# INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE POLICY AND PROCEDURES MANUAL

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Chapter 1. Background and Overview

I. History

Since its inception in 1896, the National Institutes of Health (NIH) has taken an active role in encouraging proper care and use of laboratory animals. In 1963, the first edition of the Guide for the Care and Use of Laboratory Animals (Guide) was issued by the Animal Care Panel (later renamed the American Association for Laboratory Animal Science). The most recent edition (1996) was developed by the National Research Council (NRC) and is the primary reference for research animal care and use in the United States.

In 1966, congress enacted the Pet Protection Act, now called the Animal Welfare Act (AWA). The United States Department of Agriculture (USDA) was given responsibility for implementing the Act which applied only to dogs, cats, rabbits, monkeys, guinea pigs and hamster. Although research facilities were required to be registered, to have their suppliers licensed, and to undergo inspection by Animal and Plant Health Inspection Service (APHIS) personnel, the Act did not apply directly to conduct of research using animals. The AWA has since been revised, most recently in 1990 [Public Law 104-624 – Food, Agriculture, conservation and Trade Act of 1990, Section 2503 – Protection of Pets]. Requirements for compliance with the Act have been incorporated into any research conducted or supported by any component of the Public Health Service (PHS).

In 1973, a new policy applying to all PHS awardee institutions was drafted. This Policy required compliance with the AWA and the recommendations of the Guide. It also required each institution to provide NIH with an assurance which gave a detailed plan for research, training, testing, education, experimentation or demonstration purposes. An institution’s failure to comply could lead to withdrawal of NIH approval and suspension or termination of all PHS-supported research at that institution. Individual investigators could be disqualified from receiving PHS awards. Thus, this Policy required that individual institutions assume responsibility for the quality of its animal research program and the conduct of its investigators and animal care personnel.

In 1974, the Institutional Regulations Branch of the Division of Research Grants was transferred to the Office of the Director of NIH and renamed the Office for Protection from Research Risks (OPRR), now named the Office of Laboratory Animal Welfare (OLAW). The third PHS Policy was prepared jointly by OPRR and what is now called the National Center for Research Resources, and came into effect in January 1979. It covered all vertebrates used in research and put the responsibility on awardee institutions to train staff for the management of their animal programs. This Policy gave institutions three options for obtaining NIH approvals: 1) accreditation by the America Association for Accreditation of Laboratory Animal Care (AAALAC); 2) an assurance that the institution’s own Animal Care Committee had found the institution in full compliance with the Guide; and 3) provisional assurance of plans for correction, if deficiencies found by the Committee’s annual inspection were reported to OLAW.
In July 1981, NIH issued the first comprehensive Policy which required written assurance of accreditation, either by an appropriate professional body, or by an institutional committee which included at least on veterinarian, before NIH funding could be awarded for research or teaching. The standards for evaluation were those set forward in the Guide with annual institutional committee inspections.

During the 1980s, increased vandalism, harassment, and theft of animals spurred Congress to revise the PHS Policy while, at the same time, the Institute for Laboratory Animal Research of the National Academy of Sciences updated the Guide. The final version of the PHS Policy, THE PUBLIC HEALTH SERVICE POLICY ON HUMANE CARE AND USE OF LABORATORY ANIMALS, became effective January 1, 1986. It extends to foreign institutions receiving PHS funding and to intramural institutions operated directly by NIH and other agencies of the PHS. Subsequent to the revision, Congress enacted the Health Research Extension Act which added several provisions to PHS Policy. The latter was revised to conform to the new law and was reissued in September, 1986. **Key elements of PHS Policy include:**

1. Negotiation of Animal Welfare Assurances which include commitments by the awardee Institution to its animal care and use program, to appropriate staff training and to an occupational health program for employees.
2. Establishment, according to specified criteria, of an Institutional Animal Care and Use Committee with defined responsibilities.
3. Detailed requirements for the submission of applications for awards.
4. Record keeping requirements to ensure clear accountability for the quality of the program.
5. Reporting requirements to enable funding agencies and OLAW to exercise oversight of the entire system.

Each institution subject to the PHS Policy is expected to operate its program in accordance with the U.S. Government Principles for the utilization and Care of Vertebrate Animals used in Research and Training. Recently, The USDA issued Parts 1 and 2 of the final regulations implementing the 1985 amendments to the AWA. Part 2, subpart C, pertains to research institutions. Most of the provisions included in this subpart of the USDA Regulations are similar or identical to those included in the PHS Policy. Part 3 of the Regulations describes the standards that must be met when using species of animals covered by the USDA Regulations. Many of the requirements specified in Part 3 are similar to the recommendations made in the Guide and establish standards for the care and maintenance of covered species.

**II. Authority, Composition and Functions (see Table 1)**

Each institution under authority of the AWA and/or receiving PHS support for research and teaching involving laboratory animals must operate a program with clear lines of authority and responsibility, have a properly functioning Institutional Animal Care and Use Committee (IACUC), have procedures for self-monitoring, adequate veterinary care, a program of occupational health, sound animal husbandry practices, and appropriate maintenance of facilities for housing animals.
The IACUC must have at least five members, including a veterinarian with animal care and use program responsibilities, a scientist experienced in laboratory animal research, a non-scientist and an individual who has no other affiliation with the Institution besides membership in the IACUC. The IACUC must have the full support of the Institutional Official responsible for the Program, evaluate the entire program every six months, prepare a report on the evaluation and the inspection of the facilities which is to be filed with the Institutional Official, and make recommendations to this Official concerning deficiencies with a proposed timetable for corrections. **The IACUC has the authority to suspend any research or teaching activities that involve animal use.**

The IACUC has an obligation to review all research projects proposed for PHS support involving animals prior to their receiving funding. A written report on this review shall confirm that the projects shall be conducted in accordance with PHS Policy, the *Guide*, and the AWA. At least one member of the committee shall review each proposal, but all members shall have prior opportunity to request full Committee review. **The IACUC has authority to approve, require modifications before approval, or withhold approval of proposals submitted to it for review. No activity involving animals shall begin unless it is first approved by the IACUC.**

The PHS requires IACUC review of approved, ongoing activities at least once every three years whereas the USDA requires it annually. Institutions should choose a uniform mechanism that satisfies both federal requirements. OLAW has interpreted PHS Policy to require an institutional process that provides review of proposed activities with committee approval for a specified period of time generally not to exceed three years. This initial review and approval may be accomplished by either convened Committee action or by a “designated reviewer/expedited review” process that meets the PHS Policy requirements of Section IV.C.2. During this period of approval, annual review must be accomplished to meet USDA requirements. The purpose of annual review is to confirm that no changes have taken place in the approved activity that might require further consideration by the IACUC, and to ensure that any new requirements of PHS, USDA or the institution are transmitted to the investigator. **Annual review need not require a convened IACUC or designated reviewer/expedited action but must be adequately documented.** Planned modifications must be brought to the attention of the IACUC prior to initiation.

**Table 1-1. Federally Mandated IACUC Functions**

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<td>Review, at least once every 6 months, the research facility's program, using USDA Regulations/ <em>Guide</em> as basis.</td>
</tr>
<tr>
<td>2.</td>
<td>Inspect, at least once every 6 months, all of the animal facilities, including animal study areas/satellite facilities, using USDA Regulations/ <em>Guide</em>, as basis.</td>
</tr>
<tr>
<td>3.</td>
<td>Prepare reports of IACUC evaluations and submit the reports to the Institutional Official.</td>
</tr>
<tr>
<td>4.</td>
<td>Review and investigate legitimate concerns involving the care and use of animals at the research facility resulting from public complaints and from</td>
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<tr>
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<tr>
<td>reports of non-compliance received from facility personnel or employees.</td>
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<tr>
<td>5. Make recommendations to the Institutional Official regarding any aspect of the research facility's animal program, facilities, or personnel training.</td>
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<tr>
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<tr>
<td>6. Review and approve, require modifications in (to secure approval), or withhold approval of components of proposed activities related to the care and use of animals.</td>
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<tr>
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<tr>
<td>7. Review and approve, require modifications in (to secure approval), or withhold approval of proposed significant changes regarding the care and use of animals in ongoing activities.</td>
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<tr>
<td>8. Suspend an activity involving animals when necessary; take corrective action, and report to funding agency and USDA.</td>
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</tbody>
</table>

A simple mechanism to meet USDA requirements is the annual circulation of a standard form giving current basic IACUC information, e.g. approval number, date, title, species, etc. to all investigators with IACUC-approved activities. The investigator would note that no changes have taken place or describe any changes that have occurred. Any changes to the approved activities that are deemed of sufficient magnitude to merit further consideration may then be presented to the IACUC. All of these dispositions should be documented as official IACUC actions.
Chapter 2. Who Must Apply for IACUC Protocol Approval?

Anyone wishing to conduct research or teaching using animals at Western University must file an Animal Use protocol for review and approval by the University’s Institutional Animal Care and Use Committee (IACUC) before the activity begins and before any animals are obtained. The use of animals shall include alive or dead animals obtained by the principal investigator, or through an agreement with an animal owner even if that owner is another institution, for use in a research or teaching exercise.

If activities will be conducted off site, Western University’s IACUC will require a copy of the approve protocol from that site. If the site does not have an IACUC, the site must be inspected and approved by Western University’s IACUC.
Chapter 3. Design and Review of Protocols Using Animals

I. Fundamental Protocol Design Issues

Federal regulatory policy and generally accepted ethical principles require that use of live animals be minimized and pain, distress and other harm to laboratory animals should be reduced to the minimum necessary to obtain valid scientific data. Federal policy directs the IACUC to review proposals for animal use to ensure that investigators incorporate these principles into their research.

A. Reducing and Avoiding Animal Use

PHS Policy and USDA Regulations require that investigators include in their protocols the number of animals to be use, a rationale for these numbers and the appropriateness of the species they propose to use. The number of experimental animals must be the minimum necessary to produce valid results. When possible and appropriate, a non-animal substitute or a species of lower phylogenetic order must be used. Unnecessarily duplicative research will not be permitted.

The IACUC must also take into account the necessity of a given procedure. The IACUC will monitor and document the number of animals acquired and used in approved activities. The IACUC will consider the following:

- Studies must advance scientific knowledge.
- The minimum number of animals required to obtain valid results shall be used.
- Personnel and the IACUC must consider the following questions:
  1. Are animals necessary?
  2. Has an appropriate literature search been made? Is this work already published?
  3. Has the correct animal model been selected?
  4. Has a protocol based on statistical considerations been developed?
- Animals should not be subjected to unnecessary pain or suffering.
- Necessary pain should be of minimum intensity and duration. Acceptance of pain should not be based on cost, ease of application of pain-relieving substances or for the purposes of teaching or demonstration.
- Alternative end points to death should be sought.
- Economic reasons do not justify multiple surgeries.
- Housing, feeding and care must be appropriate.
- Medical care must be provided.
- Personnel caring for and using animals must be qualified and trained.
- Euthanasia must be humane.

To achieve these goal, the “three R’s will be used: replacement of animal living systems with non-living systems or computer simulations; reduction in number of animals used by animal sharing and improved statistical design; refinement by reducing invasiveness, improved instrumentation, pain control and techniques.
The following mechanisms will be used to monitor and document the number of animals acquired and used in approved activities:

• Upon receipt, the IACUC Office will assign a number to each new protocol application. Once approved, the Animal Facilities Manager will monitor the acquisition of all animals to make certain the number of animals acquired does not exceed the approved number.

• When ordering animals, the investigator must note the IACUC approval number on the purchase requisition.

• The purchase requisition shall be sent to the Animal Facilities Manager for approval who shall forward the approved requisition to the appropriate office for final processing.

• A tracking system shall be used to maintain a record of animal acquisitions for each approved protocol. The number of animals acquired with each purchase requisition will be subtracted from the number approved for a particular protocol and a running total tabulated.

• When an investigator has purchased 75% of the number of animals approved, the IACUC Office will so inform the investigator. When an investigator has purchased 100% of the number of animals approved, the IACUC Office will so inform the investigator. If additional animals are required, the investigator shall submit an amendment to the protocol for approval. Additional animals cannot be obtained until the amendment has been approved.

• A daily inventory of animals shall be conducted by animal facility personnel. Animal cages shall be tagged with the investigator’s name and contact information, protocol number, expiration date, source, species and gender. These inventories shall be forwarded monthly to the IACUC Office to ensure that the number of animals acquired does not exceed the approved number of animals.

B. Evaluating the Justification for Laboratory Animal Use

If there is no alternative to the use of the specified animals, the IACUC shall evaluate the research and require justification for the number of animals requested. Investigators must emphasize the three R’s in developing their proposals. The IACUC will judge the adequacy of the training and skill of the investigator and laboratory personnel and the adequacy of the equipment and facilities. Where appropriate, the IACUC shall enlist the help of consultants in evaluating protocols.

C. Minimizing Pain and Distress

General Policy

Minimizing or eliminating pain and distress is a basic aim of the Animal Welfare Act and PHS Policy. Pain is inherently subjective, but the International Association for the Study of Pain and
the American Veterinary Medical Association’s Panel report on the Colloquium on Recognition and Alleviation of Animal Pain and Distress are useful references for IACUCs (see references below).

Observers must be able to recognize pain and distress in animals. Observable signs may include departures from normal behavior or appearance and physiological parameters. The IACUC must ensure that research personnel are appropriately educated on how to assess pain and distress in their laboratory animals.

Approaches must be adopted to eliminate or reduce pain. The IACUC must be familiar with the most relevant strategies to ensure that investigators are educated in the measures applicable to their proposals. **The IACUC may prohibit certain procedures altogether if it feels that pain and distress cannot be reduced to an acceptable level.**

Information and provisions for education and training on reducing or eliminating pain is available from the attending veterinarian or selected resources listed herein.

If minimization of pain and distress cannot be achieved, the IACUC must evaluate the importance of the research. The higher the anticipated distress, the stronger must be the justification of the proposal.

**D. References**

- SCAW International Conference on “Pain, Distress and Stress in Research Animals: Current Standards and IACUC Responsibility”, May 18-19, Baltimore, MD.

**II. Specific Protocol Design Issues**

**A. Animal Preparation**

All animals must exhibit good health and normal behavior prior to entering a study. Restraint or altered conditions should be planned ahead of time so that the animals will be acclimated to the new conditions prior to conducting the study.

Animals must receive a physical examination appropriate to the species prior to being used in a study to determine the presence of preexisting abnormalities or conditions which would impact the study results. For acute studies, this need be only cursory; for more involved procedures, more extensive examinations should be conducted.
B. Minimization of Pain and Distress

The appropriate use of anesthetics and analgesics is important for ethical and regulatory reasons. Pilot studies, in consultation with the attending veterinarian, may be necessary to assess the compatibility of drugs with the investigation proposed. The PI and the IACUC shall carefully consider any procedures in which alleviation of pain or distress cannot be reasonably assured. The IACUC will maintain current references of recommended doses and techniques for anesthetic and analgesic drugs for investigators on campus. Consultation with the attending veterinarian in the planning stages of the research protocol is highly recommended.

C. Surgery and Perioperative Care

Surgery and postoperative care are addressed in the Guide, PHS Policy and USDA Regulations. These regulatory documents form the basis on which the IACUC must operate. Some procedures are banned or discouraged by these regulations. For example, multiple major surgical procedures may not be performed on the same animal for cost considerations, but may be performed if it is a scientifically necessary part of the proposal, has been approved by the IACUC, or if it is necessary for the health of the animal. Paralytic agents may not be used without analgesia.

MINOR SURGERY: any procedure which does not invade a body cavity or produce permanent physiological or physical impairment.

MAJOR SURGERY: any procedure that penetrates and exposes a body cavity, requires the use of more than a single application of a short-term anesthetic or produces substantial impairment of physical or physiologic functions. Multiple survival surgeries are NOT PERMITTED unless scientifically justified and approved by the IACUC.

All surgeries must be conducted with sterile gloves and masks using autoclaved instruments (major surgery), heat-sterilized instruments (rodent surgery only) or cold-sterilized instruments (minor surgery) following proper aseptic preparation of the animal. If surgical morbidity related to sepsis is higher than expected or higher than the standard for similar procedures, reassessment and justification of the surgical protocol will be required.

Aseptic facilities for non-rodent mammals should include a surgical support area; a preparation area; operating room(s); a dressing area for surgeons and an area for animal intensive care and supportive treatment. Operating rooms should not include sinks and should contain only movable equipment such as anesthetic machines and monitoring equipment. Room surfaces should be impervious to moisture and sanitizable. If volatile anesthetics are utilized, a gas scavenging system must be provided.

With the approval of the IACUC, minor surgical procedures on non-rodent mammals may be performed without the use of a fully aseptic facility. These have been defined as procedures which do not invade a body cavity or produce permanent physiological or physical impairment. Such procedures must still be performed utilizing aseptic technique in accordance with standard veterinary procedures.
A surgical area for rodents and birds can be a room or portion of a room that is free of clutter, easily sanitized, provided for that purpose, approved by the IACUC and not used for any other purpose during the time of surgery. However, for better veterinary oversight, the IACUC requires that rodent and non-rodent surgeries be conducted in a dedicated surgical facility whenever possible. An investigator’s laboratory may be used as a survival surgery area provided such use is scientifically justified and the location is inspected and approved by the IACUC. In selecting a surgical location, every attempt should be make to minimize unnecessary traffic and decrease the potential for contamination of the wound. The location should be designed to include the following three areas:

(1) An area designated for preparation of the animal, including weighing, hair or feather removal and initial skin disinfection. The prep area should be sufficiently distant from the surgery table to minimize the potential for contamination of the surgery area by aerosols generated during animal preparation.

(2) A separate area for the conduct of surgical procedures (from skin incision to wound closure). The surgical table and immediate surrounding areas must be constructed of a material that can be washed with soap and water and then disinfected using appropriate agent (Table 1). The immediate surgical area should be disinfected prior to and between surgeries to decrease dust-borne contamination and may not be used for other purposes during the time of surgery.

(3) A separate recovery area. This should be a quiet, undisturbed location where the animals can be observed.

**Surgical Instruments**

Surgical instruments must be sterile. A list of acceptable methods for instrument sterilization is included in Table 2 below. Surgical instruments may be used on more than one animal; however, any item used on multiple animals must be cleaned and disinfected between animals (see Table 3 below). Hot bead sterilizers are preferred for this purpose, although soaking in disinfectant is also acceptable. Because the effectiveness of disinfection is directly dependent upon the contact time with the disinfectant, the surgeon should anticipate the number of surgical instruments required to guarantee uninterrupted conduct of the procedure while affording ample contact time. Disinfectant should be replace when contaminate with body fluids or tissues.

**Pre-Surgical Evaluation & Treatment**

Pre-existing health conditions may negatively affect the success of the surgical procedures. Pre-surgical evaluations should include visual inspection of the animal and assessment of the behavioral status of the animal. The animals should be alert and behaving normally and should have a smooth coat and clear eyes. Physical or behavioral abnormalities should be brought to the attention of the veterinary staff. Withholding food or water is generally not necessary in rodents or birds unless specifically mandated by the protocol or surgical procedure (e.g. gastrointestinal surgery). **Withhold food or water for more than six hours should be discussed with the**
attending veterinarian. All pre-operative antibiotic or analgesic treatment regimens should be discussed with the attending veterinarian.

Table 1. Recommended Hard Surface Disinfectants
(e.g., table tops, equipment) Always follow manufacturers’ instructions.

<table>
<thead>
<tr>
<th>Agents</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>70% Alcohol</td>
<td>Minimum contact time required is 15 minutes. Contaminated surfaces take longer to disinfect. Remove gross contamination before using. Flammable.</td>
</tr>
<tr>
<td>Sodium hypochlorite (Clorox® 10% solution)</td>
<td>Corrosive. Presence of organic matter reduces activity. Chlorine dioxide must be fresh (&lt;14 days old). Kills vegetative organisms within 3 minutes of contact.</td>
</tr>
<tr>
<td>Chlorine dioxide (Clidox®, Alcide®)</td>
<td></td>
</tr>
<tr>
<td>Gluteraldehyde (Cidex®, Cide Wipes ®)</td>
<td>Rapidly disinfects surfaces. Toxic. Exposure limits have been set by OSHA.</td>
</tr>
</tbody>
</table>

Table 2. Recommended Methods of Instrument Sterilization
Always follow manufacturers’ instructions.

<table>
<thead>
<tr>
<th>Agents</th>
<th>Examples</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical (1st choice):</td>
<td></td>
<td>Effectiveness dependent upon temperature, pressure and time (e.g., 121.6°C for 15 min. vs. 131°C for 3 min.).</td>
</tr>
<tr>
<td>Steam sterilization</td>
<td>Autoclave</td>
<td></td>
</tr>
<tr>
<td>Chemical:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gas sterilization</td>
<td>Ethylene Oxide</td>
<td>Requires 30% or greater relative humidity for effectiveness against spores. Gas is irritating to tissue; all materials require safe airing time. Carcinogenic. Suitable for catheters and implants.</td>
</tr>
<tr>
<td>Chlorine Dioxide</td>
<td>Clidox®, Alcide®</td>
<td>A minimum of 6 hours required for sterilization. Corrosive. Presence of organic matter reduces activity. Must be freshly prepared (&lt;14 days). Must be thoroughly rinsed from instruments using sterile distilled water before use.</td>
</tr>
<tr>
<td>Aldehydes</td>
<td>Gluteraldehyde</td>
<td>Many hours required for sterilization. Corrosive and irritating. Consult Biosafety Officer on proper use. Must be thoroughly rinsed from instruments using sterile distilled water before use.</td>
</tr>
</tbody>
</table>
Table 3. Recommended Instrument Disinfectants
Always follow manufacturers’ instructions.

<table>
<thead>
<tr>
<th>Agents</th>
<th>Examples</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry heat</td>
<td>Hot bead sterilizer</td>
<td>Fast. Instruments must be cooled before contacting tissue.</td>
</tr>
<tr>
<td>Alcohols</td>
<td>70% alcohol</td>
<td>Minimum contact time required is 15 minutes. Contaminated surfaces take longer to disinfect. Remove gross contamination before using. Flammable.</td>
</tr>
<tr>
<td>Chlorine</td>
<td>Sodium hypochlorite (Clorox® 10% solution) Chlorine dioxide (Clidox®, Alcide®)</td>
<td>Corrosive. Presence of organic matter reduces activity. Chlorine dioxide must be fresh (&lt;14 days old). Kills vegetative organisms within 3 min. Must be thoroughly rinsed from instruments using sterile distilled water before use.</td>
</tr>
<tr>
<td>Peracetic Acid/ Hydrogen Peroxide</td>
<td>Spor-Klenz®</td>
<td>Corrosive to instrument surfaces. Must be thoroughly rinsed from instruments using sterile distilled water before use.</td>
</tr>
<tr>
<td>Aldehydes</td>
<td>Gluteraldehyde</td>
<td>Minimum contact time required is 15 min. Corrosive and irritating. Consult Biosafety Officer on proper use. Must be thoroughly rinsed from instruments using sterile distilled water before use.</td>
</tr>
</tbody>
</table>

Surgical Preparation

Preparation of the animals should include removal of hair/feathers from the surgical site with a generous border (at least 1 cm) to avoid contaminating the incision site. Hair or feather removal should be performed in a location separate from the surgical area. The surgical site should be scrubbed with a povidone-iodine scrub (e.g. Betadine®), being careful to scrub from the center of the site toward the periphery. The site should then be rinsed with 70% isopropyl alcohol. Avoid using an excessive volume of alcohol because it contributes to hypothermia by evaporation and it might cause chemical toxicity. In lieu of Betadine-alcohol, the surgical site may be cleaned with chlorhexidine scrub followed by rinsing with chlorhexidine solution. At least three alternating preparations of germicidal scrub and rinse are considered adequate. Finally, the area should be draped with sterile drapes which will help prevent contaminants from entering the surgical field and will provide a sterile area on which to lay sterile instruments during surgery.

The surgeon must thoroughly wash his or her hands with a bactericidal scrub. The use of sterile surgical gloves is required. Dipping exam gloves in bleach or alcohol is not acceptable for this purpose. A surgical mask must be worn for all surgical procedures. A clean gown or surgical scrub top is mandatory; however, a sterile gown is preferable, especially for major surgeries.

Anesthesia

The anesthetic regimen should be determined in consultation with the attending veterinarian and must be described in the approved research protocol. Generally, gas anesthesia (e.g. isoflurane) is recommended for longer procedures that would otherwise require multiple injections of anesthesia. In any case, it must be determined that the animal is fully anesthetized prior to
initiating the procedure and that a consistent plane of anesthesia is maintained throughout the surgery. Anesthetic depth may be monitored in a number of ways. (e.g. respiration rate, corneal reflex, positive toe pinch) and may vary depending upon the species and the anesthetic agent used. For rodents and birds, it is generally not necessary or feasible to monitor the heart rate. For guidance in selection and use of anesthetics, please contact the attending veterinarian.

A record of each anesthetic episode must be kept with the individual animal medical record or, for large scale rodent studies, the group medical record; these records must be made available to the IACUC and the USDA during inspections. If intra-operative morbidity or mortality is higher than expected or higher than the standard for the procedure, a reevaluation of the surgical protocol will be required.

**Surgical Procedures**

All surgical procedures must be conducted as described in the approved protocol. Evaluation of the animals during surgery is critical. In addition to monitoring anesthetic depth as described above, maintaining normal body temperature is of particular importance to avoid hypothermia. Water-circulating heat pads are recommended for this purpose. **Electric heat pads may overheat the animal.** If these are used, the pad should be set on low, a light cloth covering should be placed between the animal and the pad and the animal must be observed frequently for signs of hyperthermia. **Because heat lamps may cause severe hyperthermia or other thermal injury, their use is prohibited.** To prevent corneal desiccation, bland ophthalmic ointment should be placed in the eyes following the onset of anesthesia. If animals will undergo survival stereotaxic surgery, blunt ear bars must be used to prevent damage to the tympanic membrane.

Neuromuscular blockers will only be approved for research procedures where scientific justification is provided for paralysis of the animal. Neuromuscular blockers may not be used alone to provide restraint and immobilization and may only be used in conjunction with drugs which produce surgical anesthesia, and hence, unawareness of the paralytic state. Due to the difficulties in assessing the level of surgical anesthesia in paralyzed animals, the use of these drugs will be approved only if it is clearly established that (1) neuromuscular blockers are essential for the proposed research and (2) that the investigator is able to monitor the animals appropriately for signs of pain and distress.

Before using a neuromuscular blocker, investigators must demonstrate to the attending veterinarian that the proposed procedure may not be performed in the absence of the paralyzing drug. This will assure that the anesthetic technique is sufficient to prevent pain and distress and confirm that escape behavior does not occur in the absence of the neuromuscular blocker.

A surgical plane of anesthesia must be induced and the animal intubated prior to administration of a neuromuscular blocker; furthermore, a surgical plane of anesthesia must be maintained during the entire time that the neuromuscular blocker is active in vivo. **Neuromuscular blockers must not be administered until after the initiation of the surgical procedure (i.e. the skin incision) to ensure that the depth of anesthesia is adequate and the animal does not feel pain.** Neuromuscular blockers should be confined solely to that phase of the procedure for
which they are indicated. They must not be used as a matter of convenience or to substitute for poor control of anesthesia.

**Nitrous oxide** alone is not an appropriate general anesthetic in most animals and cannot provide a surgical plane of anesthesia; therefore, it must not be used alone with neuromuscular blockers during surgical procedures.

The use of a pre-operative analgesic is recommended in addition to the general anesthetic during surgical procedures where neuromuscular blockers are being used.

Controlled ventilation must be initiated prior to administration of the neuromuscular blocking drug.

During paralysis, signs of reaction to pain and stress must be continuously monitored appropriate to the species (e.g. heart rate, blood pressure). If these parameters increase by 20% or more without other explanation, pain/stress may be assumed to be present and the anesthetic level should be deepened. Baseline measurements must be established at the initiation of anesthesia for comparison. If a surgical procedure is being performed, baseline measurements should be made at the initiation of the surgery (skin incision) to determine that the depth of anesthesia is adequate. Monitoring of electroencephalography (EEG) may also be helpful. However, the normal EEG appearance differs with different anesthetics and confirmation of an anesthetized state may not always be possible based on the EEG. Therefore, the investigator should be thoroughly familiar with the expected EEG pattern for the particular anesthetic used.

Core temperature, blood gases and fluid and electrolyte balance must be maintained within normal levels during the period of paralysis. If animals will be paralyzed for long periods of time (e.g. greater than 4 hours), provision must be made for periodic voiding of the urinary bladder.

**References**


Suture Selection

Closure of the muscle body wall or other internal wound closures must be done with an absorbable suture material. A non-absorbable monofilament suture material should be used for skin closure. Placement of subcuticular sutures is acceptable for skin closure and may be performed using absorbable materials. The smallest gauge suture material should be used as practicable. A list of acceptable suture materials is included in Table 4 below.

Because silk and chromic gut may cause tissue inflammation, these materials are not acceptable for wound closure.

Sutures, staples or wound clips must be removed 7-14 days following surgery. If animals will be euthanized within 14 days following surgery, removal of sutures prior to euthanasia is not necessary. A member of the veterinary staff must examine incisions that do not appear to be healing. For guidance in suture selection and use, please contact the attending veterinarian.

Table 4. Acceptable Suture Materials

<table>
<thead>
<tr>
<th>Suture</th>
<th>Characteristics and Frequent Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vicryl®, Dexon®</td>
<td>Absorbable; 60-90 days. Suitable for internal wound closure.</td>
</tr>
<tr>
<td>PDS®, Maxon®</td>
<td>Absorbable; 6 months. Suitable for internal wound closure where extended wound support is desirable.</td>
</tr>
<tr>
<td>Nylon</td>
<td>Nonabsorbable. Suitable for skin closure.</td>
</tr>
<tr>
<td>Prolene®</td>
<td>Nonabsorbable. Suitable for skin closure.</td>
</tr>
<tr>
<td>Stainless Steel</td>
<td>Nonabsorbable. Suitable for skin closure. Requires instrument for removal from skin.</td>
</tr>
<tr>
<td>Wound Clips, Staples</td>
<td></td>
</tr>
</tbody>
</table>

D. Post-Operative Recovery

Observation during post-surgical recovery is imperative. The animal, whether it will recover in or out of its cage, must be kept warm. Water-circulating heat pads are recommended for this purpose. The use of electric heat pads may overheat the animal. If these are used, the pad should be set on low, a light cloth covering should be placed between the pad and the animals/cages, and the animal must be observed frequently for signs of hyperthermia. Somnolent animals should be turned periodically to prevent burns or other thermal injury. Provisions must also be made so that a conscious animal can escape the heat source when it becomes too warm. Because heat lamps may cause severe hyperthermia or other thermal injury, their use is prohibited. A recovering animal must be watched continuously until it is lying on its belly. Unconscious animals must not be housed with conscious cage mates or left unattended.

E. Post-Operative Analgesic Treatment

Analgesia must be provided to all animals following survival surgery unless scientific justification for withholding post-operative analgesics is provided and approved by the IACUC, or if a veterinarian examines the animals and determines that analgesic administration is no
longer necessary. If post-operative analgesics cannot be administered for scientific reasons, the animals must be listed in Pain Category III (pain or distress; no relief provided).

Local pain relievers such as bupivacaine (Marcaine\textsuperscript{®}), in addition to systemic analgesia, may be indicated for some procedures that will result in significant disruption of the skin (e.g., Alzet pump placement, catheter exteriorization), as these drugs may help block the onset of pain due to disruption of the dermal nerve cells. Local analgesics are not intended for use in lieu of systemic analgesics unless it is scientifically justified and approved by the IACUC.

Major survival surgeries require at least 48 hours of post-operative analgesia and then as needed if the animal still appears to be in pain. For major survival surgeries, consultation with the veterinarian should include consideration of pre-operative analgesia.

Minor procedures require at least 24 hours of post-operative analgesia and then as needed if the animal still appears to be in pain.

For guidance on selection and use of analgesics, see Table 5 or contact the attending veterinarian.

**Table 5. IACUC-Approved Analgesics**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Species</th>
<th>Dose</th>
<th>Route</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opiate drugs:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Mice</td>
<td>.05-.1 mg/kg</td>
<td>s.c.</td>
<td>Every 12 hours</td>
</tr>
<tr>
<td></td>
<td>Rats</td>
<td>.01-.05 mg/kg</td>
<td>s.c.</td>
<td>Every 12 hours</td>
</tr>
<tr>
<td></td>
<td>Birds</td>
<td>.01-.05 mg/kg</td>
<td>i.m.</td>
<td>Every 12 hours</td>
</tr>
<tr>
<td><strong>Non-steroidal drugs (NSAIDs):</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carprofen</td>
<td>Mice &amp; Rats</td>
<td>5 mg/kg</td>
<td>s.c.</td>
<td>Every 12-24 hours</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>Mice &amp; Rats</td>
<td>5 mg/kg</td>
<td>s.c.</td>
<td>Every 12-24 hours</td>
</tr>
<tr>
<td>Flunixin meglumine</td>
<td>Mice &amp; Rats</td>
<td>1.1-2.5 mg/kg</td>
<td>s.c.</td>
<td>Every 12 hours</td>
</tr>
</tbody>
</table>

**Regulatory References**

USDA Animal Welfare Regulations §2.32(d)(1)(iv)(A) and (ix): “Procedures that may cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedatives, analgesics or anesthetics unless with holding such agents is justified for scientific reasons, in writing, by the principal investigator and will continue for only the necessary period of time…Activities that involve surgery include appropriate provision for pre-operative and post-operative care of the animals in accordance with established veterinary medical and nursing practices.”
PHS Policy IV.C.1.a-b: “Procedures with animals will avoid or minimize discomfort, distress and pain to the animals consistent with sound research design. Procedures that may cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedation, analgesia or anesthesia unless the procedure is justified for scientific reasons in writing by the investigator.”

Guide for the Care and Use of Laboratory Animals, p. 64: “An integral component of veterinary medical care is prevention or alleviation of pain associated with procedural and surgical protocols...Pain is a stressor and, if not relieved, can lead to unacceptable levels of stress and distress in animals. The proper use of anesthetics and analgesics in research animals is an ethical and scientific imperative...In general, unless the contrary is known or established, it should be assumed that procedure that cause pain in humans also cause pain in animals.”

F. Use of Antibiotics

Post-operative antibiotic treatment should be discussed with the attending veterinarian to determine its necessity. In general, post-operative antibiotics should be provided if the animals will survive long enough to develop severe infection, but may also depend on the invasiveness of the procedure and the immune status of the animals. The administration of antibiotics prior to commencing a procedure can further minimize post-operative infections.

Subclinical Infections: Animals survival alone is not a valid criterion for determining if aseptic technique is necessary or of the acceptability of a rodent surgical technique. The criterion for acceptability should be the absence of untoward, unplanned alteration of physiological functions or behavior due to perioperative infection. Failure to utilize aseptic surgical technique increases the potential for introducing bacteria and activating immune responses in reaction to the bacteria. Several studies have compared the responses of animals subjected to aseptic vs septic surgical procedures and have documented differences in behavioral, physiological and immunological parameters (see references).

References


G. Long-Term Recovery and Monitoring

Post-surgical observations include a minimum daily observation, including weekends and holidays, of the condition of the animal and the surgical site. Animals must be observed for continued recovery which may include state of arousal, indices of pain or discomfort, condition of the surgical wound, appetite, hydration status, mucous membrane or footpad color or fecal and urine production. Some surgical manipulations may require an extended period of post-operative monitoring. The appropriate duration and extent of monitoring can be determined by the veterinarian in consultation with the investigator.

The attending veterinarian must be apprised of any post-surgical complications.

H. Record-keeping Requirements

In accord with regulations, surgical and postoperative records are required for rodents and birds and must include the following: administration of anesthetics; fluid and drug, including the name, dose, route and time of administration; details of the procedure including intra-operative monitoring; daily post-operative recovery observations and treatment including administration of analgesics and antibiotics; monitoring of incision healing including suture/staple removal if applicable, and the initials of the individual performing these tasks. Any adverse outcomes should also be noted.

Each cage card must be clearly marked with the day of surgery. If antibiotics will be provided in the drinking water, special treatment cards should be placed on each cage to communicate this special care to the veterinary staff.

III. Anesthesia and Survival Surgery in USDA-Covered Species

In keeping with federal regulations, all major survival surgeries performed on USDA-covered species must be conducted in a dedicated IACUC-approved surgical facility.

USDA-covered species currently include dogs, cats, non-human primates, guinea pigs, hamsters, rabbits, least shrews, naked mole rats and any other warm-blooded animals with the exception of mice of the genus Mus, rats of the genus Rattus, and birds. Performance of survival procedures involving the use of anesthesia on USDA-covered species must comply with the most recent edition of the NIH Guide for the Care and Use of Laboratory Animals, PHS Policy and the USDA Animal Welfare Act Regulations 9 CFR §2.33(b)(5).

A. Pre-operative Management and Assessment

Steps should be taken to ensure that the surgical procedure will be carried out efficiently, professionally and with adequate record keeping (including a record of all drugs administered and the dose, time and route of administration) and that the animal’s health has been appropriately addressed prior to surgery to minimize the risk of complications during and after surgery. Consideration should be given to having preoperative hematology and serum chemistry tests.
performed prior to surgical procedures. The specific tests should be detailed in the protocol submitted to the IACUC.

**B. Intra-operative Procedures**

Acute (terminal) and chronic (survival or recovery) surgical procedures that may cause more than momentary or slight pain or distress require appropriate use of anesthetics, analgesics and tranquilizers (AATs). Most commonly used AATs have short-term and long-term effects on an animal’s ability to maintain homeostasis. Appropriate monitoring provides important clues about the animal’s homeostatic state.

**C. Intra-operative Monitoring**

Animals that are unconscious and/or intubated must not be left unattended. Monitoring must be done by trained staff from the investigator’s laboratory or the animal facility.

**Cardiovascular**

a. Heart rate must be monitored continuously either by continuous ECG monitoring, blood pressure monitor or pulse oximetry. The heart rate must be recorded every 15 minutes.

b. Mucous membrane color and capillary refill time may be monitored periodically to help assess cardiac output and oxygen saturation.

c. Direct or indirect blood pressure monitoring should be considered for major surgical procedures lasting more than 1 hour.

d. Hypotension may occur due to anesthetic agents, blood loss or evaporative water loss of exposed tissues or expired gases. Blood pressure should be maintained through the use of appropriate intravenous fluid therapy, generally 5-15 ml.kg.hr IV of crystalloids.

**Pulmonary**

a. For intubated animals, auscultation of the chest should be done to assure adequate placement of the endotracheal tube. Airflow should be audible in all lung fields.

b. Pulmonary function must be monitored by continuous capnography, pulse oximetry, observation of the respiratory rate and quality or auscultation. Pulmonary function should be recorded at least every 15 minutes.

c. Pulse oximetry and capnography should be considered for all major surgical procedures.

d. Blood gas monitoring and recording should be considered for major surgical procedures lasting more than 3 hours.
e. Mucous membrane color can be used to assess overall ability to oxygenate but is not a very sensitive measure, especially when the animal is receiving gas anesthesia in 100% oxygen.

**Temperature**

Body temperature should be monitored by digital or rectal thermometers or by electronic temperature probes placed rectally or esophageally. The temperature should be checked and recorded at least every 15 minutes. Core body temperature should be maintained at normal levels with circulating water blankets, warm-air circulating devices (e.g. Bear Hugger blanket), heated surgical table, warmed intravenous fluid therapy or other appropriate methods.

**Anesthetic Depth**

The anesthetic depth should be monitored throughout the surgical procedure. Depending on the species, this can be done by observing responses to manipulation, jaw tone, corneal and palpebral reflexes and position of the eyes.

**D. Post-operative Care and Monitoring**

Adequate post-operative care enhances the animal’s recovery, minimizes pain and distress and is a requirement of both professional and regulatory federal agencies. Adequate post-operative care includes monitoring and documenting the animal’s recovery during the anesthetic recovery period, the acute post-operative period and the long-term post-operative period.

**E. Anesthetic Recovery**

Animals that are unconscious or still intubated after the procedure must not be left unattended. Endotracheal tubes should not be removed until an animal has regained a swallow reflex. Animals must be monitored continuously until they are conscious and sternal.

All animals must be given analgesics unless scientific justification for withholding such agents is provided and approved by the IACUC. Analgesics must be given such that they become effective before the animal emerges from anesthesia. Therefore, analgesia must be administered before or during surgery.

The animal’s status must be monitored at least every 5 minutes. The following parameters should be monitored and recorded at least every 15 minutes during the anesthetic recovery period:

a. Respiratory rate, as assessed by observation, auscultation, capnography or other appropriate method. Any abnormal or deviant pattern of respiration should be noted.

b. Heart rate, as assessed by auscultation, palpation, ECG, pulse oximetry or other appropriate method.

c. Temperature
It is the responsibility of the investigator to arrange for appropriate monitoring during the anesthetic recovery phase, either by a member of the investigator’s laboratory or the veterinary staff. During the recovery period, the animal’s core body temperature should be monitored and maintained in a normal range using circulating warm water blankets, warm water bottles/bags or other appropriate means. **The use of heat lamps is not permitted.**

To avoid aspiration pneumonia, airway obstruction, pulmonary edema, tissue necrosis or edema at pressure points, a recumbent animal’s position should be adjusted every 15 minutes. In addition, capillary refill time, mucous membrane color, condition of the wound and anesthetic plane of the animal should be monitored.

**Acute Post-operative Period**

The acute post-operative period is that period when the animal regains stable physiologic functions, usually over 24-48 hours. Monitoring during this time is usually done 2-3 times daily depending on the type of surgical procedure and the condition of the animal. The Principal Investigator’s staff will monitor and record the post-operative condition of these animals at least once daily. A member of the veterinary staff must also check these animals at least once daily.

The acute post-operative period may require further treatments to stabilize the animals such as fluid therapy, analgesics, antibiotics and more intensive monitoring. If the animal is immobile, the heart rate and core body temperature should be monitored. Analgesia is required in all animals, excluding those in Pain Category III, as described in the IACUC Policy on Post-operative Analgesia.

Post-operative treatments should be administered according to the Principal Investigator’s research protocol or as determined by the veterinary staff in consultation with the Principal Investigator. This may be done by the veterinary staff or by the Principal Investigator’s staff. All medications, including name, dose, route and time of administration must be recorded in the animal’s post-operative record.

**Long-term Post-operative Period**

The long-term post-operative period is from the time of physiologic stabilization to normalization. This usually takes a minimum of 10 days for the animal to totally recover from most survival surgical procedures. Daily monitoring should continue during this time.

Parameters that should be monitored/recorded during this time include: state of arousal; indices of pain or discomfort; condition of the surgical wound; appetite; hydration status; capillary refill time; mucous membrane color; fecal and urine production and any medication administered.

All non-absorbable sutures must be removed at 7 to 14 days after the surgery and the animal’s post-operative record closed. The record is then to be submitted to the veterinary staff. Some surgical manipulations may require an extended period of post-operative monitoring. The
appropriate duration and extent of monitoring can be determined by the veterinary staff in consultation with the Principal Investigator.

F. Personnel Qualifications

The IACUC must determine if the personnel proposing and supporting surgical proposals are qualified to conduct a given procedure and, if not, how to ensure adequate instruction. Persons without formal surgical training may perform surgery when qualified by relevant experience. Various requirements may be made as to the professional background of the investigator and documentation showing ability to perform the specific surgery may be required. Persons with graduate degrees, students or technicians should only perform surgery after formal instruction in surgical techniques or with specific documentation that the proposed technique has been previously performed without complications by the person.

It is impossible to design a surgical instruction course which is applicable to all situations. Regulations require that each institution provide instruction in aseptic surgery applicable to their research programs. Generally, these courses should include instruction in aseptic technique, anesthesia and analgesia and proper surgical technique and may focus on a specific procedure.

Consultation with the attending veterinarian is required during the design and conduct of novel surgical protocols. The IACUC may conduct inspections to ensure proper personnel qualifications and offer instruction. Investigators are encouraged to seek continuing education in research surgical techniques.

Reference:


G. Euthanasia

Euthanasia in the context of biomedical research is defined as the humane killing of an animal by a method (physical or chemical) which produces rapid unconsciousness, subsequent respiratory and cardiac arrest and ultimate loss of brain function without evidence of pain or distress.

Criteria used in determining the appropriateness of a given method include (i) species of animal being used, (ii) qualifications of the person performing the procedure, (iii) minimization of distress to animals and persons performing euthanasia and safety to the latter, (iv) reliability and irreversibility of the method chose and (v) compatibility with the requirements of the research.

In accordance with PHS Policy on Humane Care and Use of Laboratory Animals and USDA Animal Car Policy #3, the IACUC requires that the methods of euthanasia are consistent with the recommendations of the most current version of the American Veterinary Medical Association (AVMA) Panel on Euthanasia unless a deviation is justified for scientific reasons and has been approved by the IACUC.

The 2000 Report of the AVMA Panel on Euthanasia was published in the Journal of the American Veterinary Medical Association on March 1, 2001 (Vol. 281, No. 5) and is also available on the AVMA website: http://www.avma.org/resources/euthanasia.pdf.

The IACUC has determined that the administration of carbon dioxide is not an acceptable method of euthanasia or anesthesia. The recommended method for rodent euthanasia is anesthetic overdose.

Physical methods: In accordance with the Report of the AVMA Panel on Euthanasia, anesthesia must be administered prior to euthanasia by a physical method unless evidence is provided that such agents would interfere with the experimental design. The IACUC will approve the use of the physical methods described below without prior anesthesia only when adequate scientific justification is provided.

Decapitation: those carrying out the method must be properly trained to do so. Equipment used to perform decapitation should be maintained in good working order and serviced on a regular basis to ensure sharpness of blades. A guillotine is sharp enough if it will cut a thick rubber band without dragging it between the blades and sticking. Thus, prior to approving protocols using decapitation for euthanasia, the IACUC requires the following: 1) after each use, the unit should be wiped clean of any biological fluids to prevent buildup of potential corrosion; 2) after cleaning, a few drops of light machine oil (e.g. “3 in 1”) should be applied to blade surfaces and blade channels and the blades run together several times to spread the oil evenly over all moving surfaces. Blades should be replaced or sharpened regularly depending upon frequency or use. Decapitation of small mice or neonatal rodents using sharp scissors or a sharp blade is allowed.

Cervical dislocation: Those carrying out the method must be properly trained to do so. Cervical dislocation may not be performed on rodents weighing greater than 200g since the large physical mass in the cervical region makes manual cervical dislocation more difficult. Decapitation should be used if a physical method is required for rodents weighing more than 200g.
Personnel responsible for performing euthanasia by decapitation or cervical dislocation must be properly trained and proficient in carrying out these techniques. Therefore, personnel who will perform decapitation or cervical dislocation without prior anesthesia must contact the attending veterinarian to receive training in these techniques prior to performing them.

References


IV. Fluid and Tissue Collection

All personnel must document to the IACUC their qualifications to handle the species being used and to perform procedures necessary to collect the fluid or tissue. The method and volume of collection must be appropriate to the species, age and physical condition of the animal. Specific guidance on acceptable volumes and frequency of collection should be sought from the attending veterinarian (need table). Specific training may be requested by the IACUC or the Attending Veterinarian. When multiple samples are required over time, additional methods must be considered to minimize pain and distress (e.g. indwelling catheters, behavioral modification, alternate routes of collection, etc.).

Biopsy generally requires local, regional or general anesthesia as well as appropriate aseptic techniques.

A. Blood Collection Limits

To prevent anemia and dehydration, the IACUC limits survival blood collection to 1.25% (1.25 ml/100 g) of the animal’s current body weight. The frequency of blood collection is dependent upon the volume collected. If the maximum volume is collected, as specified above, blood may be collected once every two weeks. The IACUC requires monitoring hematocrit or serum protein levels when more frequent collections are necessary.
All forms of mutilation used for the collection of blood, including transecting vessels and amputating digits or tails, are unacceptable and incompatible with the humane care and use of laboratory animals.

Survival blood collections may be performed without general anesthesia if peripheral blood vessels are used.

Exsanguinations must be performed under general anesthesia or following euthanasia. Survival intracardiac bleeding is not permitted without scientific justification and must be conducted under general anesthesia due to the painful nature of blood collection via this route.

B. RODENT PROCEDURES

Lateral saphenous vein blood collection: The IACUC recommends the use of the lateral saphenous vein on the hindlimb for blood collection. This technique may be performed in conscious animals and requires clipping or plucking the fur from the area around the vein and swabbing with 70% alcohol prior to puncture\(^1\). Repeated sample collection is permitted provided the volume does not exceed 1.25% (1.25 ml/100 g) of the animal’s current body weight every two weeks.

Retroorbital blood collection: The IACUC does not recommend retroorbital blood collection in rodents for serial sampling. This procedure has been associated with histopathologic and clinical changes in orbital tissues including hemorrhage, inflammation and infection\(^2\). In the absence of a suitable alternative, retroorbital blood collection must be performed under general anesthesia and after application of a topical ophthalmic anesthetic (e.g. proparacaine HCl (Ophthaine\(^8\))). Any residual bleeding must be stopped by gentle digital pressure with clean gauze and an antibiotic ophthalmic ointment must be applied to the affected eye taking care to avoid injury to the cornea. Individuals performing retroorbital blood collection must be adequately trained due to the potential for significant complications.

References


C. Tail Biopsy in Mice

To produce genetically altered rodents, it is often necessary to sample tissue for DNA analysis. Usually, the end of the tail is sampled. The following IACUC policy will ensure the humane sampling of tissue for biopsy from rodents.
In the mouse, the terminal tail ossifies between 2 and 4 weeks of age. Thus, tail sampling is recommended in mice younger than three weeks of age. In mice of this age, biopsy of the distal tail may be performed with local anesthesia after spraying the tail with ethyl chloride. Animals over 3 weeks of age should be anesthetized with a short acting anesthetic (e.g. isoflurane).

Sampling must be performed using sharp sterile scalpels or sharp scissors. If tail biopsies are performed on multiple mice, instruments must be disinfected appropriately between animals to prevent infection and DNA contamination. The use of each blade should be limited to no more than 5 times to prevent the development of a dull cutting edge. The smallest possible section of tail must be removed and adequate hemostatis achieved via a styptic (e.g. silver nitrate, cautery, tissue adhesive, etc.). It is recommended that tail samples be limited to no more than 0.5 cm of tissue.

Alternatives to tail biopsies should be considered. Tissue can be obtained by ear punching or ear snips which can also serve as identification. Small quantities of blood from distal veins (e.g. saphenous vein) may be used for analysis. PCR analyses using saliva\(^1\) and hair\(^2\) have also been described.

**References**


**D. Dosing and Handling**

Dosing with test chemicals may result in distress due either to the nature of the chemical or the procedures involved in its administration, e.g. gavage. Maximum volumes and routes must not be exceeded. Typical gavage volumes are 1-2% of body weight in mice and rats, i.e. 0.2-0.4 ml for a 20 g mouse or 1-2 ml for a 100 g rat.

Investigators must indicate that test chemicals will be administered in a volume appropriate to the chemical, species and route of administration. The least invasive means of delivery compatible with the research goals must be used. More invasive means must be scientifically justified and approved by the IACUC.

When the experimental design requires the frequent or prolonged administration of injectable medications or experimental compounds, the IACUC recommends that alternative methods be considered and discussed with the attending veterinarian. For example, osmotic (Alzet) pumps
and indwelling catheters are two examples of drug delivery refinements that minimize pain and (di)stress to the animals.

V. Antibody Production

A. Polyclonal Antibody Production

Complete Freund’s Adjuvant (CFA) is commonly used but it can cause severe inflammation and can occasionally result in ulceration at the site of injection (CCAC, 1993). Less irritating adjuvants must first be considered and CFA and Incomplete Freund’s Adjuvant (IFA) used only if no appropriate alternative is available. CFA should be used only for the initial immunization with IFA used for subsequent booster injections. Footpad injections are strongly discouraged and may only be approved with scientific justification.

The IACUC recommends the use of commercial vendors as a source of polyclonal antibodies whenever possible. Information regarding off-campus vendors is available from the attending veterinarian.

The IACUC requires that pharmaceutical grade components be used when available and that methods to preclude bacterial contamination be employed (e.g. antigen filtration prior to mixing with the adjuvant). Some pharmaceutical grade adjuvants, such as Montanide, are available and should be a primary consideration when selecting an adjuvant. The most familiar adjuvants are Freund’s and Hunter’s TiterMax®, but investigators should familiarizes themselves with alternatives such as those described below.

B. Selected Adjuvant and their Properties

Freund’s Mineral Oil Adjuvant Emulsions

Freund’s complete adjuvant (CFA) is a mixture of non-metabolizable oil (mineral oil), a surfactant (mannide monooleate) and killed mycobacteria (Mycobacterium tuberculosis or M. butyricum). Freund’s incomplete adjuvant (FIA) is the same as FCA except that it does not contain killed mycobacteria. Freund’s adjuvants are water-in-oil emulsions. If properly mixed, the antigen will be distributed over a large surface area which increases the potential for interaction with relevant antigen presenting cells in vivo. Like other water-in-oil adjuvants, FCA and FIA have a depot effect and release the antigen over long periods of time resulting in a prolonged antibody response. Both formulations can result in adverse reactions from the stimulation of cell-mediated immune responses. FCA is particularly toxic because the host response to the mineral oil and the mycobacteria can result both in local and disseminated granulomatous reactions. Less severe inflammatory reactions result when: a) the concentration of mycobacteria in FCA is less than 0.5 mg/ml; b) more concentrated aqueous antigen solutions are added resulting in an antigen-rich emulsion and reduction in the quantity of emulsion injected; c) multiple injection sites with minimal volumes of emulsion are injected at any one site and d) the injection sites are separated to avoid fusion of inflammatory lesions. FCA is to be used only for weakly immunogenic antigens and only for initial immunizations. If booster
immunizations are necessary, FIA must be used instead. The recommended volumes per subcutaneous injection site of FCA or FIA are:

**Hunter’s TiterMax®**

TiterMax® is a water-in-oil emulsion containing metabolizable oil (squalene) and a non-ionic surfactant (copolymer of poloyoxyethylene and poloyoxypropylene). Most adjuvant activity is attributed to the surfactant’s ability to activate and bind certain complement components which putatively target the antigen to follicular dendritic cells in the spleen and lymph nodes.

Some studies suggest that TiterMax® is superior to Freund’s with some protein antigens, particularly in rabbits and mice. Compared with FCA, TiterMax® can be used in smaller quantities for initial injection which minimizes the inflammatory reaction at the injection site(s) and less frequent booster injections are required.

### Recommended routes of administration and injection:

<table>
<thead>
<tr>
<th>Species</th>
<th>Injection route</th>
<th>Total # injections</th>
<th>Volume per injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse</td>
<td>IM</td>
<td>2</td>
<td>0.02 ml</td>
</tr>
<tr>
<td></td>
<td>SubQ</td>
<td>1</td>
<td>0.04 ml</td>
</tr>
<tr>
<td>Rat</td>
<td>IM</td>
<td>2</td>
<td>0.05 ml</td>
</tr>
<tr>
<td>Guinea Pig</td>
<td>IM</td>
<td>2</td>
<td>0.05 ml</td>
</tr>
<tr>
<td></td>
<td>SubQ</td>
<td>4</td>
<td>0.05 ml</td>
</tr>
<tr>
<td>Rabbit</td>
<td>IM</td>
<td>2</td>
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</tr>
<tr>
<td></td>
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<td>10</td>
<td>0.04 ml</td>
</tr>
</tbody>
</table>

**Montanide ISA Adjuvants®**

A group of oil/surfactant based adjuvants where surfactants are combined with a non-metabolizable and/or metabolizable oil. Performance of the ISA 50 and ISA 70 were found to be similar to Freund’s incomplete adjuvant for antibody production but with less inflammatory response. The surfactant in ISA 50 and ISA 70 is a major component of the Freund’s adjuvant surfactant, mannide oleate.
Syntax Adjuvant Formulation (SAF)®

This Freund’s complete adjuvant alternative is a pre-formed oil-in-water emulsion stabilized by Tween 80 and pluronic poloxyethelene/oloyoxypropylene block copolymer L121. SAF used a low toxicity, high stimulatory derivative of muramyl dipeptide, thr-MDP, and the metabolizable oil squalene.

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ANTIGEN PREPARATION

Antigen preparations should be free of extraneous microbial contamination. Millipore filtration of the antigen prior to mixing with the adjuvant is recommended. The presence of byproducts, such as polyacrylamide gel, should be avoided because of their inflammatory or toxic properties.

Avoid pH extremes, particulate matter and contamination with chemicals such as SDS, urea, acetic acid or other solvents or potentially toxic agents.

Special precautions may be necessary if the antigen is a viable microbe.

Antigen-Adjuvant Emulsions

If FCA is used, the mycobacteria should first be re-suspended by vortexing or shaking. One part or less of Freund’s adjuvant to one part antigen (v/v) is recommended. Two sterile luer-lock syringes, one containing Freund’s adjuvant and one containing the antigen, preferably in sterile saline, are used for these purposes. Glass syringes or plastic disposable syringes without rubber plungers are preferred as the oil reacts with the rubber plunger on plastic disposable syringes. The antigen solution is injected into the adjuvant through a 3-way stopcock or mixing cannula and the emulsion is prepared by pushing the solution back and forth between the syringes for several minutes. An emulsion is properly prepared when it becomes thick, is difficult to inject back and forth through the cannula and will not separate on standing; a droplet placed into a saline solution should not disperse. Emulsification is enhanced by using cold (4°C) adjuvant. Failure of the preparation to emulsify may be due to antigen contamination with SDS or organic solvents. For antigen-adjuvant preparations using adjuvants other than Freund’s, manufacturer’s instructions must be followed.

C. Animal Selection

Rabbits are the most commonly used species for polyclonal antibody production. Specific-pathogen free rabbits must be used. Their use dramatically reduces the morbidity and mortality frequently documented in rabbits infected with microbial pathogens, especially Pasteurella multocida.

Rabbits are covered under the Animal Welfare Act and, as such, all procedures pertaining to their use in research, teaching and/or testing must be entered in the animal’s medical record. Information that must be recorded includes, but is not limited to, sedation/anesthetic events, blood collection, compound administration and euthanasia. The name of any compound used,
volume administered and the site(s) where administered must be recorded. Rabbits maintained as part of long-term (>3 months) projects are expected to have periodic determinations of hematocrit as they are prone to developing anemia.

D. Restraint

Use proper restraint methods during immunization and blood collection procedures to avoid animal and personnel injuries. Acclimating animals to handling and restraining procedures prior to the initiation of immunization or other experimental procedures reduces stress in animals and personnel. Those personnel who are uncomfortable or unfamiliar with animal restraint should contact the attending veterinarian for assistance. Personnel must be trained to perform manual restraint techniques and to appropriately use commercially available restrainers. Sedation with acepromazine during immunization and blood collection reduces stress, enhances vasodilation and can prevent injury to rabbits and personnel.

E. Immunization Site Selection, Preparation and Administration

Carefully select and prepare the immunization site to preclude unnecessary pain and distress during handling and restraint and to minimize infection. Areas commonly used for physical restraint must not be immunized. These areas include the dorsal cervical/scapular and rump areas of rabbits and the dorsal cervical/scapular regions and tail base in rodents. Skin injection sites must be at least 1-3 inches apart depending on the animal’s size.

The site must be prepared in a sterile manner to reduce the risk of abscess. Clip the hair and wipe the site with alcohol to reduce the potential of infection or abscess and facilitate injection site visualization thus permitting appropriate treatment of any developing immunization site lesions. The use of sterile needles and syringes is mandatory to minimize microbial contamination.

For injections, it is essential to use a needle with a sufficiently wide bore (gauge) to permit the smooth passage of the emulsion into the animal. Attempts to force the emulsion through a small needle gauge will result in separation of the needle from the syringe and spattering of the emulsion.

Investigators proposing to use footpad and/or IP injections must provide scientific rationale to the IACUC for review prior to performing these procedures as part of an approved protocol.

F. Post-Injection Observation

Investigators or their staff must observe animals daily, including weekends and holidays, for the following: pain, swelling, abscess, fistula formation, infection or ulceration at or near the immunization site(s). Investigators identifying animals with the above signs must contact a member of the veterinary staff immediately. All observations must be entered into the animal’s medical record.
G. Blood Collection

Blood collection must follow the IACUC Policy on Blood collection in Laboratory Animals. Specific blood collection concerns pertaining to polyclonal antibody production include:

a) Survival blood samples are generally collected via tail vein or retroorbital sinus from rodents under anesthesia and via the central ear artery in rabbits with appropriate sedation/tranquilization with acepromazine. Saphenous or facial vein use in rodents does not require anesthesia. Isoflurane is commonly used with precision vaporizers for inhalant anesthesia in rodents.

b) Blood collection from rabbit ears by transecting the artery or vein is prohibited as is rodent blood collection via tail transaction or serial tail transaction.

c) Use of xylene for dilation of the ear blood vessels is prohibited.

d) Because of the risk of cardiac tamponade, pulmonary hemorrhage and pnumothorax, intracardiac blood collection is limited to terminal procedures and is performed under general anesthesia in both rodents and rabbits.

e) Enter the blood volume collected in the animal’s medical record along with any hematocrit results.

H. Alternative Techniques

Antibody production in chickens is an alternative to the use of other animals for polyclonal antibody production. Chickens offer the advantage of obtaining antibody through a non-invasive method (egg yolk).

Another alternative method in rabbits consists of placing a subcutaneous whiffle ball chamber. Immunizations are made directly into the chamber and antibody-rich fluid is harvested from the chamber. Advantages of this technique include greater flexibility in immunogen preparation, minimal discomfort and minimal tissue reaction, ease of immunization and fluid collection and recovery of large volumes of antibody-rich fluid with low cellularity and absence of lipids. This procedure does require surgical placement of the chamber.

References:


I. Monoclonal Antibodies

The production of monoclonal antibodies in the live animal is a three-step process. First, an animal is immunized to generate antibody-producing cells which are terminally harvested from the donor via splenectomy and then fused with a tumor cell line. Second, select the appropriate target cells in vitro and perpetuate their antibody secreting ability either in culture or by injection into the peritoneum of mice to yield ascites. Third, produce ascites by first treating the animals with a priming agent (e.g. Pristane) that causes irritation of the peritoneum, secretion of fluid into the peritoneal cavity and suppression of the immune response to a growing tumor. The mouse is then injected with the selected tumor cells to stimulate tumor development. Fluid is produced by the tumor and accumulates in the peritoneum for later collection. All stages of this process are potential sources of distress.

In reviewing proposals which include the mouse ascites method, the IACUC is required by federal regulations to determine that (i) the use of the ascites method is scientifically justified,
(ii) methods that avoid or minimize discomfort, distress and pain (including in vitro methods) have been considered and (iii) such alternative have been found unsuitable.

**J. JUSTIFICATION FOR THE ASCITES METHOD**

The National Research Council Committee on Methods of Producing Monoclonal Antibodies (http://grants.nih.gov/grants/policy/antibodies.pdf) states:

- “It is incumbent on the scientist to consider first the use of in vitro methods for the production of monoclonal antibodies (mAB). When hybridomas fail to grow or fail to achieve a product consistent with scientific goals, the investigator is obliged to show that a good-faith effort was made to adapt the hybridoma to in vitro growth conditions before using the mouse ascites method.”

- “In vitro methods for producing mAB are appropriate in numerous situations and it is the responsibility of the researcher to produce scientific justification for using the mouse ascites method.”

Although the IACUC may approve the use of the mouse ascites for the production of mABs, a proposal to use this method must contain sufficient information for the Committee to evaluate whether or not there is adequate justification. **Ease of purification, higher antibody yield and lower cost are not acceptable reasons to use the ascites method unless carefully and properly justified.**

**For in vivo monoclonal antibody production at other institutions,** provide the following information:

- Name of organization producing the antibodies


- Organization’s accreditation status with the Association for Assessment and Accreditation of Laboratory Animal Care International. A directory of AAALAC-accredited institutions is available at http://63.70.211.210/cfdocs/aaalacsearch.cfm.


**ALTERNATIVES**

Federal regulations require investigators to consider alternatives to procedures that may cause more than momentary or slight pain or distress to animals. As ascites production in mice may
cause more than momentary or slight pain or distress to animals, scientists must consider alternatives to this method. The IACUC will not approve protocols that do not provide scientific justification for why in vitro techniques such as hollow fiber bioreactors cannot be used.

K. Guidelines for the Ascites Method

Pain Categorization

Due to the potential for unalleviated pain or discomfort from accumulation of fluid in the peritoneal cavity, the IACUC requires that animals used for ascites production must be listed under Pain Category III (pain or distress, no relief provided because the use of anesthetics, analgesics or tranquilizers will interfere with the experimental design).

Priming

Pristane, the most commonly used priming agent for ascites production, induces a granulomatous reaction and interferes with peritoneal fluid drainage. A dose on 0.5 ml. i.p. may cause distress which is not seen with the equally efficacious dose of 0.1 to 0.2 ml. Therefore, pristane priming must be performed with doses no greater that 0.2 ml per injection unless scientifically justified in the protocol and approved by the IACUC. Scientific justification must be provided for the use of priming agents other than pristane.

Inoculation

Tumor cell lines should be tested for murine virus. Untested mice or those contaminated with murine viruses must be isolated. Hybridoma cell suspensions in 0.5 ml of media are recommended for increased mAB production.

After inoculation with ascites-producing tumor lines, mice must be observed daily (including weekends and holidays) to monitor the degree of abdominal distention and for signs of clinical abnormalities and distress (e.g. hunched posture, rough, dehydration or difficulty in ambulation). The animals must be weighed at least every other hair coat day beginning seven days after hybridoma injection.

Animals having difficulty reaching their food or water should have food pellets and a water source place inside their cage.

Harvesting Ascites Fluid

Accumulation of fluid in the peritoneal cavity causes abdominal distention, discomfort and may even cause respiratory distress. Ascites fluid must be removed before abdominal distention causes discomfort, tachypnea or interference with normal activity. Any animal with a grossly distended abdomen in which the skin is drawn tight must be tapped and/or euthanized. Animals must be tapped before ascites fluid volumes exceed 20% of the animal’s baseline body weight prior to hybridoma cell inoculation.
Ascites fluid may be collected with a sterile 18-22 gauge hypodermic needle (glass syringes are more effective for this procedure than plastic). Passive flow from the needle usually works best. The collection procedure should be performed using aseptic techniques including clipping or shaving the fur from the injection area, preparation of the site with 3 alternating washes of both betadine and 70% ethanol and using a new, sterile hypodermic needle for each mouse. To minimize discomfort, the needle should be inserted lateral to the bladder and parallel to the body wall. Anesthesia is not normally required if those performing the collection are experienced. The animals should be anesthetized if new personnel are being trained.

Animals must be observed continuously by trained personnel at least 30 minutes immediately following abdominal paracentesis for signs of hypovolemic shock and distress. If an animal appears hunched or lethargic, an equal volume of warm saline should be administered subcutaneously.

At a maximum, animals may be tapped twice and allowed to recover. The third tap, if one occurs, must be conducted following euthanasia.

Euthanasia

Animals bearing ascites tumors must not be maintained past a point where they are in good health. Animals must be euthanized promptly if they display severe signs of pain or distress or exhibit severe or persistent clinical abnormalities (ruffled coat, hunched posture, anorexia, dehydration, pallor, weight loss, inactivity, difficulty ambulating, tachypnea or dyspnea). Any animal in the moribund condition must be euthanized.

References


VI. Chronic Pathological States/Disease Induction

The justification for inducing chronic states must be carefully thought through and the limits of an allowable disease condition predetermined. A full schedule of monitoring, particularly for potentially painful conditions, must be included in any proposal. The study of naturally occurring pathological models is preferable to inducing such states artificially.

Criteria for morbidity assessment and allowable morbidity must be determined with the Attending Veterinarian during the planning stages of a protocol involving chronic pathological state/disease induction.

A. Death as an Endpoint (See Table 3-1)

As an objective and unequivocal data point, death has been used as an endpoint in cancer, infectious disease and other animal studies, especially for drug safety and efficacy studies. Increased public interest, scrutiny and regulation have led to a reevaluation of its appropriateness. Much of the current concern arises from the use of LD50 tests for chemicals and drugs to determine acute toxicity measures.

The routine use of death as an endpoint is disallowed. Endpoints other than death must always be used whenever the research objective makes it possible. Death as an endpoint must be scientifically justified in the proposal and approved by the IACUC. Drugs or techniques to alleviate pain or distress preceding death must be used unless they would interfere with the scientific objectives of the study. Any proposal foregoing the use of anesthetics, analgesics or tranquilizing drugs must be scientifically justified and approved by the IACUC.

Investigators must administer euthanasia in death endpoint experiments prior to the actual death of the animals unless experimental validity will be compromised. Moreover, animals in these experiments must be monitored at least daily (including weekends and holidays) by personnel trained and experienced in recognizing signs of morbidity. More frequent monitoring may be indicated for some experimental protocols. For experiments where scientific validity requires death as an endpoint, the experimental design must reflect a rigorous effort to minimize the number of animals.

B. Morbidity

Investigators must be able to judge and perform euthanasia on moribund animals based on objective signs of dying, professional judgment and the experimental protocol. Some known signs of illness or dying which may be applied are listed below. The specific indicators used for euthanasia must be included in the design of the experimental protocol. However, the particular combination of signs indicating euthanasia will vary depending on the experimental endpoints.
Signs for Judging Morbidity (disease/illness)

- Rapid respiration, very slow, shallow and labored respiration
- Rapid weight loss

Table 3-1. Alternative Endpoints for Studies with Potential Lethality

<table>
<thead>
<tr>
<th>Alternative Endpoint</th>
<th>Example</th>
<th>Application</th>
</tr>
</thead>
</table>
| Tumor Characteristics                        | Max. size: 1.5 cm (mouse) or 2.5 cm (rat) 10% of normal body weight, necrosis, infection | Subcutaneous or intraperitoneal tumors and hybridomas  
Organ metastases                                                                 |
| Peripheral Blood Cell Counts                 | Depends on cell type                                                     | Leukemias, infectious disease, anemia                                        |
| Prolonged Inappetence/Cachexia               | Loss of weight (20% of normal body weight) and/or condition              | Metastatic disease, chronic infectious disease  
Supportive treatment required  
(food in cage, gel packs, sc fluids)                                           |
| Inability to Obtain Feed and Water           | Tumors  
Paralysis, oro-facial or cervical lesions, other non-ambulatory condition | Many                                                                       |
| Signs of Severe Organ or System Involvement  | Respiratory: rapid or labored breathing, coughing, rales  
Cardiovascular: shock, hemorrhage, arrhythmias, anaphylaxis  
Gastrointestinal: severe diarrhea or vomiting, blood in stools  
Peripheral Nervous System: flaccid or spastic paralysis, paresis  
CNS Signs: circling, blindness, dementia, convulsion; seizures, lethargy  
Integument: severe inflammation, ulceration; extensive hair loss, | Toxicity testing; neurodegenerative disease, epilepsy, autoimmune disease |
| Moribund or Pre-moribund State               | Define with specific clinical signs and euthanize when reached           | Many                                                                       |

- Ruffed fur (rough hair coat)
- Hunched posture
- Hypothermia or hyperthermia
- Ulcerative dermatitis or infected tumors
- Loss of appetite
- Diarrhea or constipation
Signs for Judging the Moribund Condition (state of dying)

- Impaired ambulation (unable to reach food or water easily)
- Evidence of muscle atrophy or other signs of emaciation (body weight is not always proportionate)
- Obvious prolonged illness, including lethargy (drowsiness, aversion to activity, lack of physical or mental alertness), prolonged inappetence, bleeding, difficulty breathing, central nervous system disturbances, chronic diarrhea or constipation
- Inability to remain upright

Signs of pain in animals

- Animal not alert
- Abnormal movement or postures
- Inappetence or dehydration
- Guarding reaction when likely areas of pain are palpated
- Vocalization when palpated or moved
- Self-mutilation
- Restlessness or lethargy

C. Strategies for Reducing Animal Numbers in Death-Endpoint Experiments

LD50 studies are widely criticized as cruel and wasteful of animals. Because of the large numbers of animals involved, LD50 studies are no longer acceptable by some federal regulatory agencies.

Statistical methods have been developed that reduce the number of animals used without compromising experimental reliability. One approach to derive median values with relatively few samples is the up-and-down procedure. Whereas conventional methods using a dose-response design generally employ 24 to 40 subjects, LD50 values calculated through the up-and-down procedure can use as few as six animals. The up-and-down procedure yields essentially identical LD50 values as the conventional dose-response experiments. Those investigators whose work requires death as an endpoint should review current statistical approaches to reducing animals numbers.

References


VI I. Hazardous Materials

The IACUC must pay attention to proposals employing potentially hazardous materials including radioactive substances, infectious microorganisms and hazardous chemicals. These all have the potential of causing harm to animals and personnel in the facility. All such materials will be disposed of in accordance with applicable local, state and federal laws and guidelines and in consultation with Western University’ Office of Environmental Health.

VIII. Field Studies

Since federal requirements and standards focus primarily on laboratory animal care and use, field biologists in organizations devoted to the study of fish, amphibians, reptiles, birds and mammals and the National Science Foundation may be helpful with guidelines for field work with these animals.

Unique concerns in the field include the impact of a given proposal on the native populations of animals at the site. This can be due to the use of enclosures or the effect of changed behavior of the study animals on other populations in the vicinity.

Proposed studies should be assessed by the IACUC according to a number of priority questions which are similar to those used for a laboratory-based proposal:

1. Species Selection

   The most common and least sensitive species should be studied in preference to rare or endangered ones or ones known to be particularly timid and susceptible to distress.
Consideration should be given to whether the population is stable, growing, declining or marginal. If either of the latter is evident, careful attention must be given to the potential impact of the proposal.

2. Site Selection

Many animals live in a variety of habitats and the choice of a study site conducive to obtaining maximal results with minimal disruption should be given priority. The impact of other human enterprises on the site should also be considered, for example agriculture, tourists, hunting and fishing may all disrupt a study. The ownership of the site and whether permits are required to gain access or to conduct experiments are also crucial considerations. The investigator must submit copies of all necessary permits to the IACUC.

3. Methodologies to be Employed

If animals are to be captured, methods and numbers should be detailed in the proposal. Measures taken to alleviate distress and injuries should be described. A discussion of the potential impact of capture on the animals’ subsequent behavior should also be included. If the animals are to be monitored in the wild, investigators must indicate if they plan to follow the animals by their natural markings or if they will be artificially marked. If the latter, a clarification of methodology and potential trauma is necessary; e.g. paint markings may increase visibility to predators. Site manipulations may include the removal of prey, predators or the addition of either. Fences might be erected to limit the movement of populations. Individual animals may be periodically removed to take tissue samples. If these individuals are meant to survive, aseptic practices should always be employed. Potential pain or distress to an animal must be assessed and the investigator’s justification evaluated in the context of the value of the data to be obtained. Consideration should also be given to additional data that might be obtained at no further cost. Potential long term effects on individual animals, their community and other species in the vicinity must also be evaluated.

References


IX. Role of the Attending Veterinarian

Institutions using animals for teaching and research are required by law to have an attending veterinarian associated with their animals care and use program unless they only use rats and mice or receive no federal funds.

Western University will maintain a contractual relationship with a board certified laboratory animal medicine veterinarian to oversee the Animal Care Program and the Animal Facility. Western University has contracted with Dr. Marcelo Couto to serve as the attending veterinarian. He may be reached via digital pager at (909) 469-5423 or you may leave a message with the IACUC office at (909) 469-5619. Dr. Couto is routinely on campus the second Friday of each month during the hours of 12-3 PM.

Qualifications

Dr. Marcelo Couto (Western University attending Veterinarian, 2003-present) attained his DMV from the University of Buenos Aires, Argentina in 1979. He is a Diplomate of the American College of Laboratory Animal Medicine (1998) and Director of the UCLA Division of Laboratory Animal Medicine. He is also a member of the American Association for Laboratory Animal Science.

Responsibilities

The chief responsibility of the attending veterinarian is to provide for the health and welfare of the animals. Attending veterinarians must coordinate with the technical staff to ensure adequate daily animal husbandry. The details will depend on the species of animals employed and the nature of the activities in which they are used, but in all cases the care must comply with USDA Regulation, the PHS Policy and the Guide.

To reduce the risk of infectious diseases in the animal facilities, investigators are encouraged to obtain animals from reputable vendors who produce high-quality laboratory animals that are pathogen-free. Random source or wild-caught animals are obtained from a variety of sources, including pounds, shelters or farms which are not subject to the same standards. Before their use, clinical evaluation and conditioning of these animals is required to ensure that they are not carrying diseases which can be transmitted to other animals, including humans. All incoming...
animals, regardless of source, will be quarantined until it has been determined that they do not pose a health risk to other animals in the facility.

The veterinarian is responsible for monitoring animal health and providing adequate diagnosis and treatment of animals when necessary. The veterinarian may delegate responsibility for care to trained technical staff, but he/she must always be available to provide for rapid diagnosis and treatment.

The veterinarian is also responsible for overseeing the use of suitable anesthetic and analgesic agents; appropriate selection of species for research projects and surgical procedures and pre- and post-surgical care. The veterinarian should discuss with investigators the design and implementation of their study proposals and may provide written guidelines dealing with these and other issues. Consultation between the investigator and the veterinarian before submission of a proposal to the IACUC may address many concerns and expedite the review process.

USDA Regulations require the institution to provide training and instruction to personnel on humane methods of animal maintenance and experimentation. The attending veterinarian and the animal resource program staff, in conjunction with the IACUC, shall provide such training.

The attending veterinarian or his/her staff may be co-investigators or principal investigators on some projects. In such cases, the ICUC must address the potential conflict of interest by seeking the input of another qualified laboratory animal veterinarian.

PHS Policy requires institutional occupational health programs to include personnel who work in the animal resource facilities or whose activities include substantial animal contact. The veterinarian, in cooperation with appropriate health and safety officials, is responsible for the implementation and execution of the aspects of the program which are concerned with animal health and safety issues.

A. The Veterinarian and the IACUC

The veterinarian’s role on the IACUC is mandated by USDA Regulations and PHS Policy. Any veterinarians sitting on the IACUC must keep abreast of current literature on comparative medicine and laboratory animal science. The knowledge gained may lead to alternative techniques or models or species which may augment the study design. The attending veterinarian will be a voting member of the IACUC.

B. Personnel Qualifications and Training

USDA Regulations and PHS Policy put responsibility on the research institution to ensure that all personnel involved in animal care and use are appropriately qualified to conduct the proposed activities.

Western University requires investigators to be certified by the IACUC in levels I-III of Animal Care and Use (see below).

**Level I training** includes institutional policies, federal regulations and animal welfare, legal and ethical issues, the concept of the 3Rs, research issues, basic animals care/biology/techniques,
occupational health and safety and facility-specific issues. Satisfactory completion will be certified and maintained on file.

**Level II training** includes species-specific training covering the care, handling and research uses of the elected species. Satisfactory completion will be certified and maintained on file.

**Level III training** (advanced techniques, etc.) must be documented or proficiency demonstrated as determined by the IACUC. Continuing education will be required annually (1 course).

C. **Education Program Design**

The program must be flexible in design so that a heterogeneous group of investigators, technicians, students, IACUC members and veterinarians can be accommodated.

The content of the educational program is governed by legal requirements and by the specific scientific activities conducted at the institution. Certain basic procedures will be common to most programs, for example, blood sampling, injection methods, anesthesia and analgesic use. Investigators must be made familiar with the means to correct perceived deficiencies of animal care and treatment and they must be familiar with information sources for optimal methods and methods to avoid unnecessary duplication of studies. Instructional methods should be designed to heighten the users’ sensitivities to their animals and any potential adverse effects to these animals as a result of the procedures used. Training and instruction of personnel must include guidance in several areas.

- Humane methods of animal maintenance and experimentation, including the basic needs of each species of animal, proper handling and care for the various species of animals used by the facility, proper pre- and post-procedural care of animals and aseptic surgical methods and procedures.

- The concept, availability and use of research or testing methods which limit the use of animals or minimize animal distress.

- Proper use of anesthetics, analgesics and tranquilizers for any species of animal used by the facility.

- Methods whereby deficiencies in animal care and treatment are reported, including deficiencies reported by any employee of the facility. **No facility employee, Committee member or laboratory personnel shall be discriminated against or be subject to any reprisal for reporting violations of regulations or standards under the Animal Welfare Act.**

- Utilization of services (e.g. National Agricultural Library, National Library of Medicine) available to provide information on appropriate methods of animal care and use, alternatives to the use of live animals in research, unintended and unnecessary duplication of research involving animals and the intent and requirement of the Act (Source: USDA Regulations, 9 CFR Part 2, Subpart C. Section 23.1, Federal Register, August 31, 1989).
The IACUC will provide animal care and use training to all faculty and staff through its IACUC 101 course. This course will consist of on-line self-instruction covering Levels I and II training and hands on practical instruction by the attending veterinarian and Animal Facilities Manager. Practical instruction will be limited primarily to rodents but training with other species and Level III training for all species will be available on request through the IACUC by the attending veterinarian.

X. Evaluation of the Program

The program must be periodically revised and updated to fit the needs of the individuals involved and the legal requirements of the institution. The IACUC will monitor the instruction available and assess the capabilities of investigators and staff. The opinions of the individuals completing different components of the educational program will be solicited.

References


http://www.researchtraining.org

XI. Protocol Review Process

The IACUC requires submission of proposals in a format reflecting requirements of the Animal Welfare Act and other federal regulations (See Table 3-2). The IACUC Chair will assign a given proposal to a Committee member for in-depth review. This primary reviewer is responsible for presenting a description of the proposal to the Committee along with any concerns he/she may have. However each Committee member will receive a copy of each protocol. The Committee may use additional consultants to assist with specific proposals. Application forms may be requested from the IACUC Office, ext. 5619 or srobes@westernu.edu.

An electronic copy and a signed hardcopy of a protocol must be submitted to the IACUC Office two weeks prior to the meeting at which it is to be reviewed. Any new activities proposed must be submitted in writing to the IACUC and may not begin until the amendment has been formally approved.

The IACUC shall review all protocols and determine that they are in accordance with the Animal Welfare Act and PHS Policy and that the protocol is consistent with the Guide unless acceptable scientific justification for a departure is presented. The IACUC shall also determine that the protocol conforms with the institution’s PHS Statement of Assurance.
Table 3-2. Federal Criteria for Granting IACUC Approval

<table>
<thead>
<tr>
<th>Activities</th>
<th>Must be in accord with USDA Regulations/PHS Policy.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain/Distress</td>
<td>Must avoid/minimize discomfort/distress/pain. If pain/distress is caused, appropriate sedation, analgesia or anesthesia will be used. Attending veterinarian must be involved in planning. Use of paralytics without anesthesia is prohibited. Animals with chronic/severe unrelievable pain will be painlessly euthanized.</td>
</tr>
<tr>
<td>Surgery</td>
<td>Must meet requirements for sterile surgery and pre/post operative care. Cannot use one animal for several major operative procedures from which it will recover, without meeting specified conditions.</td>
</tr>
<tr>
<td>Euthanasia</td>
<td>Euthanasia method must be consistent with USDA Regulations/AVMA recommendations.</td>
</tr>
<tr>
<td>Housing/Health</td>
<td>Animal living conditions must be consistent with standards of housing, feeding and care directed by veterinarian or scientist with appropriate expertise.</td>
</tr>
<tr>
<td>Alternatives</td>
<td>There must be considered alternatives to painful procedures; also must document consideration of alternatives if animals experience pain or suffering.</td>
</tr>
<tr>
<td>Rationale and Methods</td>
<td>Must provide written narrative of methods/sources.</td>
</tr>
<tr>
<td>Duplication</td>
<td>Must provide assurance that activities do not unnecessarily duplicate previous efforts.</td>
</tr>
<tr>
<td>Qualifications</td>
<td>Personnel must be appropriately qualified.</td>
</tr>
<tr>
<td>Deviations from Requirements</td>
<td>Must be justified for scientific reasons, in writing.</td>
</tr>
</tbody>
</table>

Each Committee member will have an opportunity to express their concerns and vote on each protocol at a convened meeting of the IACUC. Decisions regarding protocol applications will be made by majority vote of the quorum. Minority opinions shall be documented in the meeting minutes. Consultants may not participate in official decisions regarding protocol applications; nor may any Committee member participate in review or approval of an application in which the member has a conflicting interest except to provide information requested by the IACUC. A Committee member who has a conflicting interest may not contribute to the quorum. The investigator may be invited to the meeting to answer questions that may arise from this discussion.

As a result of the review process, one of the following decisions shall be made by the IACUC:

1. Unqualified approval: The IACUC considers that all significant points have been adequately addressed by the investigator. With this approval, the investigator may conduct the experiments on the number of animals described in the proposal for up to three years.

2. Conditional approval, pending clarification: The IACUC considers that there are significant points needing clarification. With satisfactory written responses to issues raised by the IACUC, the protocol will be reclassified as an “Unqualifies approval” By the IACUC/
3. Deferral: The IACUC considers that there is insufficient information available or that the proposed studies are not sufficiently clear to make a determination.

4. Disapproval: The Committee feels that the investigator has not adequately met the concerns of the IACUC. The investigator will not be permitted to conduct experiments on animals under this protocol.

For conditionally approved protocols, the concerns of the Committee will be conveyed to the investigator by a formal letter from the Office of the IACUC. The investigator must address the concerns and respond to the Office of the IACUC who will forward the response to the primary reviewer. The primary reviewer will determine if the concerns have been met. If so, the primary reviewer may determine that the protocol is approved and so notify the IACUC Office which will issue a letter of approval to the investigator.

**Only research and teaching involving animals approved by the Western University IACUC may be conducted at this institution. However, proposals that have been approved by the IACUC may be administratively rejected by the Institutional Official (IO).**

**A. Continuing Review**

Each investigator must submit an Annual Renewal and Progress Report for review and approval by the IACUC Chair. The Chair may request changes to the approved protocol prior to renewing the protocol or the Chair may bring the renewal request before the full committee for review and approval. Decisions by the chair on annual renewal requests will be read into the minutes of the next regularly scheduled meeting of the IACUC. Any Committee member may request full Committee review of a protocol up for renewal.

A new protocol application must be submitted for full IACUC review and approval every three years. Investigators shall be notified 60 days prior to their protocol’s anniversary date that a progress report or new protocol is due.

Forms may be obtained from the IACUC Office (srobles@westernu.edu) or they may be downloaded from the intranet. An electronic copy and a signed hard copy must be sent to the IACUC Office.

**B. Suspension of Approved Protocols**

The IACUC may suspend a previously approved activity if it determines that the activity is not being conducted in accordance with the approved protocol, applicable provisions of the Animal Welfare Act, The Guide or the Institution’s PHS Statement of Assurance. The IACUC may suspend an activity that jeopardizes animal welfare at any time but the protocol can only be suspended after review of the matter at a convened meeting of a quorum of the IACUC and with a vote to suspend by a majority of the quorum. If the IACUC suspends an activity, the IO, in consultation with the IACUC, shall review the reasons for the suspension and take appropriate corrective action. The IO shall notify the PHS, OLAW, USDA (if applicable) and the sponsors of any suspended activities.
All cages housing animals belonging to a suspended protocol will be flagged with a sign stating “Do Not Use by Order of the IACUC”. Animals belonging to a suspended protocol will be maintained by the animals care facility personnel until the issues surrounding the suspension have been resolved. If the protocol is reinstated, the project may proceed according to the approved protocol or any new requirements by the IACUC. If the protocol is not reinstated, the disposition of the animals will be determined by the IACUC. Reinstatement of a suspended protocol shall be the vote of a majority of a quorum of the IACUC.

C. Changes to Approved Protocols

Significant and minor changes to an existing approved protocol may be requested by the investigator. Minor changes are those that do not affect the scope of the investigation, its time course, number or species of animals used, anesthetic and analgesic agents used or level of invasiveness. Significant changes do involve changes to the above categories.

The review and approval process for significant changes to a protocol will be the same as that described for full protocol application review. Minor changes will be reviewed by the IACUC Chair and the Attending Veterinarian; any concerns will be resolved with the investigator. The Chair may determine the request to be a significant change and require full IACUC review. Any approved changes will be added to the approved protocol file.
Chapter 4. IACUC Policies, Procedures and Responsibilities

There are eight basic Institutional Animal Care and Use Committee (IACUC) functions (PHS 1986, IV.B.1. – 8). These functions include reviewing the overall animal program and inspecting the animal facilities every 6 months; reviewing and approving animal study proposals initially and at least once every 3 years thereafter (annually under U.S. Department of Agriculture Animal Welfare regulations [9 CFR 1-3]; reviewing concerns about the animal care and use program; making recommendations to the institutional official about any aspect of the institution’s programs, facilities or training and suspending activities involving animals under certain circumstances.

I. Membership

The President shall appoint a Chair and members to the IACUC who are qualified through experience and expertise to oversee the institution’s animals care and use program and animal facilities. The Committee must consist of not less than 5 members and shall include at least one doctor of veterinary medicine with training or experience in laboratory animals medicine (voting member) who has direct or delegated program authority and responsibility for activities involving animals at the institution; one practicing scientist experienced in animal research (voting member); one member whose primary concerns are in a nonscientific area (voting member); one member who is not affiliated with the institution other than as a member of the IACUC and is not an immediate family member of a person affiliated with the University (voting member). The term of appointment is two years with staggered terms. The IACUC may also include the Institutional Official, to whom the IACUC reports and the Animal Facilities Manager as ex officio, non-voting members. Any individual who meets the requirements of more than one of these member categories may fulfill more than one of the requirements, but no committee shall consist of fewer than five members. Further, the committee shall not have more than three members from the same administrative unit.

OPRR and USDA both maintain that nominal compensation is permissible without jeopardizing a member’s nonaffiliated status if it is only in conjunction with service on the IACUC. The level of reimbursement varies from payment of travel and related expenses, such as parking and meals, to modest monetary payments for participation in this capacity. The dollar amount of compensation, if any, should not be so substantial as to be considered an important source of income or to influence voting on the IACUC.

II. Meetings

• Monthly meetings will be held as needed to fulfill responsibilities of the IACUC

• The University shall maintain minutes of the IACUC meetings and shall include records of attendance, activities of the Committee, committee deliberations, records of proposed activities involving animals and whether IACUC approval was given or withheld.
• **Conducting official business:** Although there is no requirement that all members be present at all IACUC meetings, the requirement that the IACUC be properly constituted in order to conduct official business is explicit in not only the PHS Policy and USDA Animal Welfare Regulations, but also in the corresponding authorizing statutes. Accordingly, the validity of IACUC actions is always predicated on the existence of a properly constituted IACUC. When it becomes apparent that an improperly constituted IACUC has approved a research or teaching proposal or taken other official action, that action is, by definition, invalid. It follows that animal-related activities without valid approval must be suspended until appropriate review and approval have occurred. In addition, prompt reporting of such findings and corrective actions to OPRR, in accordance with the PHS Policy (IV.F.3), is expected. Except as outlined below, official business will only be conducted by a convened quorum.

• Official business includes all of the activities described in the first paragraph of this chapter.

• **Convened quorum:** A “convened quorum” means a meeting of more than 50% of the members of the IACUC. This should be the traditional gathering of people in a meeting room at the same time. Other forums that provide the same opportunities for members to deliberate interactively with a quorum of other members of the committee may be functionally equivalent. Conference calls, audio-video conferences and possibly some forms of highly interactive on-line computer discussion groups may qualify in exceptional circumstances. A committee member not present due to a conflict of interest shall not be considered in determining if there is a convened quorum.

The simple polling of IACUC members does not, however, satisfy the definition of a meeting of a convened quorum and should not be used for conducting IACUC business that requires the vote of a convened quorum of the committee. For example, polling should not be considered a valid method of voting under the “full committee” review method of protocol review and is not an acceptable substitute for having a vote of a convened quorum on the suspension of a previously approved activity involving animals.

**III. Facility Inspections**

Per PHS Policy and USDA Regulations, the IACUC shall inspect all institutional animal facilities every six months to ensure that the institution maintains compliance with applicable animal care and use policies, guidelines and laws. An updated list of all facilities to be inspected will be maintained by the IACUC. The USDA Regulations require inspection of all managed animal resource facilities and any other animal containment facilities in which animals are kept for more than twelve hours. PHS Policy requires inspection of all surgical facilities and areas in which animals are maintained longer than 24 hours.

The IACUC Chair shall schedule all animal facilities inspections and shall notify the IO of the time and date of the inspection. The IACUC may determine whether the supervisory personnel of various facilities should be notified of the date and time of an inspection.
The IACUC may inspect the facilities by assigning specific facilities to subcommittees which must contain at least two members as required by USDA Regulations. No IACUC member shall be excluded should he or she wish to attend a particular inspection. Additional consultants may be used. The inspection team must have a working knowledge of the Guide and USDA Regulations in order to fully evaluate the facilities which are being inspected.

The IACUC shall prepare a written report of each inspection and any deficiencies must be noted as minor or significant. The latter is defined by USDA Regulations and PHS Policy as one of significant threat to animal health or safety. A plan and timetable for correction of all deficiencies must be included in the final report. If the institution is unable to meet the plan, the IACUC, through the IO, must inform Animal and Plant Health Inspection Service (APHIS) within 15 working days of the lapsed deadline. If the activity is federally funded, the relevant agency must also be informed. The report must be reviewed and approved by a quorum of the IACUC and signed by all those who accept the report. Minority views shall be included in the report. Apparent deficiencies shall be discussed with the person in charge of the facility to ensure that the team’s perception of the situation is correct.

A copy of each report will be sent to the IO and must be kept on file for a minimum of 3 years. Annually, the institution must notify OLAW of the dates of the semiannual inspections and the dates the report was submitted to the IO.

Maps and architectural drawings of all facilities will be maintained by the Facilities Department of Western University.

IV. Program Review

The PHS Policy and USDA Regulations both require that the IACUC conduct semiannual evaluations of the animal care and use program. The IACUC Chair shall schedule semiannual reviews of Western University’s program. Aspects of the program that should be reviewed and modified, if necessary, include IACUC functions and procedures, proposal review practices, provisions for dealing with “whistle blowers” or other concerns regarding animal care and use and the procedures employed to meet reporting requirements. The institution’s occupational health program, veterinary care procedures and personnel qualification review process should also be reviewed and modified if necessary.

V. Legal Concerns

A. Rights and Obligations of IACUC Members

IACUCs are created in response to federal law and institutional policies. Hence, Committee members must be made aware of the legal obligations of their institutions, the responsibilities of the committee and the regulatory requirements for which they may be personally accountable. Committee members must be cognizant of federal and state laws and regulations as well as the interpretations of the regulations by the primary agencies.
The Committee should be familiar with any institutional committee charter, the institution’s Animal Welfare Assurance with OLAW and any other guidelines or operating directives which impact their authority.

Any IACUC member may request, through the IACUC Chair, a legal opinion to help guide the Committee’s actions if there is any doubt about the legal ramifications of an issue before the panel. Towards this end, Western University’s legal counsel will be made available to the IACUC on issues with uncertain legal ramifications.

B. Liability

The primary responsibility for meeting applicable state and federal standards rests with the registered research facility or PHS awardee institution. Under applicable statutory provisions (7 U.S.C. Section 2149), the USDA has the authority to suspend a facility’s registration for failure to comply with the regulatory and statutory requirements and to impose a fine. OLAW has the authority to withdraw approval of an institution’s Animal Welfare Assurance thereby requiring PHS awards (e.g. NIH grants) to be immediately discontinued (an approved Assurance is a prerequisite for receipt of PHS awards).

Although there are many requirements assigned to the IACUC by the statutes and rules, they do not create specific penalties for violations by the IACUC. Liability of the IACUC is unlikely to be an issue unless flagrant violations focus attention on the Committee or individual members.

C. Public Information

Suits have been successfully initiated against institutions in which IACUCs have met in closed sessions. Most states require that meetings of decision-making committees at government-supported institutions be open to the public. OLAW has interpreted PHS Policy to make the IACUC an advisory, as opposed to dispositive, committee. This distinction has allowed IACUCs in some states to continue to hold closed sessions.

Committee members should also be aware of the Freedom of Information Act which requires that the Department of Agriculture provide copies of information, which it holds in the conduct of its business, to a member of the public who request such data. The California Public Records Act makes similar provisions. This includes information which agencies such as the USDA obtain from regulated research institutions.

Committee members must be sensitive to the need to balance the public’s right to know with the institution’s need to protect proprietary information and to the personal safety of its employees. Any information submitted to the Committee may be subject to review by the Agency and ultimately available to requests from the public. Animal procedure statements, minutes of the Committee meetings and the annual report of the institution are among the items which may be demanded by the public domain.
Western University will make every effort to protect proprietary information and the personal safety of its employees to the extent possible. Requested information will be released after appropriate editing.

D. References


Chapter 5. Evaluation of Animal Welfare Concerns

As specified in the USDA Regulations, the IACUC is to “review and, if warranted investigate, concerns involving the care and use of animals at the facility resulting from public complaints received and from reports of noncompliance received from laboratory or research facility personnel or employees” (9CFR Part 2, Subpart C, Section 2.31 (c)(4)). Also required under 9 CFR Part 2, Subpart C, is training of personnel in the “methods whereby deficiencies in animal care and treatment are reported, including deficiencies in animal care and treatment reported by any employee of the facility.”

I. Definition of Mistreatment and Noncompliance

Mistreatment is physical or psychological, wrongful or abusive treatment of an animal. This is a broad definition and gray areas exist. Noncompliance means that procedures or policies are not being followed. Western University will use whatever means are necessary to ensure that no animal is subjected to physical or psychological mistreatment or is in any other way wrongfully treated or abused. Similarly, Western University will take measures to ensure that the use of all animals by University employees, while conducting activities as a part of their official duties either on or off campus, is in compliance with all applicable guidelines and laws.

II. Institutional Commitment

The Administration of Western University advocates the finest animal care and assures the public, researchers, employees and students that there is a true desire to investigate allegations of mistreatment or noncompliance. The IACUC and veterinary staff fully support this philosophy. Under no circumstances will reporting such instances be detrimental to an individual’s standing within the University as this action is protected under the law (9CFR, Part 2, Subpart C 2.32 (c)(4). The complaint reporting procedure and contact names will be posted in each facility conducting research on or housing research animals.

III. Reporting Procedure

To report any concern regarding animal mistreatment, noncompliance or concern for human safety in research/teaching facilities, contact the Vice President for Research (shenriksen@westernu.edu; 909-469-5299), the IACUC Chairperson (dewalters@westernu.edu; 909-469-5592), the Attending Veterinarian (mcouto@gmail.com; 909-469-5432) or the Environmental Health and Safety Director (bboston@westernu.edu; 909-469-5528) for immediate action. Complainants are encouraged to fully document and sign their complaints. Every effort will be made to protect the identity of complainants but absolute anonymity cannot be guaranteed. Every complaint is taken seriously and reviewed by the IACUC.
IV. IACUC Response to Complaints

Ideally, all complaints brought to the IACUC’s attention will be documented and signed by the complainant. For undocumented complaints, the IACUC will use its judgment on whether the complaint is of sufficient substance to proceed further. All documented and signed complaints will be acknowledged as received and when appropriate the complainant will be kept informed of the outcome. The IACUC reserves the privilege to keep committee discussions and conclusions confidential.

V. IACUC Procedures for the Investigation of a Complaint

The IACUC Chairperson will designate an individual or subcommittee to handle allegations of mistreatment or noncompliance. All persons involved will be informed of the purpose of the investigation and those against whom the complaint is addressed will be given the opportunity to explain their side of the issue. Results of investigations will be documented and corrective actions recommended to the IACUC. When allegations result in an official IACUC investigation, the results will be made available to all parties involved, including the Vice President of Research who is ultimately responsible for taking corrective action.

VI. Institutional Response

The Vice President of Research, in consultation with the IACUC, has the power to impose sanctions on the investigator found responsible for the mistreatment or noncompliance. In serious cases, the IACUC is empowered by the USDA Regulations and PHS Policy to suspend a previously approved project. If the activity is supported by PHS funds, the IACUC, through the IO, will file a full report to OLAW. Following a thorough investigation of a complaint, the IO, in consultation with the IACUC, will take whatever action is deemed necessary to remedy the situation.
Chapter 6. IACUC Recordkeeping and Reporting

I. Policy and Procedures

A. Introduction

PHS Policy and USDA Regulations both include reporting and recordkeeping requirements. Tables 6-1 through 6-5 compare the two. It is crucial that the responsibility for preparing reports be clearly delineated within a given institution. The persons assigned the task must be knowledgeable of federal requirements and the institution’s animal care and use program. He/she must also be aware of the Freedom of Information Act (FOIA) and the California Public Records Act. Many of the report written may be accessible under such laws and particular care must be taken to avoid using language that may be misconstrued by the lay public. Ideally, the recordkeeping responsibilities will be assigned to one office.

B. PHS Animal Welfare Assurance

Institutions receiving support from the PHS for activities involving animals must provide an Assurance of Compliance (Assurance) with the PHS Policy. The Assurance is a written agreement in which the institution outlines in detail its policies and procedures for such treatment (see Table 6-1 for details).

The Assurance must be signed by the Institutional Official, an individual who has the authority to make the commitment on behalf of the institution, guaranteeing that PHS Policy will be complied with. The Assurance is submitted to OLAW which reviews and negotiates any necessary details and approves the Assurance. OLAW issues an Assurance number to the institution and maintains the Assurance on file in its office.

C. USDA Facility Registration

USDA Regulations require that each research facility register with the Secretary of Agriculture. Registration is required if a facility has UADA-regulated species on its premises. The registration form is submitted to APHIS and the Animal Care Sector Supervisor for the state in which the facility ahş its principal place of business (see Table 6-1 for summary).

At academic institutions, the submission is usually made by the institution, not the individual departments or schools. Usually, the Institutional Official also signs the USDA submission. The registration is updated every three years by completing a new set of forms provided by APHIS and the Animal Care Sector Supervisor. The institution is required to notify the Sector Supervisor within ten days of any change in the name, address, ownership or operations affecting its status as a research facility. A facility which has not handled animals for two years may be placed in inactive status by the Sector Supervisor. The registration can be cancelled by written request if a facility no longer used or intends to use animals.
Table 6-1. USDA Facility Registration Federal Reporting Requirements

<table>
<thead>
<tr>
<th><strong>Submit If</strong></th>
<th>USDA Research Facility Registration</th>
<th><strong>Submit To</strong></th>
<th>PHS Institutional Assurance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animals covered by USDA Regulations on premises</td>
<td>APHIS, Animal Care Sector Supervisor (on agency forms)</td>
<td>Office of Laboratory Animal Welfare (OLAW)</td>
<td></td>
</tr>
<tr>
<td><strong>File By</strong></td>
<td>Institution/Facility</td>
<td><strong>Update</strong></td>
<td>Every 3 years</td>
</tr>
<tr>
<td><strong>Update</strong></td>
<td></td>
<td><strong>Authorization</strong></td>
<td>Signed by the Institutional Official (IO)</td>
</tr>
<tr>
<td><strong>Authorization</strong></td>
<td></td>
<td>On letterhead and signed by Institutional Official</td>
<td></td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td><strong>After submission of standard form:</strong></td>
<td><strong>Content:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>APHIS supplies regulations and standards after submission. Sign 2nd form acknowledging receipt and agreeing to comply. Submit to APHIS and the Animal Care Sector Supervisor. Notify APHIS and the AC Sector Supervisor of change of operation.</td>
<td>Institutional status (AAALAC or not). List all parts of institution to be included. Describe lines of authority and responsibility. List qualifications/ responsibility/ authority and percent of time contribution of each veterinarian. IACUC membership list and procedure description. Describe personnel health program. Synopsis of training/ instruction offered to personnel involved with animals. List gross sq. ft. of each facility, species housed and average daily inventory by species.</td>
<td></td>
</tr>
<tr>
<td><strong>Reference</strong></td>
<td>9 CFR Part 2, Subpart C 2.30</td>
<td><strong>Policy IV.A.</strong></td>
<td></td>
</tr>
</tbody>
</table>

*NOTE: PHS Policy requires compliance with AWA.*

II. Annual Reporting

A. PHS

At an institution with an approved Assurance, the IACUC must submit an annual report to OLAW through the designated Institutional Official (see Table 6-2 for details). This annual report is accessible under the FOIA. To minimize security risks, OLAW does not require, and institutions do not routinely submit, copies of the semiannual reports required as described below.
Table 6-2. Annual Reporting Federal Requirements

<table>
<thead>
<tr>
<th></th>
<th>USDA Annual Report</th>
<th>PHS Annual Report</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Submit To</strong></td>
<td>APHIS, Animal Care Sector Supervisor (on agency form)</td>
<td>Through Institutional Official to OLAW</td>
</tr>
<tr>
<td><strong>Deadline</strong></td>
<td>On or before each December 1st</td>
<td>At least once every 12 months</td>
</tr>
<tr>
<td><strong>Contents</strong></td>
<td><strong>Provide Assurance That:</strong></td>
<td><strong>If Changes Have Occurred in Prior Year:</strong></td>
</tr>
<tr>
<td></td>
<td>Professionally acceptable standards for care, treatment and use of</td>
<td>Report changes in program of facilities pertaining</td>
</tr>
<tr>
<td></td>
<td>animals were followed</td>
<td>to AAALAC accreditation status</td>
</tr>
<tr>
<td></td>
<td>Alternatives to painful protocols were considered, Facilities</td>
<td>Report changes in animal care/use program</td>
</tr>
<tr>
<td></td>
<td>adhere to USDA Regulations, Exceptions to standards and regs.</td>
<td>Report changes in IACUC membership</td>
</tr>
<tr>
<td></td>
<td>were explained by investigator and approved by IACUC</td>
<td>Report date(s) IACUC conducted semiannual</td>
</tr>
<tr>
<td></td>
<td><strong>Summarize:</strong> Exceptions to standards/ regs. w/species and number</td>
<td>evaluations and submitted reports to Institutional</td>
</tr>
<tr>
<td></td>
<td>number of animals affected/ description and explanation</td>
<td>Official</td>
</tr>
<tr>
<td><strong>State:</strong></td>
<td>Location of all facilities</td>
<td><strong>If No Changes Have Occurred in Prior Year:</strong></td>
</tr>
<tr>
<td></td>
<td>Common name and number of animals used that:</td>
<td>State that there are no changes</td>
</tr>
<tr>
<td></td>
<td>• experienced no pain or distress;</td>
<td>Report date(s) IACUC conducted semiannual</td>
</tr>
<tr>
<td></td>
<td>• drugs were used to alleviate pain or distress;</td>
<td>evaluations and submitted reports to Institutional</td>
</tr>
<tr>
<td></td>
<td>• experienced pain or distress and drugs would have interfered</td>
<td>Official</td>
</tr>
<tr>
<td></td>
<td>with the research.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Common name and number of animals being bred, conditioned or in</td>
<td></td>
</tr>
<tr>
<td></td>
<td>holding not being used</td>
<td></td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>Signed by the IO</td>
<td>Include any minority views of IACUC members</td>
</tr>
<tr>
<td></td>
<td></td>
<td>List USDA Facility Registration number</td>
</tr>
</tbody>
</table>
B. USDA

On or before December 1, each facility registered with the USDA must submit an annual report to the APHIS, REAC Sector Supervisor, for the state in which the facility is registered. The report is a standard form and is usually prepared by the IACUC. It is signed by the CEO or Institutional Official and covers the previous fiscal year. Specific items to be included in the report are listed in Table 6-2.

III. Semiannual Report of Facility Inspections and Program Evaluations

A. PHS

PHS Policy requires that the IACUC inspect all facilities every six months and prepare a report which is submitted to the designated Institutional Official. The report must contain a description of the nature and extent of the institution’s compliance with the PHS Policy and Guide. Any departures must be identified and modifications proposed with a plan and timetable for correction. Minor and significant deficiencies must be distinguished. The report must also identify any facilities which are AAALAC accredited or accredited by any other professional body recognized by PHS.

B. USDA

These requirements are essentially the same as those for PHS with three exceptions. First, the USDA Regulations include additional reporting requirements if the schedule and plan for correcting a deficiency is not followed. Failure to correct a significant deficiency in accordance with the specified schedule and plan must be reported in writing within 15 business days by the IACUC, through the Institutional Official, to APHIS and any federal agency funding the activity. Secondly, USDA requires that reports be reviewed and signed by a majority of IACUC members. Finally, USDA does not require the identification of facilities accredited by AAALAC. Table 6-3 summarizes the differences between PHS and USDA semiannual reporting requirements.

IV. Suspension/Non-compliance Explanation

A. PHS

At an institution with an approved PHS Assurance, the IACUC must explain, through the Institutional Official, the circumstances and actions taken in the following instances:

1. any serious or continuing non-compliance with PHS Policy
2. any serious deviation from the provisions of the NIH Guide
3. any suspension of any activity by the IACUC.
Table 6-3. PHS and USDA Semiannual Reporting Requirements

<table>
<thead>
<tr>
<th>Submit To</th>
<th>USDA Semiannual Report</th>
<th>PHS Semiannual Report</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Designated Institutional Official</td>
<td>Same as USDA</td>
</tr>
<tr>
<td>Update</td>
<td>Every 6 months</td>
<td>Same as USDA</td>
</tr>
</tbody>
</table>
| Contents  | - Describe adherence to USDA Regulations  
- Identify departures from USDA Regulations  
- State reasons for departure  
- Identify significant deficiencies  
- Identify minor deficiencies  
- Include plan/schedule to correct deficiencies  
- Include minority views  
- Not Addressed | - Describe adherence to Guide and Policy  
- Identify departures from Guide and Policy  
- Same as USDA  
- Same as USDA  
- Same as USDA  
- Same as USDA  
- Identify facilities accredited by AAALAC |
| Other     | - Reviewed and signed by majority of members  
- Maintained by Research Facility  
- Available to APHIS and funding agency upon request  
- Report failure to adhere to plan/schedule through Institutional Official to APHIS and funding agency within 15 working days | - Must be a committee action  
- Maintained by institution  
- Available to OLAW upon request  
- No similar requirement |

B. USDA

If the IACUC suspends any activities involving animals, the Institutional Official files a report in consultation with the IACUC. After reviewing the reasons for the suspension and taking appropriate corrective action, the Institutional Official is responsible for submitting a full explanation to APHIS and any deferral agency funding the activity (see Table 6-4).

V. Recordkeeping Requirements

A. PHS

These include IACUC minutes, individual proposal records and basic reports and documents. These records must be accessible for inspection and copying by authorized OLAW or other PHS representatives.

The minutes must include records of attendance, activities of the Committee and IACUC deliberations. These minutes must be kept for 3 years. Individual proposal records include the application, proposed modifications and outcome of the review. These records must be
Table 6-4. Suspension/Non-compliance Federal Reporting Requirements

<table>
<thead>
<tr>
<th>Submit To</th>
<th>USDA: Suspension Report</th>
<th>PHS: Suspension/Noncompliance Report</th>
</tr>
</thead>
<tbody>
<tr>
<td>By Institutional Official with IACUC to APHIS and federal agency funding the activity</td>
<td>By IACUC through Institutional Official to OLAW</td>
<td></td>
</tr>
</tbody>
</table>
| Submit For | - Suspension of an activity by the IACUC  
- Not addressed  
- Not addressed | - Same as USDA  
- Serious deviation from the Guide  
- Serious or continuing noncompliance w/Policy |
| Contents | Full explanation of circumstances  
Description of corrective action taken  
Not addressed | Same as USDA  
Same as USDA  
Minority views filed by IACUC |

maintained for the duration of the activity plus an additional 3 years after completion. Basic reports and documentation include the Assurance document, semiannual IACUC reports, including minority view and accrediting body determinations.

B. USDA

These regulations are essentially the same as the PHS Policy for IACUC minutes and individual proposal records. Some differences apply to recordkeeping specifications. USDA does not require copies of Assurance documents or reports of accrediting bodies but they do require that institutions maintain records from on-site, unannounced facility inspections conducted by APHIS officials. USDA also has specific regulations applying to each live dog or cat purchased, acquired, held, transported, euthanized, sold or disposed of. Responsibility for maintenance of such records generally lies with the animal resources office. USDA requires that the records be available to authorized APHIS or federal funding agency representative but material is not normally removed unless a violation has been alleged or an investigation is being undertaken. Table 6-5 compares the requirements for the two agencies.

Western University will maintain records in accordance with the more stringent requirements.

VI. IACUC Staffing

IACUC staff generally are assigned responsibilities for: 1) screening proposals for accuracy and completeness; 2) distributing copies to Committee members; 3) keeping records of proposals received and committee decisions on the; 4) coordinating and scheduling the Committee’s meetings, facilities inspections and laboratory site visits; 5) correspondence and 6) an information resource for investigators and Committee members on regulatory issues and the status of proposals. Throughout, the staff must remember that, in addition to their primary role
Table 6-5. Recordkeeping Requirements

<table>
<thead>
<tr>
<th>Records</th>
<th>USDA Requirements</th>
<th>PHS Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minutes</td>
<td>IACUC meeting minutes w/records of attendance, activities and deliberations</td>
<td>Same as USDA</td>
</tr>
<tr>
<td>Protocol</td>
<td>- Records of proposed activities using animals</td>
<td>- Records of applications and proposals</td>
</tr>
<tr>
<td></td>
<td>- Record of proposed significant changes</td>
<td>- Same as USDA</td>
</tr>
<tr>
<td></td>
<td>- Outcome of IACUC review</td>
<td>- Same as USDA</td>
</tr>
<tr>
<td>Basic Documents</td>
<td>- Semiannual IACUC reports and recommendations</td>
<td>- Same as USDA</td>
</tr>
<tr>
<td></td>
<td>- Not addressed</td>
<td>- Assurance Document</td>
</tr>
<tr>
<td></td>
<td>- Not addressed</td>
<td>- Records of accrediting body determinations</td>
</tr>
<tr>
<td>Animal</td>
<td>Records on acquired live dogs/cats or offspring including 7 types of information</td>
<td>Must adhere to <em>Guide</em></td>
</tr>
<tr>
<td></td>
<td>Records on dogs/cats transported/ sold/ euthanized including 3 types of information</td>
<td></td>
</tr>
<tr>
<td>Other Requirements</td>
<td>- Protocol records maintained for duration of activity +3 years</td>
<td>- Same as USDA</td>
</tr>
<tr>
<td></td>
<td>- Other records maintained for 3 years</td>
<td>- Same as USDA</td>
</tr>
<tr>
<td></td>
<td>- Accessible to APHIS and Federal agency officials</td>
<td>- Accessible to OLAW &amp; other PHS officials</td>
</tr>
<tr>
<td>Reference</td>
<td>9 CFR Part 2, Subpart C 2.35</td>
<td>Policy IV.E.</td>
</tr>
</tbody>
</table>

of the implementation of PHS Policy and USDA Regulations on behalf of their institutions, the facilitation of appropriate animal-based research is generally consistent with the institution’s mission and should be encouraged.

The IACUC should have available grant applications submitted for PHS funding in order to ensure consistency in animal care and use components of the applications and the proposal for IACUC review.
Chapter 7. Animal Use in Research and Education

I. Care for Institutionally Housed Animals

A. General

Proper management of animal facilities is essential to the welfare of animals, validity of research date and health and safety of the animal care staff. A good husbandry program provides a system of housing and care that permits animals to grow, mature, reproduce and maintain good health. Good husbandry minimizes variations that can modify an animal’s response to experimentation.

Animal housing shall promote animal comfort and safety by providing sufficient space and other accommodations for normal postural and behavioral activities. The USDA Regulations and the Guide provide minimum cage size requirements/recommendations for most common laboratory animal species.

Cages should allow for adequate ventilation and enable ready access to food and water receptacles. They should be constructed of materials that can be easily cleaned and sanitized.

Many animal species are social in their natural state. Encouragement of intra- and interspecies socialization is recommended by USDA Regulations in the Guide and is widely recognized as advantageous to animals well being and their research endeavor. Unless precluded for sound scientific reason and approved by the IACUC, socialization and physical exercise will be required for animals housed at Western University and its affiliated facilities.

Temperature, humidity, air pressure and rate of turnover and noise levels all may affect animal well-being and research results. Environmental conditions appropriate for the species must be maintained for all animals housed at Western University. Any deviations from accepted standards must be scientifically justified and approved by the IACUC. Whereas environmental control in outdoor facilities is much less stringent, acceptable ranges in temperature for several species are available in USDA Regulations. Reliable methods for monitoring environmental control systems must be in place. Redundancy in heating, ventilation, air conditioning and lighting systems is highly desirable. Should environmental control systems fail, animal care personnel are referred to the emergency contingency plan for caring for animals and personnel.

Research animals must be adequately and appropriately identified and records pertaining to individual or groups of animals must be maintained. A variety of identification methods may be used ranging from cage cards to individual tattoos and tags. The use of toe-clipping to identify individual rodents is discouraged with tail tattooing or ear-tagging preferred. All individual housing areas will include, at a minimum, the following information for identification: investigator’s name and contact information, protocol number, expiration date, species, gender and source of the animals.
B. Feeding and Watering

All animals should receive food that is palatable, free from contamination and of sufficient quantity and nutritive value to maintain their good health. Specific diets should be selected based on the needs of each species with special consideration of the requirements for vitamin C by guinea pigs and some species of non-human primates. Animals should be fed at least once a day except under conditions of hibernation, veterinary treatment, pre-procedural fasts or other justified circumstances.

Standard commercial dry bulk foods, when stored properly, retain their nutritional value for 6 months (3 months for those containing vitamin C). To assure that age deterioration of food does not occur, the milling date should be known (it is usually stamped on each bag), and bags should be stored so that the oldest is used first. Large amounts of food may not be stored in animal rooms. Small quantities may be kept in animal rooms if stored in tightly covered, leak- and vermin-proof containers. These may not be moved from room to room.

Food should be provided in receptacles that are accessible to all animals in a cage or pen and place so as to minimize contamination. Food receptacles should be easily cleaned and sanitized and those functions performed on a schedule that meets Guide and USDA Regulation requirements. With limited exceptions, e.g. germ-free animals in microisolator cages, food should not be placed on the bottom of the cage. Although some species may prefer this presentation, it results in waste and contamination of the food.

Potable drinking water must be available continuously or provided as often as necessary for the health and well-being of the animal, considering the animal’s species, age, condition and any research requirements. Water may be provided in receptacles e.g. bowls, bottles or via automatic watering systems. Care should be taken to ensure that water does not become contaminated and is actually available. Supper tubes and automatic watering devices should be checked routinely for patency. Water bottles generally should be replace rather than refilled.

Any deviations from normal species specific diets and watering schedules must be scientifically justified and approved by the IACUC.

C. Bedding

Bedding material should be absorbent and free of any substances that might harm the animals or alter research data. Cedar and pine products can affect liver enzymes which may in turn affect immunologic or other physiologic parameters. The use of these products must be scientifically justified and approved by the IACUC. Animals may be place directly on bedding material or it may be place under a wire or slat-bottom cage. Bedding must be changed as often as necessary to keep the animals clean and dry and the animal room relatively odor free.

D. Animal Activity

USDA Regulations require institutions to develop plans for: 1) providing dogs the opportunity to exercise and 2) enhancing the environment of nonhuman primates to promote their psychological
well-being. Conditions and requirements for these plans are included in the Regulations. Where no regulatory requirements exist, the decision to supplement activity in animals will be made by Western University’s IACUC in consultation with the Attending Veterinarian and the investigator. Group housing of most species generally is encouraged barring any research requirements or other negative effects that may preclude it e.g. fighting or potential for disease transmission.

E. Emergency, Weekend and Holiday Care

Laboratory animals must be observed by qualified personnel every day, including weekends and holidays, to ensure their health and well being and to promote sound research practices. Skilled assistance, including veterinary care, must be readily available at all times. Names and telephone or pager numbers of those assigned these responsibilities must be prominently displayed in the facility.

F. Farm Animal Species

PHS Policy and USDA Regulations do not cover food and fiber research or teaching activities. Moreover, food and fiber animal research is often conducted under conditions that mimic farm conditions. Nevertheless, the same ethical standards shall be applied by the IACUC in considering the use of these animals as are applied to the use of animals in biomedical research.

To be relevant to commercial production, agricultural research is often conducted under conditions which are appropriate to farmers and which incorporate economic considerations. There are practices common in commercial agriculture that would not be permitted under the regulations governing biomedical research, for example, the castration of young animals without anesthesia. Any deviations from standards normally applied to other species to accommodate the special nature of commercial production and agricultural research will be carefully scrutinized by the IACUC.

To assist the investigators and the IACUC in the use of food and fiber animals in research and teaching activities, a consortium of scientific and professional organizations, industrial groups and government agencies has developed a Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching (Agri Guide).

The Agri Guide specifies that the IACUC should include:

- a scientist from the institution with experience in agricultural research of teaching involving agricultural animals.
- an animal scientist with appropriate training and experience in the management of agricultural animals and with recognized high professional credentials as verified by the scientific and professional societies in animal science, dairy science or poultry science.
• a veterinarian who has appropriate training and experience in agricultural animal medicine and is appropriately licensed or eligible to be licensed to practice veterinary medicine.

• a non-scientist affiliated with the institution in addition to a person not otherwise affiliated with the institution

• other members as required by institutional needs and applicable laws, regulations and policies.

The American Association for the Accreditation of Laboratory Animal Care has approved portions of the Agri Guide as the basis for accreditation of agricultural animal programs and OLAW encourages its use as a reference for IACUCs reviewing proposals for both biomedical and agricultural research involving farm animal species. Western University’s IACUC will use the Agri Guide when evaluating the use of food and fiber animals in research or teaching activities and will consult with food and fiber animal experts as necessary.

References


G. Facility Maintenance

1. Cleaning and Sanitation

The Guide and USDA Regulation set forth recommended frequencies and methods for cleaning and sanitation of facilities, equipment and accessories. The frequency and methods used by Western University animal care personnel shall ensure that animals are maintained in a clean,
In a dry environment, free from exposure to harmful contamination and excessive animal odors. Cleaning equipment such as mops and pails must not be moved from room to room. Feeders, water bottles, sipper tubes, etc. shall be cleaned using a mechanical washing machine that provides rinse water temperature of at least 83°C (180°F). Hand washing and disinfection of such equipment is discouraged. The supply lines of automatic watering systems shall be flushed and disinfected on a regular basis.

2. Waste Disposal

Waste disposal methods must conform to federal, state and local requirements. If waste must be stored while awaiting disposal, the storage area must be outside the animals holding and clean equipment areas. Animal carcasses and tissues require a separate cold storage area and regularly scheduled removal. Hazardous waste, including carcasses of animals exposed to radioactive or biohazardous agents, must be adequately sterilized and contained prior to removal and disposal.

3. Vermin Control

Western University will control vermin by all means necessary including placement of appropriate traps and closing as many potential sites of entry as possible.

II. Use of Animals in Research

A. Numbers

The IACUC must consider the justification for doing the experiment at all, as well as the number of animals needed to achieve meaningful results. Repetition of experiments is justifiable, for example, when changes in technology greatly enhance the resolution of the data but is less justified if it is a direct repeat of a previous study. Comparisons between species are important if certain phenomena are to be shown to be more generally applicable. The USDA Regulations require that investigators state that a proposed activity is not “unnecessarily duplicative” of previous studies. Replication within experiments may be justified and necessary due to biological variation in the test system which can obscure the effects of a given intervention if the sample size is insufficient to obtain a statistically significant result. The principle investigator (PI) must provide justification, through statistical or other means, for the number of animals used in the proposed research project or teaching exercise. The investigator is encouraged to consult with a biostatistician before submitting a protocol. The IACUC will also consult with a statistician, if necessary, as part of the protocol review process.

B. Species

PHS Policy and USDA Regulations both require that investigators provide a rationale for selecting the species of animal to be used. Western University requires that all investigators submit a rationale for their choice of species in the research project or teaching exercise. The lowest phylogenetic species appropriate to the scientific questions must be used. The IACUC will determine if personnel and facility resources are available to maintain the proposed species.
Whereas inbred animals help reduce variation within an experiment and thus the number of animals required, they also reduce the ability to generalize the results and may necessitate repetition of experiments with other strains.

III. Clinical Trials Involving Animals

The use of animals in clinical trials will be held to the same ethical standards as the use of animals in basic science research.

IV. Use of Animals in Education

A. General Requirements

Any instructional use of animals supported by PHS funds is governed by PHS Policy. The applicability of the USDA Regulations depends upon the species to be used. Western University requires that all instructional use of animals, regardless of funding source or species, be reviewed by the IACUC. All instructional proposals should clearly justify the value of animal use as part of the course, whether it is demonstration of a known phenomenon, acquisition of practical skills or exposure to research. Cadavers, tissues and/or cells secured as such will not require and IACUC protocol application submission.

B. Alternatives

Consideration must be given to alternative approaches to attaining the desired educational objectives. The IACUC must ensure that maximum effort is made to avoid pain and distress. Instructional uses involving unrelieved painful procedures are not allowed. Justification regarding the inadequacy of existing non-detrimental learning tools will be required.

C. Supervision

Faculty and students should receive instruction on the ethics of animal research prior to undertaking any experimentation. The IACUC will provide training on the proper care and use of animals to all faculty and students engaged in animal research or teaching activities. Students may not conduct animal research or teaching exercises on projects that have not been approved by the IACUC.

D. Animal Use in Veterinary Skills Laboratories

Requiring that all instructional use of animals be made non-survival would greatly increase the number of animals used and the expense of instruction. However, cost savings alone will not be accepted as an adequate reason for performing multiple survival surgical procedures. Moreover, there are federal prohibitions against multiple survival surgeries.
Instructors are encouraged to use client-owned animals or dogs and cats from humane societies that are made available for surgical neutering. Plastic models and other model systems are encouraged wherever appropriate. The use of pets with unique or terminal conditions donated by their owners to veterinary schools for research or teaching needs full IACUC review.

All protocols involving animal use, including those proposing the use of animals with known guardians, will require IACUC approval. The donation of cadavers or tissues will not require IACUC approval if the animal is euthanized for medical or humane reasons prior to acceptance by Western University (i.e. Veterinary Willed Body Program). The purchase of animal tissues for instruction will not be subject to IACUC review.

E. Animal Use in Agricultural Instruction

Food and fiber animals are not covered by PHS Policy or USDA Regulations. However, any invasive procedure, e.g. in vitro fertilization, regardless of species, must be reviewed by the IACUC. A Guide for the Care and Use of Agricultural Animals in Agriculture Research and Teaching will serve as a guide to the IACUC for evaluating the use of food and fiber animals in agricultural research or instruction.

F. References


Chapter 8. Alternative to the Use of Animals

I. General Considerations

The definition of alternative was originally developed by Russell and Burch and is defined as the three “Rs” – replacement, refinement and reduction. The term alternative refers to systems that do not employ whole live animals. Alternatives to the use of animals include in vitro model systems such as isolated organ preparations like the perfused heart or, more commonly, cell, tissue and organ cultures. Another alternative is the use of non-biological model systems. These include chemically based systems, physical models such as hemodynamic flow chambers or computer simulations. The principal investigator (PI) must provide evidence of his/her understanding of the 3R principle as defined above. The PI will be responsible for providing justification for his/her animal use relative to these concepts; i.e. Can the number of animals be reduced: Can in vivo be replaced with in vitro? Can animals or tissues be replaced with computer modeling?

II. Resource Organizations for Alternatives

Animal Welfare Information Center (AWIC)
National Agricultural Library
10301 Baltimore Bled.
Beltsville, MD 20705
(301) 504-6212
FAX (301) 504-7125
http://www.nalusda.gov/awic/

Institute for Laboratory Animal Research (ILAR)
National Research Council
2102 Constitution Avenue N.W.
Washington, DC 20418
(202) 334-2590
FAX (202) 334-1639
http://www4.nas.edu/cls/ilarhome.nsf

Johns Hopkins Center for Alternative to Animal Testing (CAAT)
615 North Wolfe Street
Baltimore, MD 21205
(410) 955-3343
FAX (410) 955-0258
http://altweb.jhsphe.edu;
National Institutes of Health
National Library of Medicine
Bethesda, MD 20894
(301) 496-6095
FAX (301) 496-4450
http://grants.nih.gov/training/t15.htm

Public Responsibility in Medicine and Research (PRIM&R)
132 Boylston Street, 4th Floor
Boston, MA 02116
(617) 423-4112
FAX (617) 423-1185
http://www.primr.org/

Scientists Center for Animal Welfare (SCAW)
Golden Triangle Building One
7833 Walker Drive, Suite 340
Greenbelt, MD 20770
(301) 345-3500
FAX (301) 345-3503
http://www.scaw.com/

3R Research Foundation
Postfach 1372
CH-3110 Münsingen
Switzerland
Tel.: +41-31-722 08 30
FAX: +41-31-721 70 80
E-mail: Secretary.3r@bluewin.ch

Fund for the Replacement of Animals in Medical Experiments
Russell & Burch Huse
96-98 North Scherwood Street
Nottingham NG1 4EE
+44 (0)115 958 4740
FAX +44 (0)115 950 3570
frame@frame-uk.demon.co.uk
http://www.frame-uk.demon.co.uk/index.htm
Chapter 9. Occupational Health

I. Purpose of an Occupational Health Program

PHS Policy and the Guide identify the need for an occupational health program for all personnel who work in laboratory animal facilities or who have substantial animal contact. The emphasis of such a program is the prevention of illness, but it also includes provisions for early diagnosis and treatment when such illnesses occur. See Table 9-1.

II. Elements of an Occupational Health Program

An effective program will have the following components: 1) pre-placement medical evaluation; 2) periodic medical surveillance; 3) educational component; 4) provisions for treating illness or injury and 5) provisions for consultation with other professional staff. The specific elements will be dictated by the extent and nature of the employee’s exposure (see table).

There are ethical and legal requirements to inform individuals of health risks and precautions which affect them. Therefore, all personnel will be informed of the health risks and precautions associated with using and caring for laboratory animals as part of their orientation and job training. Pre-placement medical evaluations will be conducted to ensure that employees are capable of the demands of the job and to provide a medical reference baseline. Employees will be periodically evaluated to ensure their continued health and safety. Provisions will be made for treating any on-the-job injury or illness. In addition to established mechanisms for reporting and treating accidents and injuries, Western University will provide investigators and animal care personnel access to medical expertise in zoonotic diseases and other health risks associated with laboratory animal care. All cases of animal bites and scratches shall be documented. Tetanus prophylaxis will be considered and, depending on the species, rabies prophylaxis and antibiotics will be arranged.

Allergy and musculoskeletal injury are the primary health risks to persons using and caring for laboratory animals. Allergies can be reduced by the provision of protective equipment to affected personnel. Musculoskeletal injuries can be minimized by use of transport carts and training in lifting and equipment use.

Infectious diseases are also a significant risk depending on the species and health status of the animals involved and the level to which a person is exposed. Infections acquired from live animals, animal tissues and excreta can serve as sources of zoonoses. Western University will carefully monitor and quarantine any animals with potential viral or bacterial infections. Particular care will be taken in all facilities handling primates as they are likely to carry infections such as Herpes Virus Simiae (Herpes B) and tuberculosis which can be transferred to humans. Routine TB testing will be conducted by the University at such time as primates are housed on campus.
# Table 9-1. Occupational Health Program for Animal Handlers

<table>
<thead>
<tr>
<th>Species Used/ Other Factors</th>
<th>Extent of Animal Contact</th>
<th>Code #</th>
<th>Procedure</th>
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<tbody>
<tr>
<td></td>
<td>Direct Regular Contact (8hrs/week or more)</td>
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<tr>
<td></td>
<td>Direct Contact Limited Exposure (less than 8hrs/ week)</td>
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<tr>
<td></td>
<td>No Direct Contact, Occasional Exposure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small Animals (Rabbits, Rodents, Birds)</td>
<td>1</td>
<td>1</td>
<td>Pre-Employment Physical Exam (including serum for banking)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>2</td>
<td>Tetanus Immunization (every ten years or following known injury or advice of Physician)</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>5</td>
<td>Rabies Immunization</td>
</tr>
<tr>
<td>Dogs, Cats, and Feral Animals</td>
<td>1</td>
<td>1</td>
<td>Infected Disease Studies (Class III or Higher)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>2</td>
<td>(Class III or Higher)</td>
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<tr>
<td></td>
<td>4</td>
<td>4</td>
<td>Work with Animal Tissues</td>
</tr>
<tr>
<td>Primates</td>
<td>1</td>
<td>1</td>
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<td></td>
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<td>2</td>
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<td>8</td>
<td>8</td>
<td></td>
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<tr>
<td>Farm Animals</td>
<td>1</td>
<td>1</td>
<td>Work with Animal Tissues</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>2</td>
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<tr>
<td></td>
<td>6</td>
<td>6</td>
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</tr>
<tr>
<td>Amphibians, Reptiles, Fish, and Other Cold-Blooded Animals</td>
<td>2</td>
<td>2</td>
<td>Work with Animal Tissues</td>
</tr>
<tr>
<td>Infectious Disease Studies (Class III or Higher)</td>
<td>1</td>
<td>1</td>
<td>Work with Animal Tissues</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>2</td>
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<tr>
<td></td>
<td>9</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Work with Animal Tissues</td>
<td>7</td>
<td>7</td>
<td>Work with Animal Tissues</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

Code #:  
1 Pre-Employment Physical Exam (including serum for banking)  
2 Tetanus Immunization (every ten years or following known injury or advice of Physician)  
3 TB test (every six months)  
4 Rabies Immunization  
5 Pre-Employment Allergy Evaluation and Education  
6 Special Education on Large Animal Diseases  
7 Special Consideration by Infectious Disease Committee  
8 Post-Employment Physical (including serum for banking)  
9 Annual Physical Exam
References


Chapter 10. Resources

American Association for the Accreditation of Laboratory Animal Care (AAALAC)
11300 Rockville Pike
Rockville, MD 20852-3035
Phone: 301/231-5353 FAX: 301/231-8282

American Association for Laboratory Animal Science (AALAS)
70 Timber Creek Drive, Suite 5
Cordova, TN 38018
Phone: 901-754-8620 FAX: 901/753-0046

American College of Laboratory Animal Medicine (ACLAM)
University of Illinois
College of Veterinary Medicine
Division of Comparative Medicine
2001 S. Lincoln - 1234 VMBSB
Urbana, IL 61801
Phone: 217/244-1829 FAX: 217/333-4628

American Society of Laboratory Animal Practitioners (ASLAP)
University of Pennsylvania
1 Blockley Hall
Philadelphia, PA 19104-6021
Phone: 215/898-9026 FAX: 215/898-0309

American Veterinary Medical Association (AVMA)
930 North Meacham Road
Schaumberg, IL 60196
Phone: 1-800/248-2862 FAX: 708/025-1329

Animal Welfare Information Center (AWIC)
National Agricultural Library
10301 Baltimore Blvd.
Beltsville, MD 20705
Phone: 301/504-5215 FAX: 301/504-5472

Applied Research Ethics National Association (ARENA)
132 Boylston Street - Fourth Floor
Boston, MA 02116
Phone: 617/423-4112 FAX: 617/423-1185
Center for Alternatives to Animal Testing (CAAT)
Johns Hopkins School of Public Health
615 North Wolfe Street
Baltimore, MD 21205
Phone: 410/955-3343 FAX: 410/955-0258

Center for Animals and Public Policy (CAPP)
Tufts University
200 Westboro Road
North Grafton, MA 01535
Phone: 508/839-5302, ext. 4750 FAX: 508/839-2953

Institute for Laboratory Animal Resources (ILAR)
National Research Council
National Academy of Sciences
2101 Constitution Avenue, N.W.
Washington, DC 20418
Phone: 202/334-2590 FAX: 202/334-1687

National Association for Biomedical Research (NABR) & Foundation for Biomedical Research (FBR)
818 Connecticut Avenue, N.W., Suite 303
Washington, DC 20006
Phone: 202/857-0540 FAX: 202/659-1902 (NABR)
Phone: 202/457-0654 FAX: 202/457-0659 (FBR)

National Library of Medicine (NLM)
8600 Rockville Pike
Bethesda, MD 20894
Phone: 1-800/272-4787 FAX: 301/496-2809

Office of Laboratory Animal Welfare (OLAW)
Division of Animal Welfare
National Institutes of Health
RKL1, Suite 1050, MSC 7982
6705 Rockledge Drive
Bethesda, MD 20892-7982
Phone: 301/496-7163 FAX: 301/402-7065

Public Responsibility in Medicine and Research (PRIM&R)
132 Boylston Street
Boston, MA 02116
Phone: 617/423-4112 FAX: 617/423-1185
Chapter 11. Selected References

- Acceptable Field Methods in Mammalogy: Preliminary Guidelines Approved by the American Society of Mammalogists; Supplement to Volume 68, No. 4, November 1987 Ad Hoc Committee on Acceptable Field Methods in Mammalogy.

- "Alternatives to the Use of Live Vertebrates in Biomedical Research and Testing," An Annotated Bibliography, prepared by the Oak Ridge National Laboratory under the sponsorship of the National Library of Medicine, Bethesda, MD.


- Biosafety in Microbiological and Biomedical Laboratories. Centers for Disease Control, Fall 1992.


- Guide for the Care and Use of Laboratory Animals. National Institutes of Health, 1985-6 (also available in Spanish).
• Guidelines for Use of Fishes in Field Research. American Society of Ichthyologists and Herpetologists (ASIH), American Fisheries Society (AFS), American Institute of Fisheries Research Biologists (AIFRB).

• Guidelines for Use of Live Amphibians and Reptiles in Field Research. American Society of Ichthyologists and Herpetologists (ASIH), The Herpetologists' League (HL) and Society for the Study of Amphibians and Reptiles (SSAR) 1987.

• ILAR News. Institute of Laboratory Animal Resources, National Research Council, Washington, DC


• Laboratory Animal Science, by the American Association for Laboratory Animal Science, Cordova, TN.


• Principles and Guidelines for Use of Animals in Precollege Education. Institute of Laboratory Animal Resources, 1989.


• Public Health Service Policy on Humane Care and Use of Laboratory Animals. National Institutes of Health, 1986 (also available in Spanish).


• Report of the American Ornithologists' Union, Cooper Ornithological Society; Wilson Ornithological Society; American Ornithologists' Union. 1988 Report of Committee on Use of Wild Birds in Research. Auk 105 (1, Suppl.): 1A-41A.


• Scientists Center for Animal Welfare Publications.

• State Laws Concerning the Use of Animals in Research. Compiled by National Association for Biomedical Research, September 1991.


• USDA Animal Welfare Regulations, 9 CFR Subchapter A, Parts 1, 2 and 3.

Chapter 12. Acronyms

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>AAALAC</td>
<td>American Association for Accreditation of Laboratory Animal Care</td>
</tr>
<tr>
<td>AALAS</td>
<td>American Association for Laboratory Animal Science</td>
</tr>
<tr>
<td>ACLAM</td>
<td>American College of Laboratory Animal Medicine</td>
</tr>
<tr>
<td>APHIS</td>
<td>Agriculture and Plant Health Inspection Service</td>
</tr>
<tr>
<td>AVMA</td>
<td>Animal Veterinary Medical Association</td>
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<tr>
<td>AWA</td>
<td>Animal Welfare Act</td>
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<tr>
<td>AWIC</td>
<td>Animal Welfare Information Center</td>
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<tr>
<td>DVM</td>
<td>Doctor of Veterinary Medicine</td>
</tr>
<tr>
<td>FOIA</td>
<td>Freedom of Information Act</td>
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<tr>
<td>Guide</td>
<td>Guide for the Care and Use of Laboratory Animals</td>
</tr>
<tr>
<td>IACUC</td>
<td>Institutional Animal Care and Use Committee</td>
</tr>
<tr>
<td>ILAR</td>
<td>Institute for Laboratory Animal Resources</td>
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<tr>
<td>NABR</td>
<td>National Association for Biomedical Research</td>
</tr>
<tr>
<td>NCRR</td>
<td>National Center for Research Resources</td>
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<tr>
<td>NIH</td>
<td>National Institutes of Health</td>
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<tr>
<td>NLM</td>
<td>National Library of Medicine</td>
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<tr>
<td>NRC</td>
<td>National Research Council</td>
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<td>OLAW</td>
<td>Office of Laboratory Animal Welfare</td>
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<td>PHS</td>
<td>Public Health Service</td>
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<td>PHS Policy</td>
<td>The Public Health Service Policy on Humane Care and Use of Laboratory Animals</td>
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<td>REAC</td>
<td>Regulatory Enforcement and Animal Care</td>
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<td>SCAW</td>
<td>Scientists Center for Animal Welfare</td>
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<tr>
<td>USDA</td>
<td>United States Department of Agriculture</td>
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