

University of Maryland School of Medicine Institutional Animal Care and Use Program

Guidelines for Surgery
Large and Small Animals
Revision Date 04/20/05

I. Regulations regarding animal surgery

A. “Large animals” vs. “small animals”:

Two sets of guidelines have been adopted by the United States Federal Government to regulate vertebrate animal use in research. The Public Health Service (PHS, <http://grants2.nih.gov/grants/olaw/olaw.htm>), which includes the National Institutes of Health, requires all research on animals that it funds to comply with the *Guide for the Care and Use of Laboratory Animals* (published in 1996 by the National Academy of Sciences). Henceforth in this document, the publication will be referred to as the “*Guide*.” PHS expects that all animal-related research conducted at institutions that receive its funding, including work that is not directly supported by PHS, to comply with the *Guide*. Furthermore, the Animal Welfare Act (AWA), which was passed by the U.S. Congress in 1966 and strengthened through amendments in 1970, 1976, 1985, and 1990, regulates care and use of most warm-blooded species employed in research. However, some species, including birds, mice of the genus *Mus*, and rats of the genus *Rattus* that are bred for use in research are exempt from the provisions of AWA. The USDA's Animal and Plant Health Inspection Service administers the AWA, its standards, and its regulations. Thus, most University of Maryland School of Medicine investigators who employ rats and mice in their research must comply with the provisions of the *Guide*, whereas investigators who use other mammalian species including nonhuman primates, cats, dogs, rabbits, ferrets, pigs, hamsters, guinea pigs, and other rodents not purposefully bred for research, must comply with both the *Guide* and regulations provided by the USDA.

Although use of some rodents (hamsters, guinea pigs, and other rodents not purposefully bred for research) is regulated by the USDA, both the *Guide* and USDA policies set somewhat different standards for surgical practices on rodents, which will be collectively referred to as “small animals, but also include amphibians and birds.” versus larger mammals. This document will collectively refer to non-human primates, rabbits, pigs, dogs, cats, ferrets, and other larger mammals as “large animals.”

It should be noted, however, that record keeping and certain other requirements for any animals regulated by USDA, including those rodent species that are not exempt from the provisions of AWA, differ from those dictated in the *Guide* for rats and mice that are bred for research. This document will thus point out some differences in surgical practices for mice and rats and other “small animals.”

B. Guide:

Pages 60-66 of the *Guide* provide general surgical guidelines for both large and small animals. Since the University of Maryland School of Medicine is a PHS-assured institution, all surgical procedures conducted on vertebrate animals at this institution (both large and small animals) must comply with the *Guide*. It is prudent for all investigators conducting surgery to be familiar with the relevant section of the *Guide*, which can be accessed online at the following address: <http://www.nap.edu/readingroom/books/labrats/contents.html>

C. USDA Policy 3:

Surgical standards for AWA-regulated species are described in USDA Policy 3. As noted previously, AWA-regulated species include all large animals as well as some small animals. Although the use of most rats and mice at the University of Maryland School of Medicine is not technically regulated by USDA Policy 3, most surgical standards for AWA-regulated small animals stipulated in this Policy are generally applicable across rodent species. Thus, it is useful for all investigators to be familiar with USDA Policy 3, which is attached to this document as Appendix 1.

D. Other regulations:

Both the *Guide* and USDA policies recognize that unique conditions exist at every institution, and stipulate some purview for the IACUC in the local interpretation and application of the law. The University of Maryland School of Medicine's IACUC has established a number of policies regulating animal use at our institution. All investigators must be familiar with the IACUC policies, which can be accessed at the following address: <http://medschool.umaryland.edu/orags/acuo/>.

II. Qualifications for surgeons

A. Guidelines from Academy of Surgeons:

The Academy of Surgical Research has formulated a number of guidelines for training investigators who conduct surgery on animals. These guidelines are attached in Appendix 2. All investigators conducting surgery should be familiar with these guidelines. A principal investigator with an IACUC-approved protocol must take the responsibility of assuring that any personnel performing surgical procedures on animals under that protocol are adequately trained.

B. Assessment of qualifications:

As part of routine audits, the attending veterinarian, IACUC members, and ACUO may review surgical practices or surgical outcomes for ongoing projects. If deficiencies are noted, the IACUC may require further training for personnel or other changes in procedures before the project can continue. Furthermore, Veterinary Resources' veterinarians and staff routinely assess postsurgical outcomes in all

animals, and may request that the IACUC office audit a protocol if problems are noted.

C. Surgical training opportunities:

The Veterinary Resources' veterinarians as well as staff are available for consultation if surgical problems occur or post-surgical complications are apparent. Investigators should feel comfortable in turning to the veterinarians and staff for assistance in solving problems. Often some fairly minor streamlining of procedures can vastly improve surgical outcomes, and thus increase the success rate for experiments. The goal of both the IACUC and Veterinary Resources is to facilitate the accomplishment of science while minimizing animal pain and distress.

III. Surgical Definitions

A. Major surgery:

Major surgery is a surgical intervention that penetrates and exposes a body cavity or any procedure that produces substantial or permanent impairment of physical or physiological functions.

B. Minor Surgery:

Any operative procedure in which only skin, mucous membranes and/or connective tissue is resected, such as simple vascular cut-down for catheter placement or implanting pumps in subcutaneous tissue. Non-surgical procedures that might require comparable levels of anesthesia and sterility include CSF collection, intracerebral inoculations and joint fluid collection.

C. Survival Surgery:

Survival surgery is any surgical procedure from which the animal recovers consciousness. Aseptic technique must be used for all survival surgical procedures.

D. Multiple Survival Surgery (only if recovering from the second surgery):

The *Guide for the Care and Use of Laboratory Animals* provides the following guidance regarding multiple survival surgeries: "*Use of one animal in **multiple major survival surgeries** is allowed only when such procedures are related components of a protocol; they must be scientifically justified in the protocol and approved by the IACUC. Cost savings is not an acceptable justification for multiple survival surgeries on any animal.*" Determination that a procedure constitutes major surgery on any animal is usually made during the IACUC review process. However, development of "permanent physical impairment" may not be recognized until after the procedure is performed. If such impairment develops after surgery, that animal cannot be used for another recovery procedure.

E. Non-survival (terminal) Surgery:

Any surgery or procedure conducted on animals that are not allowed to regain consciousness. Non-survival surgery procedures require similar record keeping as survival surgery.

IV. Acceptable surgical sites

A. Rodent surgery:

1. A separate facility for rodent surgery is not necessary. A room or part of a room that is easily sanitized and not used for other activities during surgery is appropriate. Surgery should be conducted in a disinfected uncluttered area, which promotes asepsis during surgery. The surgical surface must be impervious to water and able to be easily disinfected. The PI is encouraged to utilize procedure rooms or dedicated surgery facilities when possible.
2. To prevent cross-contamination, specific areas should be designated for animals awaiting surgery, prepping, surgery, and recovery.
3. Surgical table and instruments, e.g. microscopes, head frames, heating blankets, should be cleaned and wiped with disinfectant and allowed sufficient time to dry.

B. Large animal surgery:

Major survival surgery should be conducted in a dedicated surgical suite approved by the IACUC. The following locations are the only approved sites for large animal surgery:

1. MSTF Room G-78
2. BRB 6th Floor – Room 6-046
3. MSTF 416-A - 3 room suite

Minor surgery may be conducted in the above suites or a dedicated treatment area within the animal facility or within the MSTF 6th floor surgical area.

V. Surgical procedures (rodent and large animal)

A. Pre-surgical assessment of animals:

It is recommended that all animals have a pre-procedural assessment done before every procedure. This assessment can be recorded on the anesthetic form or recorded separately and maintained by the PI as part of the animal's record.

B. Aseptic techniques for rodent surgery:

These guidelines apply to all surgical procedures performed on rodents in which the animals are expected to recover from anesthesia. Survival surgery on rodents should be performed using sterile instruments, sterile surgical gloves, mask and aseptic procedures to reduce microbial contamination of exposed tissues.

1. Surgical instruments must be sterilized using EO gas or steam sterilization. For multiple surgeries, instruments must be disinfected at the tips between surgeries. Suggested methods include: hot bead sterilization followed by cooling with sterile saline, or cold sterilization solutions such as gluteraldehyde. After a maximum of 5 surgeries with one surgical pack, a fresh sterile surgical pack must be used.
2. Pre-operative guidelines for rodent surgery:
 - a. Prepare the animal by removing the hair from the surgical site. Perform this procedure in an area separate from where the surgery is to be conducted.
 - b. Prepare the surgical site(s) with an appropriate skin disinfectant such as Betadine. Alcohol is not an adequate disinfecting agent. Surgeons should don surgical mask, scrubs or a clean lab coat and wash hands before aseptically donning sterile surgical gloves.

C. Aseptic techniques for large animal surgery:

These guidelines apply to all surgical procedures performed on large animals. Major survival surgery should be conducted in a dedicated surgical suite approved by the IACUC. (See above).

1. Pre-operative guidelines in large animals:
 - a. Perform this procedure in an area separate from where the surgery is to be conducted.
 - b. Prepare the surgical site(s) with an appropriate skin disinfectant after the animal has been positioned.

- c. Surgeons must don surgical scrubs, surgical mask, and cap, complete a surgical scrub of the hands and don sterile gown and gloves.
 - d. A separate sterile instrument pack must be used for each animal.
 - e. Animal must be draped with sterile drapes before beginning the procedure.
2. Operative guidelines in large animals:
- a. The animal must be maintained in a surgical plane of anesthesia throughout the procedure.
 - b. A dedicated anesthetist should monitor depth of anesthesia and maintain an anesthetic record.
 - c. Close surgical wounds using appropriate techniques and sterile materials.

D. Anesthesia and Analgesia: (Refer to Veterinary Resources' formulary for dosages at <http://vetmedicine.umaryland.edu>)

1. Anesthetic and Analgesia Definitions
- a. **Anesthetic**-a drug that causes a reversible loss of conscious awareness and sensation, including pain.
 - b. **Analgesic**-a drug that causes an absence of pain in response to stimulation that would normally be painful; often, what is actually achieved following administration of an analgesic is hypoalgesia, or diminished pain in response to stimuli.
 - c. **Sedative**-a drug that produces a state of decreased motor activity, mental calmness, and drowsiness; does not imply analgesia, although most sedatives will increase the pain tolerance threshold by reducing anxiety and fear.
 - d. **Neuromuscular blocking agents**- (paralytic agent) a drug that blocks transmission at the neuromuscular junction; these drugs lack anesthetic and analgesic properties. It is not acceptable to use a neuromuscular blocking agent without general anesthesia.

2. General Anesthesia

General anesthesia provides overall insensitivity and unconsciousness. Basic elements include: unconsciousness, amnesia, analgesia, muscle relaxation, diminished motor response to noxious stimuli, reversibility.

- a. ***Inhalation anesthetics*** are gaseous or volatile agents administered via the respiratory tract. Inhalation anesthetics, when properly administered, allow one to control and regulate anesthetic depth. Disadvantages include need for specialized delivery equipment and potential toxicosis to personnel chronically exposed to anesthetic vapors. Endotracheal intubation facilitates effective and safe delivery of inhalation anesthetics. A waste gas scavenging system must be used to minimize exposure to personnel. Examples include: halothane, methoxyflurane and isoflurane.
- b. ***Injectable anesthetics*** can serve as the sole anesthetic agent, be used to induce anesthesia before inhalation anesthesia, or used to supplement regional anesthesia. To minimize the chance of a drug over dose and reduce drug-related tissue damage, drugs used for (<4 kg) laboratory animals may need to be diluted.
- c. ***Hypnotic/sedative*** drugs are widely used for inducing or managing general anesthesia. They induce a dose-dependent spectrum of CNS depression, from sleep to deep general anesthesia. Examples include: pentobarbital, sodium thiamylal, sodium thiopental, and diazepam.
- d. ***Alpha 2-adrenergic*** receptor agonists have tranquilizing, sedative, and potent analgesic properties. These drugs can be used as pre-anesthetic, anesthesia inducing or analgesic agents. Examples include: xylazine and medetomidine.
- e. ***Dissociative drugs*** induce anesthesia, have short duration of action, a wide safety margin, and cause minimal cardiopulmonary depression. To decrease undesirable actions such as muscle hypertonus and emergence delirium, they are often used in combination with hypnotics, tranquilizers, or alpha 2-adrenergic receptor agonists. Examples include: ketamine and tiletamine which is often in combination with the tranquilizer zolazepam.

- f. *Neuromuscular blocking agents* are devoid of sedative and analgesic properties. These drugs, when used during surgery, must be administered only in conjunction with general anesthetics. The investigator must remain aware that the animal is unable to respond with purposeful movements to noxious stimulation and the animal must be closely monitored (e.g. heart rate, arterial blood pressure) to ensure adequate depth of anesthesia. Examples include: succinylcholine and dimethyl tubocurarine.

3. Local and Regional Anesthesia

Local and regional anesthesia can result from topical application (Emla[®] cream) or injection of appropriate anesthetics in the region of the surgical incision (local anesthesia); injection in proximity to nerve trunk (nerve block); or injection into the subarachnoid or epidural spaces (regional anesthesia). Examples of agents that produce these types of anesthesia are lidocaine, bupivacaine, and Emla[®] cream.

4. Analgesia

- a. An integral component of veterinary medical care is prevention or alleviation of pain associated with procedural and surgical protocols. Analgesic drugs to reduce pain should be initiated during the perioperative period and continued well into the postoperative recovery period. It is often erroneously presumed that an animal is not in pain when there is no obvious change in behavior. Pain can be difficult to detect. Criteria for assessing pain in various species differ. Some species-specific behavioral manifestations of pain or distress are used as indicators, for example, vocalization, depression or other abnormal appearance or posture, and immobility. It is therefore essential that personnel caring for and using animals be very familiar with species-specific (and individual) behavioral, physiologic, and biochemical indicators of wellbeing. The selection depends on many factors, such as the species and age of the animal, the type and degree of pain, the likely effects of particular agents on specific organ systems, the length of the operative procedure, and the safety of an agent for an animal, particularly if a physiologic deficit is induced by a surgical or other experimental procedure. Consultation with an attending veterinarian is recommended since there is tremendous variation between species as to their response to analgesic drugs.
- b. Species-Specific Assessment of Pain and Distress can be a difficult task. Two helpful references are available in the Veterinary Resources and IACUC offices, for the investigator to review, and on-line at <http://vetmedicine.umaryland.edu>.

5. Guidelines for the Selection and Administration of Analgesic Drugs
- a. See IACUC website (<http://medschool.umaryland.edu/orags/acuo>) guidelines section formulary for suggested analgesic and anesthetic drugs and dosages.
 - b. Federal law requires pain relief according to the “*Guide*” and the Animal Welfare Act. The “*Guide*” on page 64 states that “the proper use of anesthetics and analgesics in research animals is an ethical and scientific imperative”. The Animal Welfare Act (AWA) provides (in section 13-3) requirements for animal care, treatment and practices in experimental procedures to ensure that animal pain and distress are minimized. These requirements include adequate veterinary care with the appropriate use of anesthetics, analgesics, or tranquilizing drugs or euthanasia. Care must be taken when choosing the proper dosage and schedule for a particular species, and different analgesics are indicated for different types of pain.
 - c. **Non-steroidal anti-inflammatory drugs (NSAID)** are effective against pain associated with inflammation, acute pain associated with soft tissue injury, burns, and pain associated with muscular-skeletal injuries or disease. Examples include: flunixin meglumine and ketoprofen.
 - d. **Opioid agonists** and ***Opioid agonist-antagonists*** are effective against most visceral and somatic pain; although generally not as effective as NSAIDs at alleviating muscular-skeletal pain (somatic pain), they may be used in conjunction with NSAIDs to treat severe types of pain. Examples include: morphine, buprenorphine and butorphanol.
 - e. **Neurogenic pain** is pain that arises from damaged nerves or from amputation. This pain is difficult to treat and rarely responds well to any of the drugs listed above. More likely to be effective are: tricyclic antidepressants such as amitriptyline, anticonvulsants such as carbamazepine, or nerve blocking agents such as lidocaine.
 - f. Medical and veterinary reports have suggested that analgesics might be most effective when administered prior to the painful stimulus, before the surgical incision and tissue manipulation.
 - g. Analgesic drugs must be given at the proper initial dose and subsequent doses must be given according to schedule and protocol.
 - h. However severe visceral or somatic pain may be best treated with NSAIDs in combination with potent opioid agonists or opioid agonists-antagonists.

E. Monitoring depth of anesthesia:

1. Monitoring depth of anesthesia is species and individual dependant. An anesthetic text should be consulted for details. The research animal must be maintained at a surgical plane of anesthesia through out the procedure. Monitoring should be documented every fifteen minutes. Heart and/or respiration rate, body temperature, and responsiveness to stimuli are monitored for all large animal survival surgeries. Specific parameters to be monitored must be specified in the approved IACUC protocol and will depend on species of animal, the procedure, and length of time that the animal is under anesthesia.
2. Anesthetic records must be maintained for procedures on large animals (see VI, A, 2).

F. Post-surgical recovery required before returning to animal facility:

1. Move the animal to a warm, dry area where trained personnel must monitor recovery.
2. Return the animal to routine housing once righting reflexes have returned and the animal can maintain normal body temperature. Do not offer food or water until the animal is fully recovered from anesthetic.
3. Administer analgesics according to the schedule defined in the IACUC approved protocol unless there is scientific justification and approval by the IACUC for not doing so.
4. Generally, remove skin closures 7-10 days post-operatively.
5. Maintain surgery, anesthesia and post-operative care records. (See Record Keeping section VI).

VI. Required record keeping

A. Large animal:

1. The pre-procedural assessment can be recorded on the anesthetic form and maintained by the PI as part of the animal's record. Pre-procedural assessment should include the general appearance and health of the animal, possibly weight and temperature/pulse/respiration as compared to normal values. More extensive assessment (CBC, ECG, Clinical chemistry screening) may be prudent depending on the type of procedure to be conducted, and may require veterinary consultation.

2. All large animals undergoing a survival or non-survival anesthetic procedure must have an anesthetic record maintained during the procedure. It is recommended that standard anesthetic forms be used to monitor the animal under anesthesia. The anesthetic form must include a description of the procedure, the protocol number, the animal identification number, the investigator's name and the anesthetist. The minimum data include: the date and starting time of the anesthetic procedure, the animal's weight, any pre-anesthetic assessment, anesthetic dose and route of delivery, intubation/extubation times, start/stop times of the procedure, volume of fluids given, and the pulse and respiratory rate. The pulse and respiratory rate should be recorded at a minimum of 15minute intervals, and more frequently if the procedure performed may affect these parameters quickly. **A copy of the anesthetic form must be delivered to Veterinary Resources within 24 hours post-procedure.**
3. All investigators are required to complete a **Post Procedural Form (PPF)** on all large animals to describe manipulations, including anesthesia, surgery, catheterization, injections of proteins, viruses, or biohazards, or euthanasia. This form asks for a description of the procedure performed, investigator contact information, animal identification and any treatments that the investigator or Veterinary Resources will give to the animal. The form is used to document what treatment was done to the animal and the frequency. Antibiotics, analgesics, fluids or other drugs given to the animal must have the dose and frequency recorded, and the person giving the treatment must initial the treatment form after each treatment. This form also documents that the animal was observed following a procedure. The animal's general condition and any specific clinical signs of problems and pain assessment must be recorded. **This form** is an essential part of the animal's medical record and **must be copied and delivered to Veterinary Resources within 24 hours.**
4. Standard anesthetic forms and Post Procedural Forms (PPF) are available from Veterinary Resources (410-706-3540).
5. **Copies of anesthetic forms and Post Procedural Forms must be delivered to Veterinary Resources (MSTF G-100) or faxed (410-706-8538) within 24 hours of completion of the procedure or treatment.**
6. These forms or logbooks are reviewed by Veterinary Resources' staff or IACUC to determine that the procedures specified in the protocol were performed and that animal well-being is maintained.

B. Small Animals: e.g. Rats, mice, other rodents, birds, and amphibians:

1. The primary record-keeping tool for the small animal investigator is a logbook or bound notebook. The investigator for each rodent procedure or surgery must keep a logbook record. For batches of rodent procedures, a

group logbook can be maintained, but for high-risk procedures or procedures with high complication rates (consult with a Veterinary Resources veterinarian), individual information must be maintained for each rodent in the logbook or a separate animal record can be maintained. The PI must have their logbook available during normal work hours for review.

2. Cage cards: must be maintained on all animal cages, and must be completely filled out, noting the date of arrival, strain, source, investigator's name and protocol number. Veterinary Resources fills out the cage cards upon arrival but the PI is responsible to check that all information is correctly completed and updated. Contact the Veterinary Resources' facility supervisor if there are any questions or problems.

VII. Post-procedural recovery and care

A. Responsibility for recovery:

It is the PI's responsibility to perform all post-procedural recovery and care unless determined in advance that a second party such as Veterinary Resources' personnel will perform the post-procedural recovery and care services.

B. Documentation:

The PI is responsible for documenting all post-procedural recovery and care activities. Specifically, documentation that post-procedural analgesics and antibiotics were given and daily observations of the animal were performed to assess for species-specific pain and distress. **For large animals, copies of Post Procedural Form must be delivered to Veterinary Resources (MSTF G-100) or faxed (410-706-8538) within 24 hours of completion of the procedure or treatment.** This form is available from Veterinary Resources (410-706-3540) or on the IACUC website (<http://medschool.umaryland.edu/orags/acuo>) guidelines section.

For small animals (e.g. rodents, amphibians and birds) follow the following procedures. Post-Surgical Record Keeping Requirements Small Animals – (e.g. Rodents/Amphibians/Birds)

PROCEDURES.

The Principal Investigator (or his/her designees) is required to maintain information on their rodents at both the cage level and within their laboratory as specified below.

I) Post-surgical Record Documentation at the CAGE LEVEL:

REQUIRED INFORMATION:

1) *Documentation of all surgical/ invasive manipulation and protocol specified therapeutic peri-operative treatment:*

Each surgical or invasive procedure performed on an animal must be documented by the investigator or their staff on a green “Small Animals Surgery/Procedure” card (provided by Veterinary Resources). This is placed on the cage behind the standard identifying cage card and provides a highly visible indicator to the Veterinary Resources staff of recent manipulation, allowing for more intensive and direct follow-up assessment on their part.

On one side of the card the investigator should list the procedure performed, the initials of the individual who performed it, the date and the number of animals in the cage that were manipulated (including their specific identification – when available). The other side of the card serves as a signoff document for the administration of protocol specified, required post-operative medications – including analgesics, antibiotics and/or other therapeutic treatments. Drugs given should be listed, along with the dose (or amount administered) and frequency of administration for the entire duration of therapy (Rx). For each treatment, a check box on the green card should be marked off and initialed by the individual giving the Rx. Please note that routine post-procedural treatments must be administered at least to the extent written in the approved protocol, and reduction in the course of Rx according to subjective clinical impression (unless specifically defined and approved in the protocol) is not permitted. Card signoff verifies that all surgically manipulated animals in the cage have received treatment. (*Listing and signing off on the administration of non-hazardous experimental or study related drugs at the cage level is not required – but may be done if considered useful by the investigator.*)

At the time of each treatment, investigators should examine manipulated animals. Marking and initialing the card also indicates that the animal’s incision and general clinical condition have been evaluated. If end-point criteria as designated in the approved protocol are present, the animal should be euthanized as specified. If significant unanticipated morbidity is present, additional monitoring is required. Consultation with a Veterinary Resources veterinarian to review an appropriate treatment plan is recommended.

When treatments are completed and the animal has made a full, functional recovery, the green cards may be folded in half and placed behind the standard cage card. When animals are sacrificed, these cards should be retrieved, disinfected (or copied) and filed with the

research/data records.

II Post-Surgical Record Documentation at the LABORATORY LEVEL:

General Methodology:

Required and recommended information maintained at the Laboratory (unless otherwise specified in the animal care and use protocol) may be integrated with research data recorded. As such, the format in which it is maintained may vary significantly from lab to lab.

REQUIRED (The IACUC requires that the following information be maintained)

1) Documentation of all surgical research manipulation

(Although this documentation may be done by retrieving and filing green surgical/procedural cage cards, investigators are encouraged to maintain independent central records of such procedures)

2) Brief documentation of post-anesthetic/peri-operative course

For example:

“Post-operative recoveries were unremarkable – All 7 animals were returned to facility cages awake and ambulatory at 3:00 PM”

“Post-operative courses generally unremarkable – 2 of the 8 animals (list specific animal identification numbers if available) had more prolonged recoveries and required additional external heat support”

“One of ten animals operated on died during recovery (list specific animal identification number if available)”

C. Post-procedural problems:

If post procedural problems are encountered, the PI should contact Veterinary Resources (410-706-3540). Emergency pager number: 410-748-4569.

VIII. Compliance with regulations

The Animal Care and Use Committee at the University of Maryland School of Medicine investigates all concerns regarding the care, treatment, and use of animals for research or teaching at the university. To report a concern, please contact any or all of the following:

Dr. Louis DeTolla
Director, Comparative Medicine
Chief, Veterinary Resources
G-100 MSTF
410-706-8537
detolla@vetmed.umaryland.edu

Ms. Angela Peiser
IACUC Coordinator
146 HSF-1
410-706-4365
ACUO@som.umaryland.edu

Dr. Larry D. Anderson
Chair, IACUC
146 HSF-1
410-706-3506
landerso@umaryland.edu

Dr. Steven Shipley
Attending Veterinarian
G-100 MSTF
410-706-3703
sshipley@vetmed.umaryland.edu

XI. References

- A. *The Guide for the Care and Use of Laboratory Animals* - <http://grants2.nih.gov/grants/olaw/olaw.htm>
- B. Animal Welfare Act, 1966, as amended
- C. University of Maryland School of Medicine Animal Care and Use Office's website <http://medschool.umaryland.edu/orags/acuo>
- D. University of Maryland School of Medicine Veterinary Resources' website <http://vetmedicine.umaryland.edu>
- E. Journal of Investigative Surgery, Volume 2, pp. 263-368, 1989, Taylor & Francis, Inc.: Washington, DC
- F. University of Pittsburgh, Division of Laboratory Animal Resources

XII. Resources

- A. Veterinary Resources Veterinarians (410-706-3540)
- B. IACUC: 410-706-4365
- C. IACUC Web site: <http://medschool.umaryland.edu/orags/acuo/>
- D. Veterinary Resources Web site: <http://vetmedicine.umaryland.edu>

compromise the validity of the scientific study. Proper anesthesia, analgesia, and euthanasia are required for all such procedures. Drugs administered to relieve pain or distress and emergency drugs must not be used beyond their expiration date. Facilities allowing the use of expired medical materials in acute terminal procedures should have a policy covering the use of such materials and/or require investigators to describe in their animal activity proposals the intended use of expired materials. The attending veterinarian and the Institutional Animal Care and Use Committee (IACUC) are responsible for ensuring that proposed animal activities avoid or minimize discomfort, distress, and pain to the animal. These responsibilities cannot be met unless the veterinarian and the IACUC maintain control over the use of expired medical materials.

Pharmaceutical-Grade Compounds in Research

Investigators are expected to use pharmaceutical-grade medications whenever they are available, even in acute procedures. Non-pharmaceutical-grade chemical compounds should only be used in regulated animals after specific review and approval by the IACUC for reasons such as scientific necessity or non-availability of an acceptable veterinary or human pharmaceutical-grade product. Cost savings alone are not an adequate justification for using nonpharmaceutical-grade compounds in regulated animals.

Surgery

AWA regulations require that survival surgeries be performed using aseptic techniques and that major operative procedures on nonrodents be performed only in dedicated surgical facilities. Nonsurvival surgeries require neither aseptic techniques nor dedicated facilities if the subjects are not anesthetized long enough to show evidence of infection. Research facilities doing surgical demonstrations while traveling must use aseptic techniques and dedicated surgical facilities. Motel meeting rooms and auditoriums do not qualify as dedicated surgical facilities.

Nonsurvival surgeries not performed aseptically or in a dedicated facility must at least be performed in a clean area, free of clutter, and using acceptable veterinary sanitation practices analogous to those used in a standard examination/treatment room. Personnel present in the area must observe reasonable cleanliness practices for both themselves and the animals. Eating, drinking, or smoking are not acceptable in surgery areas, and locations used for food handling purposes do not qualify as acceptable areas for performing surgeries.

Pre- and Post-Procedural Care

All animal activity proposals involving surgery must provide specific details of pre- through post-procedural care and relief of pain and distress. The specific details must be approved by the attending veterinarian or his/her designee. However, the attending veterinarian retains the authority to change postoperative care as necessary to ensure the comfort of the animal. The withholding of pain and/or distress relieving care must be scientifically justified in writing and approved by the IACUC. The appropriate use of drugs to relieve pain and/or distress must be specified in the animal activity proposal to avoid possible delays due to investigator concerns that a treatment regimen may interfere with the study. Furthermore, the specified drugs for relief of pain and/or distress must be readily available for use as described in the proposal.

While an animal is under post-surgical care, the ownership of the animal is not to change. If the animal is taken to an off-site location, such as a farm, for post-operative care, that location should be identified as a site of the research facility. An animal is not to be taken to an off-site location before it fully recovers from anesthesia unless justified in the animal activity proposal. Appropriate post-operative records must be maintained in accordance with professionally accepted veterinary procedures regardless of the location of the animal.

Program of Veterinary Care

Facilities which do not have a full-time attending veterinarian must have a written Program of Veterinary Care (PVC). This Program must consist of a properly completed APHIS Form 7002 or an equivalent format providing all of the information required by the APHIS form. The attending veterinarian must visit the facility on a regular basis, i.e., often enough to provide adequate oversight of the facility's care and use of animals but no less than annually. Records of visits by the attending veterinarian must be kept to include dates of the visits and comments or recommendations of the attending veterinarian or other veterinarians.

The PVC must be reviewed and updated whenever necessary (e.g., as a new species of animal or a new attending veterinarian is obtained, or the preventive medical program changes). It must be initialed and dated by both the attending veterinarian and the facility representative whenever it is changed or reviewed without change. The preventive medical program described in the PVC is expected to be in accordance with common good veterinary practices (e.g., appropriate vaccinations, diagnostic testing). It should include zoonotic disease prevention measures and, if necessary, special dietary prescriptions.

Health Records

Health records are meant to convey necessary information to all people involved in an animal's care. Every facility is expected to have a system of health records sufficiently comprehensive to demonstrate the delivery of adequate health care. For those facilities that employ one or more full-time veterinarians, it is expected there will be an established health records system consistent with professional standards that meets and probably exceeds, the minimum requirements set forth in this policy. For facilities that do not employ a full-time veterinarian, it is suggested the health records system be explained as part of the written PVC, to ensure involvement of the attending veterinarian in developing the system. For all facilities, health records must be current, legible, and include, at a minimum, the following information:

- **Identity** of the animal.
- **Descriptions of any illness**, injury, distress, and/or behavioral abnormalities **and the resolution** of any noted problem.
- **Dates, details, and results** (if appropriate) of all medically related observations, **examinations, tests**, and other such procedures.
- Dates and other details of all treatments, including the name, dose, route, frequency, and duration of **treatment with drugs or other medications**. (A "check-off" system to record when treatment is given each day may be beneficial.)
- Treatment plans should include a **diagnosis** and **prognosis**, when appropriate. They must also detail the type, frequency, and duration of any treatment and the criteria and/or schedule for re-evaluation(s) by the attending veterinarian. In addition, it must include the attending veterinarian's **recommendation concerning activity level** or restrictions of the animal.

Examples of procedures which should be adequately documented in health records include, but are not limited to, vaccinations, fecal examinations, radiographs, surgeries, and necropsies. Routine husbandry and preventive medical procedures (e.g., vaccinations and dewormings) performed on a group of animals may be recorded on herd-health-type records. However, individual treatment of an animal must be on an entry specific to that animal. As long as all required information is readily available, records may be kept in any format convenient to the licensee/registrant (e.g., on cage cards for rodents).

Health records may be held by the licensee/registrant (including, but not limited to, the investigators at research facilities) or the attending veterinarian or divided between both (if appropriately cross-referenced), but it is the responsibility of the licensee/registrant to ensure that all components of the records are readily available and that the record as a whole meets the requirements listed above.

An animal's health records must be held for at least 1 year after its disposition or

death. (Note: Some records may need to be held longer to comply with other applicable laws or policies.) When an animal is transferred to another party or location, a copy of the animal's health record must be transferred with the animal. The transferred record should contain the animal's individual medical history, information on any chronic or ongoing health problems, and information on the most current preventive medical procedures (for example, the most recent vaccinations and dewormings). For traveling exhibitors, information on any chronic or ongoing health problems and information on the most current preventive medical procedures must accompany any traveling animals, but the individual medical history records may be maintained at the home site.

Euthanasia

The method of euthanasia must be consistent with the current Report of the AVMA Panel on Euthanasia. Gunshot is not an acceptable method of routine euthanasia for any animal. Gunshot as a routine method of euthanasia not only endangers surrounding animals, buildings, and personnel, but it is likely to cause distress to other animals. It should only be used in situations where other forms of acceptable euthanasia cannot be used (such as emergency or field conditions where the animal cannot be appropriately restrained) or in cases where gunshot will reduce danger to other animals or humans. Only personnel skilled in the use of firearms, using appropriate firearms, and familiar with the "kill point" of an animal should perform the euthanasia. If the firearm is not aimed so that the projectile enters the brain and causes rapid unconsciousness and subsequent death without evidence of pain or distress, this method does not meet the definition of euthanasia. (All State and local laws relevant to gunshot must also be met.)

Appendix 2

Guidelines for Training in Surgical Research in Animals, Academy of Surgical Research.

Journal of Investigative Surgery, Volume 2, pp. 263-368, 1989, Taylor & Francis, Inc.: Washington, DC. Reproduced with permission. All rights reserved.

Current awareness of animal welfare motivates those in surgical research to apply all knowledge of good surgical technique, anesthetic methods, and postoperative care to their research animals. There are advantages to being proactive rather than reactive in implementing adequate surgical training guidelines and certification programs in experimental surgical research. These advantages accrue not only to experimental animals, scientists, and science, but also to the public and its perception of animal welfare.

The purpose of this document is to assist institutions and individuals in ensuring that surgical procedures performed on laboratory animals are conducted with skill and compassion. It was developed following two panel discussions on Animal Welfare in Surgical Research at the 1986 and 1987 scientific sessions of the Academy of Surgical Research. The Academy is currently developing a certification examination for persons without professional degrees who are involved in performing surgical procedures for research purposes.

The Board of Directors of the Academy of Surgical Research recommends that these voluntary guidelines be employed by institutions and individuals involved in experimental surgery to ensure compliance with current laws, standards, and regulations employed by certification agencies and governmental regulatory agencies. Ultimately, the responsibility for assuring competence of individuals involved in surgical research is the responsibility of attending veterinarians and animal care and use committees in the various institutions.

Need for Guidelines in Training

Governmental agencies in many countries have developed standards, laws, and regulations concerning experimental surgery on animals. The common theme in these regulatory statutes is that proper technique and facilities be used for the performance of experimental surgery on animals. State governments have set up board examinations to ensure that people who perform surgery on humans and client-owned animals are competent. No such certification has been employed for personnel performing surgery on laboratory animals. In reality, surgical procedures are utilized in many investigations into human and animal health issues by persons who do not have professional degrees in a surgically oriented profession. To ensure that personnel performing surgery on lab animals are competent, scientists and institutions should voluntarily develop policies and training programs to meet all applicable laws, regulations, and standards to make sure that scientific results are valid and that animal welfare needs are met.

The Academy of Surgical Research has endorsed the facilities standards of the American Association for the Accreditation of Laboratory Animal Care (AAALAC) which are based on the Guide for the Care and Use of Laboratory Animals developed by the Institute of Laboratory Animal Resources of

the National Academy of Sciences for the National Institutes of Health. Countries other than the United States have similar standards for facilities.

This document does not address standards for facilities, but offers guidelines for meeting the training requirements for personnel who are involved in experimental surgery.

Personnel Requiring Training

In actual practice persons with a wide variety of educational backgrounds perform surgery on animals in research institutions. These include persons with MD, DVM, DDS, and PhD degrees, or the equivalent, as well as graduate students and technicians.

Perhaps the most controversial area for discussion when attempting to follow current laws and regulations is whether persons with an earned degree in a given health science field should automatically be considered competent in experimental surgery. Personnel with these various backgrounds should be evaluated separately and will be discussed separately in this document.

1. MD. Not all physicians have been trained in surgery on animals due to the diversity of curriculum requirements between medical schools. All physicians have at least received didactic and observational training in surgery on humans. Physicians trained in surgical specialties should be considered to be competent in their particular field of expertise. For example, it would be inappropriate to require a training course in cardiothoracic surgery in animals for a physician who is either certified or who is in training in the specialty. However, such a person may not be competent in interspecies variations in anatomy, anesthesia, analgesia, and postoperative care methods. For survival surgical procedures, a team approach is recommended. This should include consultation and oversight of operative technique, anesthetic and analgesic selection, and postoperative care by a DVM. If support services are provided by competent personnel, then the need for a formal training program for such physicians could be waived.

It is recommended that the experience and background of physicians be taken into account when evaluating their ability to perform a particular surgical protocol on laboratory animals. If they participate in multidisciplinary team approach with persons who are qualified by experience or training to work with animals, this should be taken into consideration to negate any lack of experience they may have with a particular species or procedure. It is also acceptable to provide physicians with a waiver from training requirements if they have a documented history of successful performance of an experimental surgical protocol including minimal operative and postoperative complications.

2. DVM. All veterinarians have received didactic and operative training through experience in clinical surgical procedures, anesthetic and postoperative care techniques in animals. However, relatively few have received such training in experimental surgical techniques or in laboratory animal species. Veterinarians who have received training or certification in laboratory animal medicine, surgery, or

anesthesiology are most likely to have appropriate experience. It is more likely that physicians with specialty training would be more competent to perform such complex surgical protocols as organ transplantation or cardiac surgery. However, veterinarians should be considered competent in comparative anatomy, anesthesia, analgesia, aseptic surgical technique, and postoperative care of laboratory animals. Veterinarians who are not competent in the actual performance of experimental surgical protocol should be included in a team approach to minimize complications by consultation in anatomic, anesthetic, and postoperative techniques.

It is recommended that veterinarians with an appropriate background in training in laboratory animal medicine, surgery, and anesthesia be exempt from training requirements in experimental surgery performed on laboratory animals. Veterinarians who perform complex surgical procedures (ie, organ transplantation, cardiopulmonary bypass) on laboratory animals for which they do not have training or experience should seek training in the particular procedure. Veterinarians should be included in a team approach to minimize problems associated with experimental surgical protocols.

3. DDS. Dentists and oral surgeons generally do not receive training in surgical procedures on laboratory animals. However, they receive both didactic and operative training in dental and oral surgical procedures on humans. Dentists should be considered competent in their area of expertise; however, like physicians, they may require a training course that covers interspecies variations or should elect to utilize a multidisciplinary approach to minimize operative and postoperative complications.

It is recommended that dentists and oral surgeons be exempted from training in surgical procedures on animals that are included in their area of expertise on humans. However, they should receive training in anatomy, anesthesia, analgesia, and postoperative care for experimental surgical procedures on animals. This training requirement may be waived if they seek a multidisciplinary approach to performance of surgical procedures on animal species with which they are unfamiliar or if they have a documented history of performing a procedure in laboratory animals with minimal operative and postoperative complications.

4. PhD. Relatively few persons with graduate degrees from biomedical research programs have received formal training in experimental surgery on laboratory animals. However, scientists who have either had appropriate training or who have become competent in particular surgical procedures through experience should be recognized as competent to perform those procedures without further training. Other doctoral degree research scientists and graduate students seeking a doctoral degree in biomedical research should be considered to have the same requirements as persons with a PhD degree.

It is recommended that doctoral degree scientists in biomedical research be required to have formal training in proper surgical techniques before undertaking experimental

surgical protocols. The need for formal training may be obviated by taking a multidisciplinary collaborative approach with persons who are qualified by experience and training to perform the particular experimental surgical protocol on laboratory animals. Likewise, a documented history of performing the experimental surgical protocol with minimal operative and postoperative complications may be used as evidence to exclude the scientist from the formal training requirement. It is strongly recommended that graduate students expecting to perform experimental surgical protocols on laboratory animals during their career receive formal training in experimental surgery at the earliest opportunity in their career.

5. Technical Staff. Non-doctoral degree personnel may perform experimental surgical protocols on laboratory animals under the direction of investigators with doctoral degrees. Personnel in this category may have a wide variety of backgrounds, including certification as a technician in various fields. Regardless of the background, personnel in this category should not be considered qualified in the area of experimental surgery without documentation of previous training and experience. Personnel in this category may be valuable members of a team approach in experimental surgical protocols in the areas of aseptic preparation, anesthesia, surgical assistance, and postoperative care. Personnel in this category should be allowed to perform survival surgery on animals only after successfully completing a formal training program or by having a documented history of performing a particular procedure with minimal operative and postoperative complications. The Academy of Surgical Research seeks to provide a voluntary certification program for personnel in this category.

Ethical Training

This section recognizes that personnel with professional degrees in various specialties may not need formal training beyond that received in their predoctoral training. Physicians, veterinarians, dentists, and some technical specialties have ethical training as part of their background. This training at least implies that they seek training to develop expertise in areas, including such areas as experimental surgical protocols, with which they are unfamiliar prior to performing such a procedure. Adherence to this self-regulation is an integral part of becoming a professional.

It is also recognized that personnel without such a background in their training may have developed expertise in experimental surgical protocols through either experience or formal training. This experience, if it can be documented, should be taken into consideration when determining which individuals should receive formal training in experimental surgery.

It is also important to emphasize that ongoing continuing education is an important part of training and certification of professionals. Continuing education should be included in the judgment of a person's qualifications.

Components of Training Courses

Comprehensive training in experimental surgery may be a time-consuming and expensive undertaking and may not be necessary in all circumstances. It should include both didactic and

operative components. Less comprehensive courses may be utilized for personnel with previous experience or appropriate backgrounds. Areas that should be included in comprehensive training programs or in evaluating the background of personnel performing experimental surgery on animals are as follows:

- Ethical and legal considerations
- Species selection
- Model selection
- Selection of individual subjects
- Differences between rodent and nonrodent species in costs, facilities, and aseptic technique required
- Physiology and pathology relevant to the surgery and the experiment
- Basic knowledge of the healing process
- Facility requirements
- Instrument types, care, handling, and sterilization
- Management of sterility when performing surgical procedures in multiple rodent subjects
- Restraint and handling
- Anesthesia, analgesia, and euthanasia including drug selection
- Fundamental principles of good surgical technique
- Injections
- Presurgical preparation
- Common minor surgical techniques
- Common major surgical techniques
- Supportive therapy
- Operative and postoperative monitoring
- Emergencies during and following surgery

Personnel with appropriate degrees and backgrounds may acquire the knowledge necessary to perform a particular surgical technique through consultation with a veterinarian and/or surgeon. For a person performing a specific and relatively minor procedure merely performing the first few procedures under supervision may be all that is required and may not require a didactic course. Didactic portions of this training may be included in other training courses in proper care and use of laboratory animals sponsored by an institution with an optional laboratory course offered separately.

Laboratory courses may be either comprehensive or merely a specific surgical procedure performed under the direction of a competent instructor dependent upon the subject audience and the goals of the training. Certain aspects of surgical training can be performed without the use of laboratory animals. This can include lectures, audiovisual aids, and nonanimal models for certain techniques. For instance, students should learn to tie knots and suture patterns on nonanimal models prior to performing actual surgical procedures. However, there is not an acceptable substitute to actually performing the surgical procedure of interest on an animal under the supervision of a qualified instructor.

Recommendations

1. Institutions should ensure that all persons performing survival or nonsurvival surgical procedures on laboratory animals be qualified by experience and training to perform such

procedures. Personnel not qualified to perform such procedures should be required to have formal training or make collaborative arrangements with qualified personnel before performing the experimental protocol.

2. The comments regarding backgrounds of persons with doctoral and nondoctoral degree training listed in the Personnel Requiring Training section of this document should be used as a guideline for institutions making the evaluation of experience and training.
3. Institutions with persons performing experimental surgical protocols should either provide an appropriate course for personnel requiring training or provide the opportunity to pursue such training at another institution.
4. Training courses should be provided by qualified instructors in facilities which adhere to all applicable laws, regulations, and standards. A veterinarian should be included in the training program.
5. Training courses should utilize lectures, audiovisual aids, and nonanimal models prior to allowing students to perform surgery. Numbers of animals utilized and species selected should be based on the minimal number and lowest taxonomic status on animal necessary to meet the goals of the course.

Summary

This document is not meant to be a regulatory statement but rather to be utilized as a guideline for research institutions who are trying to adhere to the training regulations detailed by various governmental agencies. It is our hope that institutions and individuals will take a proactive stance in requiring adequate training and experience for persons performing experimental surgery on laboratory animals. Only by adherence to voluntary standards that ensure humane care and use of laboratory animals in research can we expect to avoid more stringent laws and regulations. More importantly, by adhering to these voluntary standards the quality of animal research can be improved, which should result in more effective and efficient use of our resources.

References

Canadian Council on Animal Care: Guide to the Care and Use of Experimental Animals. Ottawa, Ontario, 1980.

Department of Agriculture, Animal and Plant Health Inspection Service, Animal Welfare: Proposed Rules, Fed Reg 1989; 54(49): 10, 822-10,954.

Foundation for Biomedical Research: The Biomedical Investigators Handbook. Washington, DC, FBR, 1987.

Fox JG, Cohen BJ, Loew FM: Laboratory Animal Medicine. New York, Academic Press, 1984.

Kaplan HN, Timmons EH: The Rabbit: A Model for the Principles of Mammalian Physiology and Surgery. New York, Academic Press, 1979.

Kitchell RL, Erickson HH, Carstens E, et al: Animal Pain. Perception and Alleviation. Bethesda, MD, American Physiological Society, 1983.

Lang CM: Animal Physiological Surgery, ed 2. New York, Springer-Verlag, 1982. Markowitz J, Archibald J, Downie HG: Experimental Surgery: Including Surgical Physiology. Baltimore, Williams & Wilkins, 1964.

Swindle MM, Adams RJ: Experimental Surgery and Physiology: Induced Animal Models of Human Disease: Baltimore, Williams & Wilkins, 1988.

Swindle MM: Basic Surgical Exercises Using Swine. New York, Praeger, 1983.

US Department of Health and Human Services: Guide for the Care and Use of Laboratory Animals. National Institutes of Health, Publication No. 85-23, Bethesda, MD, Revised 1985.

Waynforth HB, Experimental and Surgical Technique in the Rat. New York, Academic Press, 1980.