/11/16	11/24/03
15.	Housing Animals Outside and/or Removal from Central Animal Facility	10/19/15	12/22/03
16.	Post-Approval Monitoring	04/27/15	04/28/03
16.1	Neoplasia in Rodents	01/11/16	11/23/09
17.	Occupational Health and Safety Program (section 5.E)	02/22/16	10/23/06
18.	Ordering Animals	inactive	inactive
19.	Pain and Distress, Determination of Levels	05/18/15	05/28/03
20.	Pet Policy (refer to University policy on pets)	inactive	inactive
21.	Physical Restraint	05/18/15	05/28/03
22.	Reporting Animal Deaths	12/07/15	01/23/06
23.	Rodent Cage Density	10/19/15	11/28/05
24.	Storage of Controlled Drugs	04/28/14	10/26/04
25.	Survival Surgery	02/01/16	02/24/03
25.1	Testing for Biological Materials	01/23/17	1/24/11
26.	Animal Identification	12/07/15	05/18/09
27.	Use of Expired Medical Materials	12/07/15	01/23/06
27.1	Visitor Policy	6/23/14	10/22/07
28.	Votey Satellite Facility, Oversight Plan for	inactive	inactive
29.	Weaning	01/23/17	11/28/05
30.	Aged Animals	05/18/15	01/23/12
31.	Random-Source Animals	05/18/15	2/27/12
32.	Non-Pharmaceutical Grade Drugs	11/28/16	2/25/13

Attachment B:
Committee Forms

All forms and form instructions are located in the forms section of our website and should be downloaded each time you need one. (SEE: http://www.uvm.edu/iacuc and click on “All Forms”)

Attachment C:

Animal Use Protocol Amendment Algorithm

Submit completed amendment form and revised protocol pages to IACUC.

Chair, in consultation with the veterinarian, decides if the amendment is significant or minor.

Significant
For example, large change in #s of animals, any increase in numbers of USDA covered animals, change in PI, increase in invasiveness, change in species, increase in pain or discomfort, change in method of euthanasia, changing route of administration of drug.

vs

Minor
For example, small change in #s of non-USDA animals or addition of new personnel (not change in PI)

Posted for Proposed Designated Review

Full review may be requested by any member during this time

Placed on next available agenda

Chair assigns Committee reviewer. Protocol and amendment request are forwarded to the reviewer. Any clarifications are resolved.

Designated Review

Chair or designee and veterinarian signs approval and sends back to the investigator. Amendments are reported at next meeting.

Administrative Review

Chair or designee and/or veterinarian signs approval and sends back to investigator. Amendments are reported at next meeting. No veterinarian signature needed on personnel changes.

Attachment D:

Performance of Repeat Procedures (1 Adapted from Colorado State University https://vpr.colostate.edu/RICRO/IACUC November 18, 2016)

Background

Proper use of animals, including the avoidance or minimization of discomfort, distress, and pain while simultaneously minimizing the numbers of animals needed when consistent with sound scientific practices, is imperative1. Furthermore, the *Guide2* specifies that the Institutional Animal Care and Use Committee (IACUC) should weigh study objectives against animal welfare concerns in accordance with the tenets of the Three R's. The IACUC is often confronted with a situation where procedures may have to be repeated in an individual animal in order to achieve study objectives. This document discusses examples of common scenarios that can be used as a roadmap to IACUC decision making. Regardless of the procedure to be performed there should be appropriate justification as to why a procedure needs to be repeated, an indication of the interval between the repeats as well the total number of repeats together with a statement of the anticipated long term effects of the repeated procedures on the animal clearly articulated in the protocol. The total numbers of procedures that can be performed is dependent on the skills of the individual performing it, the nature of the procedure, other procedures previously performed on the animal, future procedures that may need to be performed, the temperament of the animal, and health as well as physiological status of the animal.
The changes within this document must be handled in compliance with the VVC process described in NOT-OD-14- 126 and in the IACUC reviewed and approved Protocol Review Process document.

Procedures and guidance

Oral gavage

Oral gavage is a widely used method for safely administering known quantities substances to animals by properly trained (experienced/qualified) personnel. Oral gavage is part of accepted routine toxicological testing accepted by agencies like Food and Drug Administration and Organization for Economic Cooperation and Development's 28 or 90-day oral toxicity, where substances are administered daily during that time period. The maximum dosing volume is 1.5 ml for a 30-gram mouse (10 ml/kg), and 16 ml for a 400-gram rat (10-20 ml/kg)3. When performed properly, the procedure can be used to administer 50-200 µl into the stomach of mice daily for up to 20 weeks.

Fluid collection

Studies often require repeated (timed) collections of fluid e.g. blood, cerebrospinal fluid, rumenal fluid, urine, synovial fluid, intraocular fluid, semen, milk, tracheal wash, broncho-alveolar lavage, etc. In some rare instances this can be achieved by "free catch" such as for urine or collecting feces after defecation, however, for the most part the process requires penetration of a cavity typically with a needle, cannula, catheter or trocar with or without anesthesia and/or analgesia or even use of an assistive device e.g. electro-ejaculator or artificial vagina. Most of these procedures are relatively benign and pose little or any adverse impact when done correctly by a properly trained (qualified or experienced) individual. Animals should be monitored during and after the procedure, and be provided appropriate analgesia or anesthesia. The veterinarian should be notified in case of development of complications to facilitate resolution of the problem.
The circulating blood volume for most common laboratory species is 55-70 ml/Kg (5-7% of the body weight). The value is influenced by the status of the animal including age, body condition and health. Up to 10% of the total blood volume (1% of the body weight) can be safely removed in a normal healthy animal. This volume may be collected once in 3-4 weeks4. This period allows the animal to recover from the potential adverse effects of blood loss. Again the same 3-4 week recovery period should be followed. If you are collecting 0.75% of the body weight a recovery period of 2 weeks may be sufficient,

and for 0.5% a week's recovery is okay and for 0.05% blood can be collected daily. The same total amount of blood can also be removed as multiple quantities over a 24 hour period. If necessary fluids can also be administered to support the blood volume, especially for collections at the upper end of the limit.
The table below provides examples of maximal amounts of blood that can be collected.

Species[5]	Body weight	Blood volume	Maximum survival collection volume
Mouse	20-63 g	1.6-3.2 ml	0.2-0.4 ml
Rat	250-520 g	20-40 ml	2.5-5.2 ml
Guinea pig	700-1200 g	40-80 ml	7-12 ml

The table below provides common sites for blood collection in a number of laboratory animal species.

Species	Site
Mouse	Saphenous, tail, and facial and veins
Rat	Saphenous, tail and jugular veins
Guinea pig	Saphenous, tarsal and jugular veins, vena cava
Pig	Ear, saphenous, tail, cephalic, femoral and mammary veins, vena cava
Rabbit	Ear and jugular veins
Cow	Jugular, caudal (tail) and mammary veins
Sheep	Jugular and cephalic veins

The following table indicates the common routes for administration of substances.6 Suggested maximum volumes to be administered are shown in parenthesis. For most mammalian species these volumes can be safely administered: 5-20 ml/kg orally; 5 ml/kg subcutaneously; 0.05 ml/kg intramuscularly; 10 ml/kg intraperitoneally; and 5 ml/kg intravenously as a bolus or 2-4 ml/kg continuous infusion.7

	Oral (µl/g) [max dose]	Subcutaneous (µl/g) [max dose]	Intraperitoneal (µl/g) [max dose]	Intramuscular [max dose]	Intravenous bolus (µl/g) [max dose]
Frequency	Daily	No more than three times daily	Daily	No more than two sites daily	Daily
Mouse Example for a 30 g mouse	10 [50] 300 µl [1.5 ml]	10 [40] 300 µl [1.2 ml]	20 [80] 600 µl [2.4 ml]	[0.05]*	5 150 µl
Rat Example for a 400 g rat	10 (40) 4 ml [16 ml]	5 (10) 2 ml [4 ml]	10 (20) 4 ml [8 ml]	[0.1]	5 2 ml
Mini pig	10 (15)	1 (2)	1 (20)	0.25 (0.5)	2.5

Substances to be administered should be sterile and if possible the pH should be near neutral.
*Note that intramuscular injections in mice are discouraged unless scientifically-justified.

Rumen fluid is sometimes collected for research or clinical purposes. The rumen of an adult dairy cow contains 184 liters (49 gallons) of fluid. An adult sheep or goat rumen is about 3-6 gallons (11.4 – 22.8 liters). Rumen fluid can be collected either through a permanent fistula or using a stomach. Creating of a fistula makes it easy to collect rumen fluid and is usually the preferred method for long term repeated fluid collection. The process requires surgery to create the fistula as well as regular cleaning and maintenance of the fistula. Use of a stomach tube is fairly straight forward, however, it causes a temporary discomfort to the animal, and has the potential to cause esophageal and oropharyngeal irritation or trauma, and the potential for aspiration pneumonia. Use of a stomach tube does not require surgery and a recovery period. Rumen fluid can be collected repeatedly by a trained or experienced individual provided due care is take to avoid the potential adverse impact of the procedure e.g. alteration of rumen microbiome, dehydration, digestive disturbances, trauma and/or aspiration pneumonia especially if a stomach tube is used. When 5 or more gallons of rumen fluid is removed daily, it is necessary that the fluid be replaced with water.

Aseptic technique and appropriate pain management are required for collection of synovial fluid (arthrocentesis). The amount of fluid that can be collected will be dependent on the joint cavity as well as the species. The knee joint often provides the most accessible and largest practical volume of fluid. The amount of fluid in the joint is typically very small. The human knee joint contains about 4 ml of synovial fluid. The equine stifle joint has about 20 ml of synovial fluid and the carpal joint has about 10 ml. For pharmacokintetic studies arthrocentesis can be done at 0, 6, 12, 24 and 72 hours and can be repeated with a rest of 1-2 weeks (Frisbie, 2014)11. Arthrocentesis can be safely performed every week for 10-20 weeks.

Cystocentesis should be performed after cleaning the puncture site with antiseptic solution. If urine is not obtained at the first attempt change the needle before making the second attempt. The procedure should be aborted after the third unsuccessful attempt. The needle should not be redirected during the procedure. Cystocentesis may induce mild transient hematuria, bruising and urine leakage. Healthy bladders heal relatively quickly. It is possible to collect urine daily by cystocentesis especially if the procedure is ultrasound guided which minimizes the possibility of trauma (Lappin, 2014)12.

Nasal swab and buccal swabs can be performed non-invasively using a sterile cotton tip applicator, or similar device. They can typically be conducted with manual restraint. If the animal is uncooperative, then the procedure should be aborted. Nasal and buccal swabs can be collected up to 3 times a day. As long as there is no evidence of trauma such as nose bleed, these swabs can be collected up to 30 consecutive days.

Saliva can be collected from the oral cavity. If the animals are conditioned to produce saliva using training methods as described in the protocol, saliva can be collected up to 3 times daily. If medication is needed to collect saliva, it should be given no more than once daily.

Feces can be collected up to 3 times daily by manual collection from animals larger than rabbits using a lubricated fecal loop. Voided feces can be collected as often as desired.

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[1] United States Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training. Principle III and IV. http://grants.nih.gov/grants/olaw/references/phspol.htm#USGovPrinciples

[2] Guide for the Care and Use of Laboratory Animals (2011), National Research Council, National Academy Press, Washington, DC. P27- 28.

[3] Diehl KH, Morton R, Morton D, *et al* (2001). A good practice guide to the administration of substances and removal of blood including routes and volumes. Journal of Applied Toxicology 50(5): 600- 613.

[4] Diehl KH, Hull R, Morton D, *et a*l (2001). A good practice guide to the administration of substances and removal of blood, including routes and volumes. Journal of Applied Toxicology 21: 15- 23.

[5] Adapted from Joslin JO (2009) Blood collection techniques in exotic small mammals. Journal of Exotic Pet Medicine 18(2): 117- 139.

[6] Adapted from Diehl KH, Hull R, Morton D, et al (2001). A good practice guide to the administration of substances and removal of blood, including routes and volumes. Journal of Applied Toxicology 21: 15- 23.

[7] Turner PV, Brabb T, Pekow C, Vasbinder MA (2001). Administration of substances in laboratory animals: routes of administration and factors to consider. Journal of the American Association for Laboratory Animal Science 50 (5): 600- 613.

[9] Koch MA (2006) Experimental modeling and research methodology. Chapter 18, P 606- 607. Suckow MA, Weisbroth SH, Franklin CL (eds.). 2nd edition. The Laboratory Rat. Academic Press/Elsevier, Amsterdam.

[10] Iwarsson K, Lindberg L, Waller T (194) Common non- surgical techniques and procedures. Chapter 16, P267. Svendsen P, Hau J (eds.) Handbook of Laboratory Animal Science. Volume 1. CRC Press, Inc, Boca Raton, FL.

[11] Frisbie D (2014). Personal communications. [12] Lappin, M (2014). Personal communications.

Attachment E:

Formulary for Research Rodents at the University of Vermont October 2016

Anesthetics Mice Rats

Isoflurane 4% induction, 1 – 3% maintenance

Pentobarbital 40 – 85 mg/kg IP

Ketamine/Xylazine 80 – 100 and 10 mg/kg IP, respectively

Local anesthetics incisional blocks pre-operatively

Bupivicaine 0.25% no more than 8 mg/kg (< 0.3 ml/100 g BW)

Lidocaine 2% (dilute to 0.5%) no more than 7 mg/kg (<0.14 ml/100 g BW)

Analgesics

Buprenorphine 0.05 – 0.1 mg/kg SC q 6 – 12 hr 0.01 – 0.05 mg/kg SC q 6 – 12 hr

Ketoprofen 2 – 5 mg/kg SC q 24 hr 2 – 5 mg/kg SC q 24 hr

Carprofen 5 – 10 mg/kg SC q 24 hr 4 – 5 mg/kg q 24 hr

Meloxicam ~ 5 – 10 mg/kg PO q 24 hr 2 – 5 mg/kg q 24 hr

Antibiotics

Trimethoprim-sulfa (in water) 60 mg/kg (based on trimethoprim) see vet techs

Enrofloxacin (in water) 85 mg/kg (see veterinary technicians for dosing)

Fluid replacement (warmed saline or lactated Ringer's solution) 20 – 30 ml/kg IP or SC