

# Institutional Animal Care and Use Committee

## Mission

The committee's charge is to oversee the care and use of animals in research, testing, and education at the University of Mississippi Medical Center (UMMC); to review all proposed and ongoing research protocols involving the use of live animals; to ensure compliance with all federal, state and institutional policies; and to ensure the inclusion of adequate and proper record-keeping and surveillance.

## General

The Associate Vice Chancellor for Research (Dr. John E. Hall) is the University of Mississippi Medical Center's Institutional Official, and in consultation with the Vice Chancellor for Health Affairs (Dr. Daniel W. Jones) appoints representatives to the committee (IACUC). The IACUC is charged to evaluate the institution's animal program, procedures, and facilities, to ensure that they are consistent with the recommendations in the *Guide for the Care and Use of Laboratory Animals*, the *Animal Welfare Act*, and the Public Health Service Policy on Humane Care and Use of Laboratory Animals. Other committee duties include inspection of the facilities (where animals are housed and used), evaluation of programs, submission of reports to responsible institutional officials, review of proposed uses of animals in research, testing, and education (protocols), and establishment of a mechanism for receipt and review of concerns involving the care and use of animals at the institution.

## Regulatory Authority

The IACUC is mandated by the *Animal Welfare Act* (Public Law #89-544) to evaluate the care, treatment, housing, and use of animals, and for certifying compliance with the Act by the research facility. Similarly, the Public Health Service Policy on Humane Care and Use of Laboratory Animals, via the Health Research Extension Act of 1985, requires the Institutional Animal Care and Use Committee to assure compliance with the guidelines and provisions of this law. Also, the Institute of Laboratory Animal Resources (ILAR), National Research Council (NRC), publishes the *Guide for the Care and Use of Laboratory Animals* to assist institutions in caring for and using animals in ways judged to be scientifically, technically, and humanely appropriate. The *Guide* is also intended to assist investigators in fulfilling their obligation to plan and conduct animal experiments in accordance with the highest scientific, humane, and ethical principles.

## **Committee Composition**

The institution is licensed by the United States Department of Agriculture, certificate number 65-R-0102. Likewise, through the Division of Assurances, Office of Laboratory Animal Welfare (OLAW), the institution maintains an Assurance Statement (#A3275-01) with the Public Health Service (PHS).

The IACUC is composed of institutional veterinarians, research scientists who use animals in their projects, individuals who do not have a science background, and a member of the community who is not associated in any way with the medical center to represent general community interests. Committee members serve overlapping terms. Investigators are encouraged to solicit the expertise and guidance of IACUC members for all aspects of animal care and use. Committee members offer a valued resource for assisting UMC animal-based researchers in accurately completing the Animal Activity Protocol form and in addressing regulatory issues.

## **Protocol Review**

All activities requiring the use of laboratory animals (grant or contract applications, training, student laboratories) must be reviewed by the IACUC to ensure regulatory compliance. The animal activity protocol form may be downloaded from the Office of Research web site [<http://dor.unc.edu>] by clicking on institutional compliance, then clicking on IACUC. Each component of ALL questions must be addressed/answered. Responses should be included with the appropriate question, avoid the use of attachments. The *Guide for the Care and Use of Laboratory Animals* outlines numerous issues and topics that should be considered in the preparation and review of animal care and use protocols. These include:

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

This Section of the UMC Laboratory Animal Facilities Training and Procedural Manual contains a blank Animal Activity Protocol form, as well as a form with explanatory responses to the questions. Investigators are encouraged to consult these documents and solicit the aid of IACUC members for accurate completion of the protocol form. Once completed the Animal Activity Protocol original and 11 copies should be submitted to the IACUC office (U-020).

### **Maintaining Animal Activity Protocol Forms**

All Principal Investigators will be sent a copy of their IACUC-approved Animal Activity Protocol form. The approved protocol will include an IACUC protocol number and signatures of the IACUC Chairperson and the Attending Veterinarian. Investigators should maintain these documents in their laboratories and **ensure that all personnel involved in the animal activity are familiar with this document and its contents.**

### **Significant Changes and Protocol Amendments**

Investigators often must adjust/amend/change various components of their Animal Activity Protocol. **Any** modifications (minor or major) must receive IACUC approval prior to initiation. Major changes require full IACUC review and approval prior to conducting any new or modified procedures. This type of change or amendment usually can be accomplished by sending a memo (electronically) describing the changes to the IACUC Chairman and IACUC Assistant Director. A list of both major and minor amendments can be found on the IACUC website (SOP: Minor vs. Major Amendments to Animal Activity Protocols). The proposed change/amendment subsequently will be reviewed by the IACUC. The Office for Laboratory Animal Welfare (OLAW) has defined major changes as:

- changes in the objectives of the study.
- proposals which switch from nonsurvival to survival surgery.
- changes in the degree of invasiveness of a procedure or discomfort to an animal.
- changes in species or in the approximate number of animals used.
- changes in personnel involved in the animal procedures.
- changes in anesthetic agents, the use or withholding of analgesics, and methods of euthanasia.
- changes in the duration, frequency, or number of procedures performed on an animal.

### Animal Activity Protocol Annual Continuing Review

IACUC approval of an Animal Activity Protocol is for one year. Each year, the Principal Investigator will receive electronically, an Annual Renewal Form, 30 days prior to the protocol's anniversary date to inquire (1) whether the protocol is to be renewed for an additional year (2) if there are any modifications from the original submission and (3) if there were any adverse events. If the protocol is to be renewed, an IACUC subcommittee will review the information and present a summary report at the monthly meeting prior to granting a one year continuation of the work. Occasionally, investigators will be requested to supply the IACUC with additional information (i.e., the current status of the work, progress in the protocol, refinement of procedures).

### Animal Activity Protocol Resubmission

An Animal Activity Protocol may be approved only for three consecutive years. At the end of this time period a complete, full protocol must be re-submitted. Investigators will be contacted 90 days prior to the anniversary date and expected to re-submit the entire Animal Activity Protocol and **include updated relevant information on the new submission** (project progress since last submission, changes in objectives, justification of animal numbers, etc.). Appendix K must be included.

An Animal Activity Protocol may be assigned to an IACUC subcommittee for more extensive document revisions. Protocols not addressed by the investigator within 90 days of subcommittee contact will be withdrawn from IACUC consideration.

### Physical Restraint Considerations

Physical restraint is the use of manual or mechanical means to limit some or all of an animal's normal movement for the purpose of examination, collection of samples, drug administration, therapy, or experimental manipulation. Mechanical restraint devices should be suitable in size, design, and operation to minimize discomfort or injury to the animal.

Animals to be placed in restraint devices should be considered for training to adapt to the equipment and personnel. Prolonged (limiting animals normal movement for periods greater than that required for single injection administration or collections) restraint, including chairing of nonhuman primates, should be avoided unless it is essential for achieving research objectives or veterinary health maintenance and the restraint activity is approved by the IACUC. Ideally, the least restrictive system of restraint should be utilized. When restraint devices are used,

they should be specifically designed to accomplish goals that are impossible or impractical to accomplish by other means or to prevent injury to animals or personnel. The following are important guidelines for restraint:

- Restraint devices are not to be considered for normal methods of housing.
- Restraint devices should not be used simply as a convenience in handling or managing animals.
- The period of restraint should be the minimum required to accomplish the objectives.
- Animals to be placed in restraint devices should be considered for training to adapt to the equipment and personnel.
- Provision should be made for observation of the animal at appropriate intervals, as determined by the IACUC.
- Veterinary care should be provided if lesions or illness associated with restraint are observed. The presence of lesions, illness, or severe behavioral change often necessitates temporary or permanent removal of the animal from restraint.

Appendix G of the UMMC Animal Activity Protocol form specifically addresses this issue. Investigators requiring animal restraint are required to describe the **type** and duration of **restraint**, as well as the **justification** of the process. The UMMC IACUC requires special provisions for any proposal requesting restraint in excess of 12 continuous hours. Please consult the IACUC Policy Statement: Prolonged Physical Restraint for any additional information.

### **Food or Fluid Restriction**

When experimental situations require food or fluid restriction, at least minimal quantities of food and fluid should be available to provide for development of young animals and to maintain long-term well being of all animals. Restriction for research purposes **must be scientifically justified**, and a program should be established to monitor physiologic or behavioral indexes, including criteria (weight loss or hydration status) for temporary or permanent removal of an animal from the experimental protocol. Watering must be consistent with section 3.83 of the AWA. Special attention should be given to ensuring that animals consume a suitably balanced diet because food consumption may decrease with fluid restriction. The least restriction that will achieve the scientific objective should be used. In cases of conditioned-response research protocols, the use of highly preferred food or fluid as a positive reinforcement (instead of restriction) is recommended.

Question 12 (nonstandard food and water) and Appendix I of the UMMC Animal Activity Protocol form specifically address this issue. Investigators are required to provide a complete **explanation** and **justification** for any proposal requesting food and water restriction. Also, investigators should describe the methods for assuring that the animals are in good health, detailing the frequency of animal checks and responsible personnel. Please consult the IACUC Policy Statement: Food and/or Fluid Restrictions for any additional information.

## **Multiple Major Surgical Procedures**

Major surgery penetrates or exposes a body cavity or has the potential to produce substantial impairment of physical or physiologic function. Multiple major survival surgical procedures on a single animal are discouraged but may be permitted if scientifically justified by the user and approved by the IACUC. Special circumstances may dictate that the USDA grant approval. Justification for multiple major survival surgical procedures may include closely related components of a research project, conservation of scarce animal resources, or for clinical reasons. Cost savings alone is not an adequate justification for the conduct of multiple major survival surgical procedures.

Appendix H of the UMMC Animal Activity Protocol form specifically addresses this issue. Investigators are required to provide a complete **explanation** and **justification** for any proposal requesting multiple major survival surgical procedures. Please consult the IACUC Policy Statement: Multiple Major Surgical Procedures for any additional information.

## **Personnel Qualifications and Training**

The *Animal Welfare Act* and the Public Health Service Policy require institutions to ensure that people caring for or using animals are qualified to do so. Institutions should provide formal or on-the-job training to facilitate effective implementation of the program and humane care and use of animals. Training programs are designed to inform personnel on issues dealing with animal husbandry, veterinary medicine, occupational health and safety, regulatory affairs, Laboratory Animal Facilities support services, and IACUC policies. Investigators, technical personnel, trainees, and visiting investigators who perform animal anesthesia, surgery, or other experimental manipulations must be qualified through training or experience to accomplish these tasks in a humane and scientifically acceptable manner.

Training programs at UMC consist of formal presentations, web-based programs ([www.citiprogram.org](http://www.citiprogram.org)), informal one-on-one training sessions, informative newsletters, and nationally recognized training programs (AALAS). Formal presentations are sponsored by the IACUC. Typically, these sessions, offered quarterly for new employees, present information pertinent to UMMC, including veterinary issues, reporting activities, and regulatory affairs. Training sessions are announced in UMMC-sponsored electronic publications (Research Waves) and through IACUC-issued monthly email updates. Additionally, all UMMC personnel working with animals are required to complete the "Training Requirements Verification" form (available on the IACUC website).

Specific requirements of the UMC Training Program include: Principal Investigators must verify that they are established investigators by providing a *curriculum vitae*. They must complete the training requirements registration form and successfully pass the two required web-based training modules. All personnel working with animals must attend at least one formal training session. All personnel

working with animals must attend the LAF facilities tour. All persons working with animals must complete and submit the Occupational Health and Safety documents as well. Training verification forms are available and kept on file in the Office of Research . No persons, with the exception of students in a regularly scheduled class or non-UMMC scientists authorized by the IACUC, may use live animals at UMMC unless their training is completed and verified. In addition, Principal Investigators and their personnel are encouraged to supplement their training with the use of material available in the Learning Resources Center and the LAF office.

### Investigative Assurances

The UMMC Animal Activity Protocol form includes a section on Investigative Assurances specifically addressing regulatory issues dealing with unnecessary duplication and alternative procedures. A principle statement reads “ review of the available resources and previous experiments, have determined that the proposed activity is not unnecessarily duplicative of previously reported activities.” This question requires that investigators conduct searches (using 2 different search engines) to document that his/her research does not unnecessarily duplicate previous experiments.

Additional search information is required for consideration of alternatives to procedures that may cause more than momentary or slight pain or distress to the animals. This question requires investigators to note the **source** of the search (Index Medicus, AWIC, Medlar, Toxline) and list the **key words** used in the search and the **date** of the search. Further, section 2.31 of the AWA notes that a **written narrative** description be included of the methods and sources used to determine that alternatives were not available. Animal Activity Protocols rarely are considered pain or distress free, thus necessitating a review. A search template form, and PowerPoint presentation can be downloaded from the IACUC website. In addition, reference librarians are available for assistance with conducting the search.

### Institutional Assurances

All institutions conducting animal-related activities supported by the U.S. Public Health Service (PHS) must maintain an Animal Welfare Assurance with the OLAW. The Assurance is a legally binding institutional commitment to the PHS that all animals at the research facility meet the care and use requirements of the NIH. The statement is on file in the Office of the Vice Chancellor, the Office of Research, and the Laboratory Animal Facilities. This document is necessary for eligibility to receive PHS support. OLAW recommends that the core content of the Assurance statement be made widely available for information and education. The seven sections of the Assurance are:

- 1. Applicability**

The Assurance is applicable to all research, research training, and biological testing activities, involving live, vertebrate animals supported with PHS funds.
- 2. Institutional Policy**

The Assurance signifies that the institution will comply with the USDA *Animal Welfare Act* and all other statutes and regulations relating to animals. The institution is guided by U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training. The institution maintains programs in accordance with the *Guide* and ensures that all personnel (working with animals) understand their responsibilities for compliance.
- 3. Institutional Program for Animal Care and Use**

The Assurance describes the lines of authority and responsibilities for compliance with the PHS Policy. Names and qualifications of the IACUC members are provided as well as the charge of the IACUC. Also, this section describes the physical structure of the animal facilities, the occupational health program, and the institution's training program.
- 4. Institutional Status**

This section provides a mechanism for the IACUC to report its internal findings (inspection report) to the Institutional Official.
- 5. Record Keeping Requirements**

The Assurance specifies various documents to be maintained by the institution. Included in this are the institution's Assurance Statement, IACUC meeting minutes, Animal Activity Protocols, inspection reports, and records from accrediting bodies.
- 6. Reporting Requirements**

This section specifies that the Institutional Official must report to the OLAW annually. This report will include any changes in the institution, dates of facility inspections, reports of these inspections, and information about Animal Activity Protocol review.
- 7. Endorsements**

The name and signature of the Institutional Official (Dr. John E. Hall) and the name and signature of the PHS official is included in this section.

### **Animal Facility Tour Policy**

The policy on visitation to the Laboratory Animal Facilities is based on ensuring animal health, minimizing the risk of zoonoses, and an increased awareness of animal models. All LAF environments are registered with the Institutional Biohazards Committee as ABSL-2. Impromptu visits and tours of the University Medical Center Laboratory Animal Facilities by non-authorized UMMC employees and individuals not employed by UMMC are not allowed. If such visits are necessary, the Director of the LAF in consultation with the Director of Student and Employee Health must be notified in advance. A 24-hour notice is requested. This policy will help investigators schedule the most ideal time to conduct a tour/visit. As part of new investigator training, tours of the LAF by the Facility Manager and/or LAF Supervisor are now required. They are conducted twice weekly and can be arranged by calling 4-1385.

### **Laboratory Animal Facilities Security**

Animal housing areas are secured through the use of card key locks on entrance doors into the animal facilities. The Laboratory Animal Facilities office is responsible for badge activation. Components of the occupational health plan enrollment and training verification must be completed prior to admission. Additionally, many animal rooms have a unique door locking mechanism. Investigators must sign-out keys to these locks, thus assuming responsibility for their use. The LAF office coordinates the issuance of all animal housing area keys.

Investigators and their laboratory staff must maintain the security to animal housing space. UMMC personnel working in this area should not prop doors open or allow unauthorized persons to enter the facility. Please note and report all non-authorized people in the animal housing area to the LAF office. UMMC-issued identification badges should be worn when working in this area. Security breaches are considered major institutional violations and may result in the loss of privileges to work in this area.

### **Reporting Animal Care & Treatment Deficiencies**

The *Animal Welfare Act* provides a mechanism for personnel to report deficiencies in the care and treatment of animals at the institution by an 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 any regulations or standards under the Act. UMMC personnel should contact Dr. Susan Warren (IACUC Chair), Dr. Andrew W. Grady (Director, LAF), or any member of the UMMC IACUC or the HOTLINE for Reporting Non-compliance (see the IACUC website). Reports will remain confidential and will receive full investigation. As well, personnel reporting suspected deficiencies will be informed of the investigation,

the findings of such investigation, and any corrective measures. For more information, consult the IACUC Policy Statement: Management of Suspected Protocol Noncompliance.

## **Semi-Annual Program & Facility Review**

A major function of the IACUC is to evaluate all aspects of the institution's program for animal care and use. There are three principal components of the IACUC's review process: 1) **Protocol Review**, 2) **Facility Inspection**, 3) **Program Review**.

### **Protocol Review**

Review of Animal Activity Protocol documents is discussed in Section I. The IACUC reviews the protocol form for completeness, appropriate animal husbandry, relevant veterinary care, occupational safety, etc. The IACUC meets monthly to review Animal Activity Protocols. Furthermore, an algorithm for submission of the completed form to the IACUC is provided.

### **Facility Inspection**

Semi-annually, the IACUC inspects UMMC facilities that house and support animal husbandry and animal use laboratories. Individual investigator laboratories that support animal research are also inspected on a semi-annual basis. Facility inspections typically are composed of an IACUC subcommittee that physically tours and inspects animal care and laboratory use rooms in the medical center. The general time frame (June & December) for the inspections is announced to the Principal Investigators and their laboratory personnel, as well as the LAF care staff. An inspection checklist, which serves as the basis of the inspection and promotes consistency of inspections, is also sent to the PI. During these inspections, the site visitors evaluate:

- husbandry practices: Are the animals in good health? Are the cages, racks, work surfaces, and room clean? Are surfaces sanitizable? Is there documentation of these husbandry activities? Is there evidence of vermin?
- storage of supplies: Only necessary, ancillary items should be stored in the animal room. Storage should be neat and orderly. No storage of supplies should occur on/adjacent to animal housing/caging.
- occupational safety: Is there evidence of an active occupational safety program? Are safety precautions taken? Proper signage posted?
- observation of expiration dates: Check all drugs and supplies for expiration dates. Only maintain items that have not expired.
- surgical facilities: is the area appropriate for aseptic surgical procedures?

- Equipment function: are hoods certified? Autoclaves verified? Gas anesthesia units serviced?

### **Program Review**

The IACUC's review of programs is comprised of ongoing evaluation of operating procedures for the care and use of laboratory animals. Typically, program review formally occurs in conjunction with the semi-annual facility inspection. Programmatic review involves an examination of actual practices and an evaluation of how well they work. The IACUC program review may include verification of written protocols with actual animal work, examination of various regulatory documents for accuracy, review of surgical/post-surgical care procedures, validation of sanitation procedures, etc. Deficiencies in the review of programs will be discussed and recommendations toward correcting shortfalls will be enacted. Program review is considered to be of critical importance for AAALAC accreditation.

## **Algorithm for Animal Activity Protocol Submission to the UMC Institutional Animal Care and Use Committee**

Download form from Office of Research web-site  
<http://dor.umc.edu>  
ext. 5-5006  
Office of Research U-020

Principal Investigator writes proposal in spaces provided on form. Answers all questions. Complete ONLY the necessary APPENDICES. Avoid the use of attachments. The IACUC recommends that PI's consult with the LAF veterinary staff and members of the IACUC. Additional information concerning writing a protocol is available on the IACUC website.

PI submits the Animal Activity Protocol form electronically by the first or first working day of the month in order to be included for that month's consideration. Protocol is assigned a primary and secondary reviewer. All committee members have access to review and make comments. A pre-meeting interaction (personal, email, etc) between the reviewer(s) and PI may occur. Item #14 (lay summary) and #16 (experimental design) and the narrative/assurance section of the proposal will be forwarded to the reference librarians for assistance with the literature search.

IACUC meeting conducted on the third Tuesday of the month.

IACUC Chair will correspond with the Principal Investigator concerning the disposition of the protocol. Any modifications to the document as a result of meeting discussions will involve additional interaction between the review team and PI in order to produce an acceptable document. Once the document is approved, a single, signed copy needs to be returned to the IACUC office.



# Laboratory Animal Facilities Business Affairs

## **Mission**

The Laboratory Animal Facilities (LAF) operates as a research-support entity for the University of Mississippi Medical Center. Efforts by the LAF are 100% service-based to UMMC research programs. Support functions include daily animal husbandry requirements, animal quarantine and conditioning programs, animal surgical and anesthetic support, and laboratory animal veterinary care programs.

## **Administration**

Services and operation of the Laboratory Animal Facilities are under the direction of Andrew W. Grady, D.V.M., M.S. The departmental office is located in the Arthur C. Guyton Laboratory Research Building, **G-201**. The central office telephone number is **(601) 984-1385** and the FAX number is **(601) 984-1742**. The LAF is subdivided into three primary components: Business Operations, Animal Care/Husbandry, and Veterinary Services.

### **1. Business Operations**

Operational management of the LAF is the responsibility of Mrs. Tammy Seaton. Mrs. Seaton manages LAF accounts payable, accounts receivable, primary liaison between the LAF and purchasing/receiving, and management of LAF personnel records. Inquiries related to these topics should be directed to Mrs. Seaton.

### **2. Animal Care/Husbandry**

The Facility Manager for the LAF is Mr. Eddie Clardy. Mr. Clardy is certified by the American Association for Laboratory Animal Science (AALAS) as a Laboratory Animal Technologist and a graduate of the Institute of Laboratory Animal Management. Mr. Clardy is responsible for assisting investigators with caging and husbandry needs, management of the animal husbandry, care, and sanitation program, and management of the LAF animal care personnel. Issues related to these matters should be directed to Mr. Clardy.

### **3. Veterinary Services**

Veterinary services are the principle responsibility of Dr. Linda K. Fulton. Dr. Fulton is a trained laboratory animal veterinarian and directs all aspects of the veterinary care program at UMC. Primary duties include management of veterinary support staff, oversight of animal health services, management of surgical/anesthesia support, clinical management, and record keeping. All veterinary medical matters should be referred to Dr. Fulton or the veterinarian on-call (pager # 601-881-7693).

## **Facilities**

The central LAF operates and maintains approximately 29,000 ft<sup>2</sup> of animal housing and support space. The Arthur C. Guyton Laboratory Research Complex serves as the principle operation basis for the LAF. The business and director's office are located in this facility, as well as many animal housing areas, quarantine and conditioning facilities, surgical support space, and animal husbandry support functions. The eighth floor of the Research Wing is another major component of the LAF. This space contains numerous conventional animal housing rooms, surgical support space, and husbandry support functions. Finally, the James D. Hardy Clinical Sciences Building (sub-basement) provides a transgenics core area of animal housing and husbandry support functions.

## **Emergency Veterinary Care**

A member of the LAF veterinary staff is on-call and available at all times. The UMC pager for emergency veterinary services is reached by dialing **601-881-7693** from any touchtone telephone. After dialing the number, at the prompt, enter your call-back number and hang up. The veterinary staff member will return your call ASAP.

## **Maintaining LAF Security**

Security aspects of the LAF are of great importance to the institution. Only UMMC personnel with animal-based research needs are granted access into the animal housing areas. UMMC-issued identification badges should be worn when working in these areas. Access to each animal housing area is controlled via an electronic card reader. Personnel completing IACUC-mandated training and applicable occupational health questionnaires and risk assessments are granted access. Additionally, many animal rooms have unique door locks. Investigators must sign-out keys to these locks, thus assuming responsibility for their use. The LAF office coordinates the issuance of all animal housing area keys.

Badge/card access is unique to each individual and ID badges must not be shared or exchanged. Security breaches are considered major institutional violations and may result in the loss of privileges to work in the LAF.

## **Services**

The Laboratory Animal Facilities provides services in support of a wide range of UMC faculty (PhD, MD, DDS) and their extensive research protocols. Numerous protocols have the requirement for LAF services, thus scheduling conflicts may occur. All Principal Investigators are asked to contact the LAF office (**4-1385**) to

schedule/ reserve the use of LAF facilities and/or technical assistance. Advanced notice will allow the LAF to better serve the UMMC research program.

Principal Investigators are asked to notify the LAF office for all cancellations/postponements. This consideration will aid our mission of supporting other research activities. Note that cost for reservation of LAF space (e.g., surgery suite, procedural area, necropsy) may be charged to the investigator for all cancellations less than 24 hours!

### **Animal Care & Husbandry**

The LAF staffs trained personnel to conduct all aspects of the animal care and husbandry program. Principle oversight of this area is the charge of the Facility Manager. Both the Facility Manager and the Assistant Supervisor (Ms. Sharon Rand) are certified by AALAS as Laboratory Animal Technologist (LATg)

This arm of the LAF organization is responsible for implementing the requirements of the *Animal Welfare Act* and adhering to the provisions of the *Guide for the Care and Use of Laboratory Animals*. Primary functions include managing of animal husbandry concerns (feeding, watering, cage sanitation), ensuring environmental controls are maintained, providing general room care, assisting with the animal conditioning program, and implementing the enrichment program. A Fee Schedule (<http://lab-animal-facility.umc.edu/businessaffairs/feeschedule.html>) is provided for all animal care and husbandry services. Please forward all animal care and husbandry comments, questions and concerns to Mr. Eddie Clardy at **4-1385** or Mrs. Rand at **4-1387**.

### **Veterinary Health Program**

Veterinary services are the responsibility of the LAF. The *Guide for the Care and Use of Laboratory Animals* places the ultimate responsibility for veterinary services on the Attending Veterinarian. Numerous aspects of the veterinary care program may be conducted by persons other than the veterinarian, but a mechanism for direct and frequent communication must be established to ensure that timely and accurate information is conveyed to the veterinarian involving problems associated with animal health, behavior, and well-being. Methods of disease prevention, diagnosis, and therapy should be those currently accepted in veterinary practice. The choice of medication or therapy should be made by the veterinarian in consultation with the investigator.

The LAF implements veterinary medical services/programs dealing with preventive medicine; surveillance, diagnosis, treatment, and control of disease, including zoonosis control; management of protocol-associated disease, disability, or other sequelae; anesthesia and analgesia, surgery and postsurgical care; assessment of animal well-being; and euthanasia. The LAF veterinary staff provides guidance to investigators and laboratory personnel involved in the care and use of animals to ensure appropriate handling, immobilization, sedation, analgesia, anesthesia, and euthanasia. The Attending Veterinarian is responsible for guidance and oversight of

all surgical programs and post- surgical care. Veterinary services should be scheduled through the LAF office (**4-1385**) or by pager **601-881-7693**.

### **Diagnostic Labwork**

The LAF veterinary staff collaborates with several commercial diagnostic laboratories to assist with clinical pathology specimens (serum chemistry, hematology, microbial cultures and sensitivities, histopathology, etc.). Also, the LAF conducts numerous diagnostic tests in-house. Diagnostic services are billed to the Principal Investigator responsible for the animals (cost + 12%). Some diagnostic services are covered expenses (quarterly tuberculin screens of primates, fecal/skin parasitology screens, veterinary exams) and are not reflected in invoices. Veterinary diagnostic services are often necessary to aid the LAF veterinary staff in formulating the optimal treatment regime for animal health related concerns. The LAF veterinary staff will suggest diagnostic services where appropriate. Also, personnel may wish to implement diagnostic services as baseline screening data. Information derived from diagnostic lab services is included in the LAF programs for health monitoring (Section II, page 5). Contact the LAF veterinary staff (**4-1385**) for all diagnostic labwork services.

### **Necropsy**

Necropsy services are a valued research component. The collection of tissues and biological fluids is often a necessary part of an animal study. Also, a diagnostic necropsy may provide postmortem answers to antemortem animal health concerns. The LAF veterinary staff will conduct or assist with necropsy services for research protocols. Laboratory charges (histopathology, hematology, serology, microbiology) will be assessed to the investigator. The LAF recommends that all non-rodent or rabbit species be necropsied at euthanasia, as part of the program of disease surveillance and prevention. Investigators may schedule veterinary necropsy services through the LAF office at **4-1385**.

### **Euthanasia Services**

The LAF will conduct laboratory animal euthanasia services for Principal Investigators. Techniques employed must be approved by the IACUC and documented on the Animal Activity Protocol form. All LAF-conducted euthanasia services are consistent with the 2007 Report of the AVMA Panel on Euthanasia (see Euthanasia section) ([http://www.avma.org/issues/animal\\_welfare/euthanasia.pdf](http://www.avma.org/issues/animal_welfare/euthanasia.pdf) ) Investigators desiring LAF-conducted euthanasia services should contact the LAF office (**4-1385**) to schedule these activities. A service charge will be assessed to the investigator covering supplies, any chemical agents, technical time, and carcass disposal.

## **Health Monitoring Program**

Disease prevention is an essential component of comprehensive veterinary medical care. Effective preventive medicine programs enhance the research value of animals by maintaining healthy animals and minimizing nonprotocol sources of variation associated with disease and inapparent infections. Several areas of the LAF health monitoring program are discussed:

### **1. Vendor Health Surveillance Programs**

Animal suppliers (commercial sources, collaborators at other institutions, etc.) readily provide UMMC with animal health history information. Larger animal sources (Harlan Sprague Dawley, Charles River Laboratory, Myrtle's Rabbitry) generate health monitoring screens of colony animals. Dogs, cats, and nonhuman primates are received with health histories (vaccination status, treatments, serologic information, etc.) upon arrival. All animal health information is reviewed by the LAF veterinary staff to safeguard UMMC colony animals. Investigators wishing to receive animals from non-commercial sources (collaborators at other institutions) must consult with the LAF veterinary staff prior to receipt of animals. A recent health history of these animals will be required. In most cases, these animals will need to be assigned isolated animal housing space to protect other UMMC colony animals. Additional diagnostic testing may be required on these animals.

### **2. UMMC Animal Health Surveillance Programs**

Unexpected deaths and signs of illness, distress, or other deviations from normal in animals should be reported promptly to the LAF veterinary staff, ensuring appropriate and timely delivery of veterinary medical care. The UMMC animal health surveillance program is designed to address colony health vs. individual animal health concerns. Components of this program include quarterly tuberculin skin testing, physical examinations, and body weights of nonhuman primates; evaluation of all veterinary medical problems; periodic serum sampling from colony rodents; placement of viral antibody free (VAF) "sentinel" rodents in colony rooms. Necropsy information gathered as part of the euthanasia is also a valuable component of the health monitoring program. Results of these surveillance programs will be discussed with Principal Investigators to develop appropriate strategies for correcting any animal health concerns.

A special note regarding subclinical rodent infections: Subclinical microbial infections, particularly viral etiologies, occur frequently in conventionally housed rodents. Many of these infectious agents may

produce subclinical conditions yet induce profound immunologic changes or alter physiologic, pharmacologic, or toxicologic responses. Examples include Sendai virus, Kilham rat virus, mouse hepatitis virus, lymphocytic choriomeningitis virus, and *Mycoplasma pulmonis*. The scientific objectives of a study, animal strain susceptibility to the infectious agent, and risk of infection to other UMMC colony animals must be evaluated by the veterinary staff and Principal Investigator to determine courses of action to address positive serologic assessments.

### 3. **Quarantine/Conditioning Programs**

Procedures used for quarantine, acclimation, and conditioning are specialized aspects of the LAF health monitoring program. Quarantine is the separation of newly received animals from existing colony animals until the health status of the newly received animals has been determined. Procedures utilized in these LAF programs are reflective of individual animal health status vs. colony health. During this period, animals may be given frequent tuberculin skin tests, serologic/hematologic assessments, physical examinations (nonhuman primates); vaccinations, physical examinations, anthelmintic therapy, serologic/hematologic assessments, permanent identification (dogs, cats); permanent identification (rabbits). These processes allow the LAF veterinary staff to maximize the health status of the research animals and safeguard the investigator's investment. Of equal importance is the acclimation and stabilization period. Regardless of the animal species, newly received animals should be given a time period for physiologic, psychologic, and nutritional stabilization prior to their use in a research protocol (See section IV, 3 for recommendations).

### **Antibody Production**

Animal Activity Protocols may require the production of monoclonal and polyclonal antibodies. The LAF veterinary staff is available to assist with protocols for antibody production in rodents and rabbits. Consultation or technical assistance for production and harvest of antibodies should be scheduled through the LAF office at **4-1385**.

### **Technical Assistance**

LAF personnel are available to assist Principal Investigators and their laboratory staff with numerous technical activities. Activities may include special sanitation procedures, minor dosing/administration procedures, weighing animals, and assistance with room and

equipment set-up. All LAF technical assistance will be charged to the Principal Investigator. It is imperative that any utilization of LAF technical assistance be scheduled through the LAF office to receive Facility Manager and veterinary approvals. LAF technical assistance will be provided only when all federally regulated animal husbandry and care activities have been satisfied.

### **Animal Transportation**

Services related to animal transportation may include the physical pick-up and delivery of farm animals in UMMC vehicles, services surrounding the arrival of commercial vendor's animals, and transportation of animals by the LAF to areas other than their primary housing space.

Farm animal (pigs) transportation services are invoiced based upon mileage traveled. Rabbits, guinea pigs, pigeons and rodents are assessed a per shipping carton charge (delivery charge). This charge (per box) covers expenses associated with animal ordering and receiving, technical time associated with cage/room set-up, technical time for removal from the shipping containers, and disposal of shipping containers. Also, a delivery charge is assessed for LAF transportation of animals (typically dogs, cats, pigs) to an investigator's laboratory. This charge covers expenses associated with technical time commitments and sanitation of the transportation equipment. LAF activities associated with new animal delivery and receipt are coordinated by the Operations Manager and Facilities Manager. LAF animal transportation services to investigator's laboratories must be scheduled in advance with the office (4-1385).

### **Transferring Animals Between Protocols/Investigators**

Commonly, research animals (especially rodents) may be originally purchased off of one specific protocol then transferred to another protocol or investigator. Any such transfer should include the LAF to assure appropriate animal accounting information. Animals should only be used for procedures and activities outlined in the given protocol for which they were ordered unless appropriate transfer documents have been completed.

Transfers between investigators are completed with a signed copy of the "Transfer Form". This form identifies the animal (s) and protocol number (s) as well as requiring the signatures of both the transferring and receiving investigator. Transfer forms are available in the LAF office (G201) and an example form as appendix C of this section. The LAF office can assist in coordinating transfers. Billing information/invoices can only be altered after the signed form is completed.

### **Animal Anesthesia Support Services**

The LAF operates and maintains several surgical suites as well as ancillary anesthetic equipment (anesthetic machines, pulse oximeters, cardiac monitors,

ventilators, circulating hot water heating pads). Use of these items in support of research protocols is managed by the LAF veterinary staff. Investigators will be assessed a nominal charge to cover any expenses associated with the use of the equipment. All use of LAF surgical/anesthetic support equipment must be coordinated through LAF veterinary services.

Technical support also is provided on a fee basis (per hour) for anesthetic services. The LAF veterinary staff is qualified to provide numerous forms of animal anesthesia (inhalation and injectable). Principal Investigators requiring technical support for anesthesia services must schedule these activities through the LAF veterinary staff (**4-1385**). This scheduling period is the ideal time to discuss the anesthetic regime and identify supplies and equipment necessary to support the procedure.

### **Anesthesia, Surgery & Postsurgical Support**

Careful preparation of all animal surgeries and anesthesia will ensure uneventful and successful outcomes. The many surgical programs and their unique needs (anesthesia, instruments, equipment, drugs) dictate that these programs and the LAF veterinary staff must coordinate their efforts to minimize potential problems. Some specific areas that must be considered:

- 1. Schedule proposed procedure with the LAF office**  
What is/are the dates of the surgery? Start time? Is anesthesia assistance needed? Is surgical assistance needed? Species and animal weight? Animal identification numbers? Desired surgical location? Ancillary equipment required?
- 2. Pre-surgical fasting of animal**  
Most nonrodent animals should receive a minimum of eight hours of food fasting, co-ordinate this issue with the LAF office [see NPO (fasting) procedures, Section IV,11].
- 3. Surgical Procedures**  
Are the procedures described in the Animal Activity Protocol? Are the necessary anesthetic agents and drugs on hand? Are there provisions for monitoring and documenting anesthesia? Are the surgical instruments sterile?
- 4. Postsurgical Animal Care**  
Post operative monitoring is the investigator's responsibility. LAF veterinary staff may be called upon to assist. Arrangements must be made to have continuous monitoring of the patient until extubated (swallowing reflex present). Thereafter, frequent monitoring and documentation must be made to assess recovery. Document the use of post-procedural analgesics, antibiotics, and nursing care.

Additional details on these issues and issues related to animal euthanasia, necropsy procedures, and animal carcass disposal may be found in the LAF office. Contact the LAF office at **4-1385** for additional information.

## **LAF Procedural or Surgical Room Reservation**

The use of LAF procedural areas and surgical suites must be scheduled and controlled through the LAF office. Research protocols may have the need for these types of facilities at random intervals. The LAF will provide a sanitized area for the conduct of these animal activities on a fee basis. Investigators should reserve these areas as early as possible through the LAF office (**4-1385**). It is essential to request any technical assistance or ancillary equipment, such as suction canisters, ECG, pulse oximetry, vascular catheters, fluids, surgical supplies, at the time of scheduling. As well, Principal Investigators are asked to notify the LAF office for all cancellations/ postponements. This consideration will allow the LAF to support other UMMC research activities. Cancellations of less than 24 hours will result in room charges assessed to the investigator!

## **LAF Billing Policy**

Monthly charges are issued from the LAF office on an itemized statement. These invoices are sent to the Principal Investigator by the 10<sup>th</sup> of each month for charges incurred in the previous month. Charges are based upon daily receipts for supplies purchased, daily inventory of animals, animal purchases, special room reservations, and LAF service fees. A Fee Schedule (<http://lab-animal-facility.umc.edu/businessaffairs/feeschedule.html>) is provided in Section II, Appendix B.

All invoices should be signed, coded, and returned directly to the LAF office (**G-201**) by the 15<sup>th</sup> of the month following the month in which the invoice is received. If the invoice is outstanding on the 15<sup>th</sup>, a late notice will be sent allowing ten (10) days for payment to be made. Failure to pay for LAF services may result in termination of services and notification of the department chair and the UMMC Vice Chancellor for Research.

# Occupational Health & Safety Program for UMC Personnel with Laboratory Animal Contact

## Purpose

The 1996 *Guide for the Care and Use of Laboratory Animals* requires that an occupational health and safety program be a part of the institution's animal care and use program. The focus of the program should be on maintaining a safe and healthy workplace. Oversight of the occupational health program is provided by Dr. Rebecca R. Waterer, Director, Student-Employee Health. The Department of Environmental Health and Safety (EHS) is responsible for assuring safe work practices at the institution (<http://ehs.umc.edu>). Together, the IACUC and the LAF work with Student-Employee Health and EHS to promote occupational health and safety. The operational and day-to-day responsibility for safety in the workplace resides with the laboratory or facility supervisor.

## Student & Employee Health Office

The UMMC Student & Employee Health Office is located in N-128. The office telephone number is **4-1185**.

## Environmental Health and Safety Department

The Department of Environmental Health and Safety can be contacted at **4-1980**. Additional information is available at <http://ehs.umc.edu>.

## Enrollment

Enrollment and inclusion in the occupational health plan (OHP) is initiated at each person's in-processing and orientation. Baseline health information is obtained by the Student-Employee Health office, vaccination status is reviewed, and ID tuberculin testing is provided. Employees requiring LAF access (those listed on IACUC-approved protocols, LAF employees, service/maintenance personnel) must complete IACUC "Training Requirements Registration" (<http://iacuc.umc.edu/Forms/TrainingForm51507.doc>) [see Section V, Security Concerns, "LAF Access"]. A component of this training requirement is completion of two occupational health and safety forms, Health Screening Questionnaire and Risk Assessment Survey.

Employees requiring access must complete the two forms and electronically submit the documents. With electronic submission, the Health Screening Questionnaire is securely routed to Student-Employee Health while the Risk Assessment Survey is routed to the IACUC and LAF. The Health Screening Questionnaire and transmission will remain confidential and comply with all HIPAA requirements.

## **Personal Hygiene**

### **1. Protective Clothing**

UMMC personnel working with animals should wear appropriate protective clothing when working with laboratory animals. Protective clothing may include scrub suits, laboratory coats, back supports, safety glasses, face masks, face shields, ear plugs, ear muffs, exam gloves, shoe covers, hair bonnets, rubber gloves, and aprons. The animal activity should dictate the type of personal protective clothing to be worn. Personnel should not wear garments worn in animal rooms outside of the institution. The institution provides laundering services for animal related needs.

### **2. Shower Facilities**

The LAF has a separate shower facility for men and women employees in the Laboratory Research Building, G-041 and G-042 and in the 8<sup>th</sup> floor research wing facility R-821.

### **3. Policy Regarding Eating, Drinking, and Smoking in the LAF**

University policy strictly forbids eating, drinking, smoking, or applying cosmetics in animal rooms or procedural areas. The application of cosmetics, eating, and drinking presents a potential zoonotic hazard for personnel. Also, these items adversely contribute to our vermin control program. These activities should only occur in LAF-designated areas (G-020 & R-821). The Medical Center campus is a tobacco-free designated area.

## **Occupational Health Program for New UMC Employees**

All personnel with laboratory animal contact or exposure to LAF environments must be enrolled in the UMC Student & Employee Health office occupational health and safety program. New personnel should discuss their involvement with animals with Principal Investigators in order to make informed decisions concerning vaccinations, zoonoses, and health prophylaxis. All new employees are required to complete a medical history form and undergo a physical examination prior to assuming their assigned duties of handling/working with animals. This is a routine component of UMC personnel in-processing and all new personnel are automatically forwarded to the Student & Employee Health office via the Human Resources office. All UMC employees are required to have a Tuberculin skin test at this time. Personnel with exposure to laboratory animals will be provided (1) Health Screening Questionnaire and (2) Risk Assessment Survey. The Health Screening Questionnaire will be reviewed by the employee health physician. The Risk Assessment Survey will be reviewed by the IACUC/LAF. An individual's "risk" is obtained from a combination of their personal health history and potential hazards that exist in the workplace. As well, an immunization history will be obtained, if additional vaccines are needed (tetanus booster, rabies) they will be offered at this time. Also, the Hepatitis B vaccine will be offered to the new employee during this in-processing.

Completion of this occupational health information is critical towards assuring an employee's health and safety. Only those persons completing this information and having an appropriate medical risk assessment will be granted electronic card key access into the LAF areas.

### **Occupational Health Program for Existing UMC Employees**

All employees with laboratory animal contact will be requested to undergo annual Tuberculin skin testing. Annually, personnel will be asked to update their Health Screening Questionnaire at the time of TB skin testing. As above, these forms will be reviewed by the employee health physician for their risk assessment. An individual's "risk" is obtained from a combination of their personal health history and potential hazards that exist in the workplace. Personnel who's job requirements have changed (working with different species, working with differing hazards, etc) are urged to notify the UMC Student and Employee Health office during this annual review.

Completion of this occupational health information is critical towards assuring an employee's health and safety. Only those persons completing this information and having an appropriate medical risk assessment will be granted electronic card key access into the LAF areas.

### **Laboratory Animal Related Injury Protocol**

Injuries sustained from laboratory animal bites, scratches, animal contact, or associated caging/equipment (other than nonhuman primates) should receive prompt medical attention. Zoonotic threats are possible with all laboratory animals, thus appropriate action should follow any injury. All injuries should be recorded on the standard Employee Injury Report (<http://secure.umc.edu/meds/servlet/InjuryForm>). The injured employee should report to the Student & Employee Health office (N-128) for evaluation during normal working hours (M-F, 7:30 am - 4:00 pm) or to the UMC Emergency Room after hours and on weekends and holidays. Injuries that are of a serious or potentially life-threatening nature (significant trauma, head injuries, etc.) should be sent to the UMC Emergency Room immediately for evaluation and treatment. Also, medical emergencies within the Medical Center may call **4-1111**.

### **Biosafety Requirements for Work with Nonhuman Primates**

The Centers for Disease Control has designated all activities involving the use or manipulation of tissues, body fluids, and primary tissue culture from macaques as a minimum of biosafety level 2 (BL-2). While the various research protocols may entail differing technical manipulations of macaque tissues, body fluids, and/or primary tissue culture, **all Principal Investigators working with nonhuman primates must register**

**with the Institutional Biohazards Committee.** Contact Dr. Susan Wellman at 4-1631 or Ms. Kim Eaves at 4-5010 for further information.

### **Nonhuman Primate Related Injury Protocol**

Nonhuman primates present a significant zoonotic potential to personnel involved in their husbandry, care, and experimental manipulation. First Aid Kits, or “Primate Exposure Kits” are found in all non-human primate use areas. Injuries sustained from nonhuman primates (bites, scratches, fluid exposures, or cuts/scratches from primate caging and equipment) are emergencies and should proceed immediately with the following process:

1. Immediately following a bite/scratch/exposure, soak or scrub the wound/exposure site with water and iodine soap (betadine) for a minimum of 15 minutes. Exposures to the eyes or other mucous membranes should irrigate the exposed area with the 1 liter bag of 0.9% Sodium Chloride Injection and the primary I.V. set (tubing).
2. CALL FOR HELP! Notify co-workers or other personnel in order to receive assistance quickly.
3. The employee should report ASAP (after step #1) to the Student & Employee Health office (N-128) for evaluation during normal working hours (M-F, 7:30 am - 4:00 pm) or to the UMC Emergency Room after hours and on weekends and holidays. A UMMC Employee Injury Report will be initiated. Complete the information on the injury report and include identifying information of the contact nonhuman primate.
4. Upon arrival at the Student & Employee Health office or the UMC Emergency Room, the employee will be evaluated according to the “Recommendations for Prevention of and Therapy for Exposure to B Virus (*Cercopithecine herpesvirus 1*)” (*Clin Inf Dis* 2002; **35**: 1191-1203) and “Guidelines for the Prevention and Treatment of B Virus Infections in Exposed Persons” (*Clin Inf Dis* 1995; **20**: 421-439).
5. The Laboratory Animal Facilities veterinary staff will be notified of the exposure. Appropriate laboratory data will be obtained from the contact nonhuman primate.
6. All follow-up will be arranged by the Student & Employee Health office.

Exposures to aerosolized fluids (sneeze, cough, urine spray) from nonhuman primates are of equal importance as any other hazardous exposure. Evidence supports viral transmission from primates to man via these agents with exposures to the mucous membranes of the eye. Personnel exposed to these fluids should exercise caution and flush the eye and proceed with the above safety procedures.

### **Animal Activities During Pregnancy**

It is recommended that all pregnant employees with exposure to any laboratory animals exercise universal precautions in the workplace. Personnel that are planning a pregnancy or are pregnant should update their personal medical history, namely the Health Screening Questionnaire. Pregnant employees should refrain from cleaning cat bedding and cages for the duration of the pregnancy to minimize the risk of becoming infected with *Toxoplasma gondii*. Also, precautions should be exercised when working with volatile anesthetics and numerous chemical agents. Consult the UMMC Student & Employee Health office for related questions.

### **Animal Experimentation Involving Hazardous Materials**

Special safeguards should be instituted for animal experimentation involving hazardous agents, including radioisotopes and biohazards. The Department of Environmental Health and Safety (<http://ehs.umc.edu>) offers resources to appropriately manage potentially hazardous studies. The Radiation Safety Committee (RSC) provides oversight for all studies utilizing radioisotopes. The RSC is responsible for providing guidelines for the use of radioisotopes, training of individuals, and the procurement, distribution, and disposal of the materials. The UMC Radiation Safety Office provides oversight and may be contacted about all radioisotope issues (4-1078). The Institutional Biohazards Committee (IBC) provides oversight for all studies utilizing recombinant DNA, microbiological agents, and activities utilizing nonhuman primates. The IBC will register all projects using these agents and ensure regulatory compliance.

### **Animal Transportation in the University Hospital**

Occasionally, laboratory animals are involved in research studies requiring their transport to an area within the University Hospital (imaging areas, Interventional MRI). Appropriate safeguards must be in place to ensure the protection of both human patients that may follow the research animal, as well as approaches to protect the health of the experimental animal. Written approvals may be required with these protocols (signed by an appropriate administrator from the hospital area).

## **Zoonoses**

Zoonotic concerns are diseases of animals that may be transmitted to humans. Although zoonotic diseases are not common in modern facilities, their prevention and detection must be an important concern of all personnel who work with laboratory animals. Human susceptibility to infectious diseases carried by animals may occur even when the animals show few/no signs of illness. Microorganisms in the normal flora of a healthy animal may cause serious illness in persons lacking protective immunity. Personnel should be aware of these possibilities and take precautions to minimize the risk of infection. Additional information may be obtained from the Student & Employee Health office, the LAF veterinary staff, or selected references (Occupational Health and Safety in the care and use of Research Animals. National Research Council, National Academy Press, 1997).

## **Allergies to Laboratory Animals**

A special precaution is necessary regarding allergies. Allergies to laboratory animals are the most common occupational problem among workers in a research animal environment. Typical signs include allergic rhinitis, conjunctivitis, asthma, and atopic dermatitis. The most common exposure is to rodents. Many allergic problems are attributed to dander and debris from the skin/fur of the animal. Equally important allergens are associated with urine proteins from these animals. Personnel should minimize exposures through the judicious use of safety equipment/ clothing: long-sleeve laboratory coats, gloves, face masks, and eye protection. Health Screening Questionnaires contain extensive information about allergic conditions and should prompt personnel to discuss this health condition with the Student/Employee Health office.

## **Physical/Chemical Injuries in the LAF**

Numerous occupational hazards are present in the animal facilities, including physical and chemical injuries. Physical injuries may result from thermal burns (cagewashing facility, autoclaves), falls resulting from wet/moist surfaces, and from the lifting/movement of caging and equipment. Chemical injuries may result from the diverse types of detergents, acids, and disinfectants used in support of the animal husbandry program. UMMC personnel are advised that these occupational hazards are present and should take precautions to safeguard themselves and fellow workers.

## **Occupational Health Training Options**

Potential problems related to the use of laboratory animals have been categorized according to the exposure “risk”. Several Power Point presentations have been developed dealing specifically with these Risk Groups. Groups have been assigned based upon the

Following format:

Risk Group I	No direct animal contact (Physical Facilities, Environmental Services, Campus Police, Receiving, etc.)
Rick Group II	Work with rodents, amphibians, fish
Rick Group III	Work with larger animal species
Rick Group IV	Work with nonhuman primates

Specific training presentations related to the various risk categories are available for viewing (<http://iacuc.umc.edu>)

# LAF Policies & Procedures

## **General**

The implementation of reliable, consistent animal care and husbandry depends upon dedicated personnel and standardized practices. The Laboratory Animal Facilities has established numerous Standard Operating Procedures in an effort to deliver consistent animal care programs. This section of the *Training and Procedural Manual* is devoted toward assisting UMC personnel with frequently asked questions. Many of the topics discussed contain abbreviated text from IACUC-approved procedures.

## **Veterinary Health Program**

Veterinary services are the responsibility of the LAF. The *Guide for the Care and Use of Laboratory Animals* places the ultimate responsibility on the Attending Veterinarian (Director, LAF). Numerous aspects of the veterinary care program may be conducted by persons other than the veterinarian, but a mechanism for direct and frequent communication must be established to ensure that timely and accurate information is conveyed to the veterinarian involving problems associated with animal health, behavior, and well-being. Methods of disease prevention, diagnosis, and therapy should be those currently accepted in veterinary practice, thus the choice of medication or therapy should be made by the veterinarian in consultation with the investigator. Any veterinary care procedures instituted by the investigator's laboratory must be communicated to the LAF veterinary staff for inclusion in the clinical records.

The LAF implements veterinary medical services/programs dealing with preventive medicine; surveillance, diagnosis, treatment, and control of disease, including zoonosis control; management of protocol-associated disease, disability, or other sequelae; anesthesia and analgesia, surgery and postsurgical care; assessment of animal well-being; and euthanasia. The LAF veterinary staff provides guidance to investigators and laboratory personnel involved in the care and use of animals to ensure appropriate handling, immobilization, sedation, analgesia, anesthesia, and euthanasia. The Attending Veterinarian is responsible for guidance and oversight of all surgical programs and post-surgical care. Veterinary services should be scheduled through the LAF office (4-1385) or by pager # 601-881-7693.

## **Emergency Veterinary Care**

A member of the LAF veterinary staff is on-call and available at all times. The UMC pager for emergency veterinary services is reached by dialing 601-881-7693 from any touchtone telephone. After dialing the number, at the prompt, enter your call-back number and hang up. The veterinary staff member will return your call ASAP.

## **Animal Ordering/Procurement**

Investigators may order only animals that are covered on their IACUC-approved protocol(s). All animal transfers must be coordinated through the LAF such that IACUC managed animal accounting is accurate and appropriate LAF billing is achieved. (url link & See Section II Transferring Animals). All animal orders are administered by/through the LAF office. The investigator is responsible for securing the necessary purchase order or master order number from the Purchasing Department for placement of the order. The LAF utilizes commercial vendors and licensed USDA dealers for all animal purchases. Animal/colony health history information is required for all incoming animals prior to arrival.

Documentation of all animal orders must be made on the LAF-issued Animal Order Form ([http://lab-animal-facility.umc.edu/forms/ANIMAL\\_ORDER\\_FORM.doc](http://lab-animal-facility.umc.edu/forms/ANIMAL_ORDER_FORM.doc)). Forms may be obtained through the LAF office (**G-201, 4-1385**). Investigators must complete the entire form and detail specific information for the order (age, sex, strain, weight, etc.). Signed order forms may be sent via FAX @ **4-1742**. All animal orders must be received by the LAF office **prior to 4:00 pm Tuesday** for delivery the following week. The commercial vendors often place certain constraints on fulfilling an order. Equally important, the LAF may need to assign special housing for incoming animals. Investigators should anticipate and confirm the arrival dates of all animal orders. All animal purchases must conform to the policies of the UMC Purchasing Policies and Procedures Manual (pg 45) detailing specific procedures for master orders and standard orders. UMC Purchasing Policies and Procedures (see Sections V, VI, VII, & VIII of Policies & Procedures,) (Purchasing Policies & Procedures can be found on the UMC Intranet under Departments – Purchasing). No animal purchase can be placed on an SPPO (Small Procurement Purchase Order).

Commonly, unique rodent models (transgenics, knock-outs) may be acquired from colleagues at other institutions. Procurement for these animals must also utilize a LAF-issued Animal Order Form ([http://lab-animal-facility.umc.edu/forms/ANIMAL\\_ORDER\\_FORM.doc](http://lab-animal-facility.umc.edu/forms/ANIMAL_ORDER_FORM.doc)), regardless if the animals are purchased or donated. This form will prompt the LAF veterinary staff to solicit animal health surveillance information on these animals prior to their arrival at UMC. Receipt of this health history is critical for all incoming rodents and is required to ensure appropriate animal housing.

All orders for fish, amphibians, and reptiles must also use the LAF-issued Animal Order Form. The form will prompt the LAF to assure appropriate housing is provided and assure that accurate census information is maintained.

Dogs are purchased through Class A or Class B USDA dealers. The LAF encourages investigators to use Class A dogs for chronic research studies. dogs must complete a 21-day quarantine/conditioning program, during which time they will receive vaccinations, anthelmintics, diagnostic tests, and veterinary evaluations. Dogs will only be released for use upon the completion of the conditioning period. Even after this period of conditioning, the health of Class B dogs cannot be guaranteed.

UMC research scientists often support the LAF in the negotiation and purchase process of nonhuman primates. The LAF can supply investigators with nonhuman primate sources. Investigators are free to make preliminary arrangements (negotiate price, specifics about the animals [sex, age], and discuss target receipt date) then file an animal order form. The veterinary staff must review individual clinical records of all nonhuman primates prior to any agreements on their acquisition. The LAF office assumes sole responsibility for the progression of the

animal order beyond this point. Details surrounding the USDA Shipping Papers, health certificates, necessary clinical records, methods of transportation, and arrival date must be initiated and implemented by the LAF office. **It is the responsibility of the investigator and the IACUC to ensure that the primates have not or will not be involved in more than one major operative procedure.**

### **Animal Receipt**

All vendors/animal suppliers deal directly with the LAF for the receipt of UMC animals. Animals are received at the east end of the Laboratory Research Building (LAF loading dock). The LAF office issues a weekly receipt schedule of all incoming animals. Unless otherwise specified, the LAF is responsible for the safe, efficient off-loading of animals. Animals will be carefully examined for any inconsistencies in the order, placed into appropriate housing, and properly identified. **The investigator is also responsible for order verification and should notify the LAF office within 24 hours of any discrepancies in an animal order.** The LAF office will coordinate credit/reshipment with the vendor. If the LAF office is not notified of discrepancies or other problems within 24 hours of receipt of animals, it is unlikely that the vendor will consider credit/reshipment. The LAF veterinary staff will initiate quarantine/conditioning procedures on many incoming species, including rodents with suspicious health histories. For other animals, especially rodents, birds, and swine, an acclimation/ stabilization period is recommended prior to the initiation of the research program. Survival surgical procedures are discouraged in any animal prior to the end of the conditioning period (see below). Investigators are responsible for knowing the animal receipt date and anticipate/confirm the animal's arrival at UMC.

### **Animal Quarantine & Conditioning Program**

It is recognized that all laboratory animals experience some stress from transportation, new environments, new feed, etc. To allow the animals an opportunity to stabilize metabolically and acclimate to their surroundings, the LAF recommends various species-specific conditioning periods.

Rodents	2 days
Guinea pigs	2 days
Fish/amphibians	5-7 days
Ferrets	7 days
Rabbits	7 days
Pigeons	7 days
Pigs	7 days
Cats	21 days
Dogs	21 days
Primates	6 weeks

For many UMC laboratory animals, this time period allows the LAF veterinary staff to provide species-specific care procedures, including vaccinations, disease diagnostics, physical examinations, regulatory identification, and veterinary medical treatments. These efforts are

necessary to help ensure a healthy animal for the research study.

### **General Animal Care Procedures**

All UMC laboratory animals must be cared for in a manner consistent with the mandates of the *Animal Welfare Act* and the recommendations of the *Guide for the Care and Use of Laboratory Animals*. Through implementation of these husbandry practices, UMC programs are accredited with the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC). Animals housed in the central animal facilities are cared for by the LAF staff. Generalized/basic species-specific care practices are provided.

### **Rabbit Colony Care**

Rabbits are housed in plastic/stainless steel caging providing waste collection, fresh water, and feed hoppers. Cage preparation and daily care activities are the responsibility of the LAF. Care activities include the proper size caging, preparation of litter pans, checking automatic water lines, placing feeders on cages, and completing animal care identity cards. Animals are checked at least daily by the LAF staff. Daily checks involve feeding, checks of the water system, observation for any animal health problems, and room care (sweep, mop, dust). Twice weekly, the litter pans are removed and exchanged for sanitized pans, and the soiled pans are sanitized. Bi-weekly, the stainless steel rack and cages are exchanged for freshly sanitized caging. Cages and equipment that become excessively soiled between scheduled changes are exchanged for sanitized items prior to the scheduled change. Other care activities include maintenance of feed drums, sanitizing feed hoppers, maintenance of the air filtration system, and checks of the temperature/humidity/lighting. Each rabbit room has a posted room check list of animal and room care activities. The check list details procedures and husbandry issues to be addressed. Rabbits are provided with protocol compatible environmental enrichment. Such types of environmental enrichment may include food items as treats or species specific manipulada.

### **Canine Colony Care**

Canines are housed in 32 ft<sup>2</sup> pens/runs equipped with an automatic watering system. Cage preparation and daily care activities are the responsibility of the LAF. Each morning, dogs are fed in their home cage. Dogs are relocated to clean runs (typically across the aisle) or allowed to exercise in the corridor. Then, the soiled runs are cleaned with high pressure water. Bi-weekly, runs are sanitized with a commercial pressure sprayer (water + detergent). Dogs are not wetted during either the cleaning or sanitizing process. Feed hoppers are exchanged for sanitized feeders weekly. The LAF care staff and vet staff ensure the proper identification of all dogs (verification of AVID microchips with care card) During daily cleaning the animal care staff will note and apprise the LAF veterinary staff of all animal health problems (anorexia, diarrhea, lameness, skin abrasion, etc.).

### **Canine Post-Operative Care**

Canines are typically housed in stainless steel caging in temperature controlled recovery units during the immediate post-operative phase. Husbandry of these animals is the joint responsibility of the LAF care staff, veterinary staff and investigative team. Post-operative monitoring and the provision of analgesia are the responsibility of the investigator and veterinary staff. Freshly sanitized caging will be provided for each recovery dog. The LAF veterinary care staff will coordinate with the investigative staff to ensure the appropriate provision of food and water. Unless specified, these animals will be provided fresh water and food by the LAF veterinary care staff. Every effort is made to ensure proper animal husbandry and a comfortable environment. Cages are sanitized upon the removal of a dog from the recovery cage. Investigators are encouraged to return dogs to the runs or to the experimental housing area as soon as the animals stabilize post-surgery. The LAF veterinary staff will assist investigators with this decision. Each canine post-operative room has a posted room check list of animal and room care activities. The check list details procedures and husbandry issues to be addressed.

### **Cat Colony Care**

Cats are housed in stainless steel caging providing elevated resting (perch) surface, litter box, fresh water, and feed bowls..

Minimally, each cat is allotted a minimum amount of floor space based upon the weight of the animal [AWA subpart A (b)1.ii. and the Guide, page 28]. Cats weighing less than 8.8 lbs. (4 kg) are provided 3.0 ft<sup>2</sup> floor space. Cage preparation and daily care activities are the responsibility of the LAF. Care activities include the proper size caging, preparation of litter pans and boxes, placing feeders and water bowls on cages, and completing animal care identity cards. Animals are checked at least daily by the LAF care staff. Daily checks involve feeding and watering, observation for any animal health problems, and room care (sweep, mop, dust). At least three times per week, litter boxes are changed. Bi-weekly, the stainless steel rack and cages are exchanged for freshly sanitized caging. Cages and equipment that become excessively soiled between scheduled changes are exchanged for sanitized items prior to the scheduled change. Other care activities include maintenance of feed drums, sanitizing feed hoppers and water bowls, maintenance of the air filtration system, checks of the temperature/humidity/lighting, and provision of species and protocol appropriate environmental enrichment. Each cat colony room has a posted room check list of animal and room care activities. The check list details procedures and husbandry issues to be addressed.

### **Rat, Mouse, Gerbil, & Hamster Colony Care**

Care procedures and activities for the various rodent colonies are very similar. Separation of species will be observed in all cases. Care practices pertain to rodents housed in polycarbonate or polypropylene shoebox cages. Cage preparation and daily care activities are the responsibility of the LAF. Care activities include maintaining the proper caging and bedding, placing the appropriate lid on the cage, selection feeders (if applicable), procuring the appropriate watering system (water bottles/sipper tubes or automatic lixits), and completing animal care identity cards. Paper towels and nestlets may be placed in each cage for provision of environmental enrichment. Animals are

checked at least daily by the LAF care staff. Daily checks involve feeding and watering, observation for any animal health problems, and room care (sweep, mop, dust). Twice weekly, cages are removed and exchanged for sanitized cages. Cage lids are changed and sanitized every two weeks. Water bottles, sipper tubes, and feed hoppers are changed weekly. Shelf racks are sanitized monthly. Cages and equipment that become excessively soiled between scheduled changes are exchanged for sanitized items prior to the scheduled change. Other care activities include maintenance of feed drums, maintenance of the air filtration system, and checks of the temperature/humidity/lighting. Each rodent colony room has a posted room check list of animal and room care activities. The check list details procedures and husbandry issues to be addressed.

### **Pig Colony Care**

Pigs may be housed in stainless steel cages or chain-linked runs equipped with automatic watering fixtures. Cage preparation and daily care activities are the responsibility of the LAF. Daily, the soiled cages/pens/mats are then cleaned with high pressure water. Bi-weekly, cages/pens/mats are sanitized with a commercial pressure sprayer (water + detergent) or transported to the mechanical cagewash unit. Pigs are not wetted during either the cleaning or sanitizing process. Feed hoppers are exchanged for sanitized feeders weekly. The LAF care staff ensures the proper identification of all pigs and reports all animal health problems (anorexia, diarrhea, lameness, skin abrasion, etc.) to the LAF veterinary staff. Each pig colony room has a posted room check list of animal and room care activities. The check list details procedures and husbandry issues to be addressed.

### **Pigeon Colony Care**

Pigeons are housed in stainless steel cages equipped with feed hoppers and water bowls. Cage preparation and daily care activities are the responsibility of the LAF. Care activities include the preparation of litter pans, placing feeders and water bowls on cages, and completing animal care identity cards. Animals are checked at least daily by the LAF care staff. Daily checks involve feeding and watering, observation for any animal health problems, and room care (sweep, mop, dust). Twice weekly, the litter pans are removed and exchanged for sanitized pans, and the soiled pans are sanitized. Bi-weekly, the stainless steel rack and cages are exchanged for freshly sanitized caging. Cages and equipment that become excessively soiled between scheduled changes are exchanged for sanitized items prior to the scheduled change. Other care activities include maintenance of feed drums, sanitizing feed hoppers and water bowls, maintenance of the air filtration system, and checks of the temperature/humidity/lighting. Each pigeon colony room has a posted room check list of animal and room care activities. The check list details procedures and husbandry issues to be addressed.

### **Frog Colony Care**

Frog colonies at UMC may include both *Xenopus* and *Rana* species. Housing and environmental parameters may be quite different for these species (*Xenopus* habitat of calm water, cool ambient temperature; *Rana* habitat of running water, normal room temperatures).

Meeting the habitat needs of these animals requires much consideration and must be coordinated with existing investigators and the LAF. Details concerning the husbandry and care of these species may be obtained by contacting the LAF veterinary staff or the Facility Manager.

### **Nonhuman Primate Colony Care**

Nonhuman primates are housed in appropriately sized stainless steel, aluminum, or plastic caging, equipped with an automatic watering system or bottle bracket. Cage sizes conform to the AWA Subpart D 3.80b. (2)I. And the Guide, page 28. Group 3 monkeys (3-10kg) are provided minimally 4.3 ft<sup>2</sup> floor space and Group 4 monkeys (10-15 kg) are provided 6.0 ft.<sup>2</sup> Cage preparation and daily care activities are the responsibility of the LAF. The soiled cages are cleaned daily with high pressure water. Primates are not wetted during the cleaning process. Litter pans in plastic behavioral chambers are removed three times weekly and exchanged for sanitized pans, and the soiled pans are sanitized. Feed hoppers are exchanged for sanitized feeders weekly. Caging systems are sanitized bi-weekly. The LAF care staff ensures the proper identification of all nonhuman primates (verification of tattoo with care card) and notes all animal health problems (anorexia, diarrhea, lameness, skin abrasion, etc.) with the LAF veterinary staff. Cages and equipment that become excessively soiled between scheduled changes are exchanged for sanitized items prior to the scheduled change. Other care activities include maintenance of feed drums, sanitizing ancillary equipment and cage accessories, maintenance of the air filtration system, checks of the temperature/ humidity/ lighting, and provision of species and protocol appropriate environmental enrichment. . Each primate colony room has a posted room check list of animal and room care activities. The check list details procedures and husbandry issues to be addressed.

### **Nonhuman Primate Environmental Enhancement**

Current animal husbandry knowledge emphasizes the basic needs of nonhuman primates to receive varying forms of environmental enhancement. This “enrichment” program is likewise dictated by the Animal Welfare Act (9 CFR, 3.81). Forms of enhancement include both the structural environment and the social environment. The structural environment may include “resting boards, shelves/perches, toys, foraging devices, nesting materials, tunnels, swings, or other objects that increase opportunities for expression of species-typical postures and activities” (Guide). Social enhancement “usually involves physical contact and communication among members of the same species” (Guide). The LAF provides numerous forms of environmental enhancement and is continually evaluating new forms. Appendix C of the IACUC’s Animal Activity Protocol form specifically addresses environmental enrichment and is required for all proposals involving nonhuman primates.

### **Environmental Enhancement for Other Species**

While there is no legal mandate for environmental enhancement for other species, numerous studies have demonstrated the positive, beneficial effect on laboratory animals. Relatively simplistic forms include providing nesting materials for mice, climbing structures for rats, and play objects/chew toys for rabbits, pigs, cats, and dogs. The LAF stocks a wide variety

of these items and provides these forms of environmental enrichment unless specifically excluded in the study protocol.

**Cage Size Requirements**

<u>Animal</u>	<u>Weight</u>	<u>Floor area/animal</u>	<u>Height</u>	<u>#/UMC cage</u>
Mice	<10 (grams)	6 (inches <sup>2</sup> )	5 inches	23 (lg) 10 (sm)
	10-15	8	5	18 7
	16-25	12	5	13 5
	>25	15	5	9 4

Rats	<100 (grams)	17 (inches <sup>2</sup> )	7 inches	8
	100-200	23	7	6
	201-300	29	7	5
	301-400	40	7	3
	401-500	60	7	2
	>500	70	7	2

<u>Animal</u>	<u>Weight</u>	<u>Floor area/animal</u>	<u>Height</u>	<u>#/UMC cage</u>
Hamsters	<60 (grams)	10 (inches <sup>2</sup> )	6 inches	14
	60-80	13	6	11
	81-100	16	6	9
	>100	19	6	7
Guinea pigs	≤350 (grams)	60 (inches <sup>2</sup> )	7	4
	>350	101	7	2

<u>Animal</u>	<u>Weight</u>	<u>Floor area/animal</u>	<u>Height</u>
Rabbits	<2 (kg)	1.5 (feet <sup>2</sup> )	14 inches
	2-4	3.0	14
	4.1-5.4	4.0	14
	>5.4	5.0	14

Cats	≤4 (kg)	3.0 (feet <sup>2</sup> )	24 inches
	>4	4.0	24

Dogs all dogs provided floor space based on the USDA formula:  
 AMathematical square of the sum of the length of the dog in inches, plus 6 inches.≡

$$X = (\text{length} + 6")^2 / 144 \qquad X = \text{feet}^2$$

Pigs	<15 (kg)	8.0 (feet <sup>2</sup> )
	15-25	12.0
	26-50	15.0

Pigeons 0.8 (feet<sup>2</sup>)

Nonhuman <1.0 (kg) 1.6 (feet<sup>2</sup>) 20 inches

Primates	1.0-3.0	3.0	30
	3.0-10.0	4.3	30
	10.0-15.0	6.0	32

### **Special/Unique Animal Housing Requirements**

Scientific protocols may contain provisions for specialized animal housing or unique, nonstandard caging. Examples include metabolic caging/racks, unique feeding or watering devices, and cage activity accessories. These special considerations often present problems for the facility management due to lack of proper planning and limited equipment inventory. Several investigators may have requirements for these types of cage arrangements simultaneously, thus we must carefully plan the caging availability. It is imperative for investigators to notify the Facility Manager or LAF office of any nonstandard caging and housing needs before the project begins. This advanced notice will allow the LAF to efficiently manage caging resources. The LAF Animal Order Form contains a section entitled, **Specific Instructions** where any special provisions should be indicated.

### **Customized Animal Husbandry Procedures**

Animal husbandry practices and procedures often are tailored to accommodate the scientific needs of a study. Examples include feeding at a specified time, feeding a unique diet, provision of specified quantities of water, and altering cage care management due to treatments (increased urination due to study, development of diarrhea due to study). The LAF often is asked to participate in these specialized animal activities. Investigators are reminded that any special husbandry procedures must be documented in the Animal Activity Protocol form and approved by the IACUC. Any involvement of the LAF to assist with these studies (feeding special diet, water restriction, cage cleaning at specific time) must be routed through the LAF office. Investigators and their personnel should not make special arrangements with individuals. Requests that are directed through the LAF office can be disseminated to all members of the animal care and veterinary staff and lead to consistent animal care practices.

### **Animal Identification**

Proper animal identification is necessary to ensure consistent animal husbandry, accurate veterinary care, and valid scientific results. The LAF staff is responsible for ensuring the legible identification of all laboratory animals at UMC. Forms of identification may include cage cards (rodents, rabbits, guinea pigs, fish, amphibians), leg bands (birds), ear tags (rodents, pigs), collars (cats, dogs), tattoos (rodents, dogs, cats, rabbits, primates, pigs), and microchips (dogs, cats, primates, rabbits). **All USDA-issued identification tags are property of the USDA and must be returned to the LAF for holding.** All animals, regardless of the primary form of identification, will have a care card. These cards must contain the following information: source, strain/stock, names/locations/phone of responsible investigators, pertinent dates, protocol number, and animal identification, when applicable. Occasionally, investigative personnel segregate animals into study groups and require new cage cards. Animal care cards must be created for all new caging and must contain all information noted above. Alternately, blank care

cards are found in all LAF areas. Care cards not only provide information to investigative personnel, they serve a valued regulatory function for the LAF and IACUC. These cards become the principle mechanism to maintain accurate animal inventories and provide data for animal use reports. Care cards also play an important role in per diem charges.

### **Vermin Control Program**

A universal problem in animal housing areas involves the control and/or elimination of vermin (insects and feral rodents). Conventional insecticides are contraindicated, as they may have a significant health impact on laboratory animals, especially rodents. The primary defense against vermin infestation is a sound, efficient sanitation program. Housekeeping issues in LAF areas and in laboratories will greatly aid efforts to control vermin. The LAF also employs the use of a non-toxic boric acid insect bait in animal housing areas. This bait is safe to use in animal rooms. Feral rodents may become a tremendous problem to research programs, infecting laboratory animals with numerous pathogens. Occasionally, laboratory rodents may escape and likewise spread pathogens. These free-roaming rodents are controlled through the use of commercial traps that safely contain the rodent. Traps are checked daily and captured animals are humanely euthanized. In these instances, the animals should be sacrificed due to the unknown microbial contamination. LAF policy is to sacrifice all captured rodents found outside of the primary housing area.

### **Weekend & Holiday Animal Care**

Animal care and husbandry activities occur 365 days per year. Members of the LAF animal care staff rotate on a schedule for weekend/holiday animal care duties. Weekend animal care activities are inclusive of all routine animal care responsibilities, excluding cagewashing services. The aspects of care described for the various species (feeding, watering, cage and room husbandry) will be provided on weekends and holidays.

### **Maintenance Requests in the LAF**

Maintenance items in the LAF must receive prompt attention. Facility management makes frequent checks/observations of the physical plant to note problem areas (peeling paint, non-sealed surfaces, leaks, lighting problems, etc.). The LAF maintains a Maintenance Log that identifies the problem, notes when and to whom the problem was reported, and any progress toward correcting the maintenance request. Principal Investigators and their laboratory personnel should contact the LAF office (4-1385) regarding all LAF physical plant maintenance items.

### **Animal Housing Room Appearance**

The *Animal Welfare Act* and the *Guide* highlight the importance of maintaining animal rooms in an organized, clean manner. Animal housing areas that double as procedural space must be regarded primarily as a housing room. These areas must receive the same sanitation measures afforded to conventional rooms (daily room care procedures, ancillary equipment/supplies sanitation, documentation of these activities).

Storage of supplies and equipment in animal rooms is discouraged and must be limited to those items necessary for the animal's primary care. Consult the LAF and the IACUC to verify the maintenance of these materials in animal rooms. A spartan appearance is ideal. Cage racks, equipment carts, etc. should be on casters to allow easy movement and sanitation procedures to proceed unobstructed.

### **Animal Room Thermostats & Humidistats**

Regulation of the animals environment is an important variable that must be controlled rigidly. The temperature and humidity of an individual animal room must be regulated to conform to the recommendations of the *Guide*. Thermostats and humidistats located in animal housing rooms or support space are set by the LAF to maintain compliance. Personnel must not attempt to adjust thermostats/humidistats. Adjusting these controls can have a tremendous impact on surrounding rooms. Rooms/areas that need adjustments (too hot, too cold, too humid) should be brought to the attention of the LAF office. The Facility Manager then will take corrective actions with the assistance of the UMC Physical Plant.

### **Maintaining Clinical Veterinary Records**

Clinical veterinary care records are critical regulatory documents that the institution must maintain. Records must be accurate and current. This documentation should reflect all clinical situations (any health concerns, surgical records, post-procedural care, anesthetic records). Numerous aspects of the veterinary care program may be conducted by persons other than the veterinarian(s), but a mechanism for direct and frequent communication must be established to ensure that timely and accurate information is conveyed to the veterinarian involving problems associated with animal health, behavior, and well-being. For all situations involving animal health, investigators should contact the LAF veterinary staff (**4-1385**, pager **601-881-7693**). The veterinary staff can provide veterinary support, detailed follow-up, and maintain the accuracy of the clinical record.

### **NPO (fasting) Procedures**

Experimental manipulations and presurgical requirements often dictate that animals be fasted for a controlled amount of time. Principal Investigators are responsible for the implementation of NPO instructions. It is recommended that all such procedures be routed through the LAF office (**4-1385**). The LAF utilizes pink NPO cards to highlight and alert care staff not to feed the animal(s). In presurgical preparations, the veterinary staff recommends that

animals be given free access to water (maximize hydration) and fasted from their ration.

Completion of the NPO cards is important in order to reduce potential complications. Cards may be found on pegboards within the hallways of the LAF housing areas. All blanks should be completed! In most cases 12 hours of fasting is sufficient and NPO procedures may not exceed 24 hours. Personnel completing the card should note the animal's identification number, the time/date the fasting period begins, the time/date the fasting period ends, and the name and telephone extension of the responsible person. The LAF **will** feed all animals with inaccurate NPO information. Likewise, all animals will be fed 24 hours beyond the initiation of the NPO orders. Instances may arise where animals have been fed prior to manipulations or surgery. In these cases, the investigator should consult the LAF veterinary staff concerning the use of the animal.

<b>NPO</b>	
Investigator Name _____	
Species _____	Tattoo # _____
In _____	Out _____
Time/Date	Time/Date
Signature _____	Ext # _____

### **Laboratory Animal Surgical Programs**

All laboratory animal surgical manipulations must be approved by the IACUC. The principle tenets of the UMC laboratory animal surgical program are derived from Brown et al, *Guidelines for animal surgery in research and teaching*. Am J Vet Res. 1993; 54(9), 1544-1559. Surgical programs may be classified as survival or nonsurvival. All survival procedures must be conducted under aseptic conditions. Nonsurvival procedures are those in which the animal is euthanatized before recovery from surgery and may be conducted under less stringent conditions if approved by the IACUC.

Rodent survival surgical procedures must be conducted in a surgical facility or a dedicated space in the laboratory. This rodent surgical space must be managed appropriately to minimize contamination from other room activities during the surgical procedure.

Nonrodent aseptic surgery should be conducted only in IACUC-approved surgical facilities. Careful presurgical planning should include all members of the surgical and post-surgical care team. The plan should identify personnel, their roles, and the equipment and supplies required for the procedures planned. Additionally, this plan should specify the requirements of postsurgical monitoring, care, and record-keeping, including the personnel who will conduct these duties.

All surgical procedures should receive careful monitoring and documentation. Monitoring includes frequent checks of anesthetic depth, cardiopulmonary function, and

assessment of clinical signs and conditions. The LAF utilizes an anesthetic monitoring form (Section IV, Appendix B) for all surgical cases. As noted in Section II, **Animal Anesthesia Support Services**, the LAF can provide technical support for anesthesia services. Also, note in Section II, **LAF Procedural/Surgical Room Reservation** that facilities for the conduct of these procedures must be scheduled through the LAF.

### **Postsurgical Animal Care**

The Principal Investigator and veterinary staff share responsibility for ensuring that postsurgical care is appropriate. The LAF veterinary staff is responsible for the guidance and oversight of postsurgical animal care. The Principal Investigator is responsible for implementing the postsurgical care, including monitoring and provision of analgesia. An important component of postsurgical care is the observation of the animal and intervention as required during recovery from anesthesia and surgery. Animal housing during recovery should be consistent with good nursing care; clean, warm environment with ease of observation and intervention. Particular attention should be given to thermo-regulation, cardiovascular and respiratory function, and post-operative pain or discomfort during the recovery period. Other considerations include fluid therapy, use of analgesics, wound care, and maintenance of post surgical records (Section IV, Appendix C). It is particularly important to document all post-procedural care (*Guide for the Care and Use of Laboratory Animals*). Checks of physiologic status (heart rate, respiratory rate, capillary refill time, pulse quality, body temperature, hydration, urine production) are important indicators of the animal's condition. As well, all medications (antibiotics, analgesics, fluid therapy) should be documented and maintained with the animal. Surgical and postsurgical records should be returned to the LAF office immediately following the postsurgical care period.

Principal Investigators may contract with the LAF veterinary staff for the provision of post-operative care. In these cases, the LAF veterinary staff will provide the monitoring and any necessary treatments for the animals. These services must be scheduled in advance to avoid charges for emergency veterinary care.

### **Animal Transportation**

Careful consideration should be given to any animal movement/relocation at UMC. All animals must be properly restrained/housed prior to transportation in the university. The routes of transport vary depending upon the origin and destination. **ALL ANIMAL TRANSPORTATION CARRIERS/TRANSFER CAGES MUST BE COMPLETELY COVERED (towel, drape, blanket) WHEN BEING TRANSPORTED THROUGH THE CORRIDORS, ELEVATORS, OR ANY PUBLIC ACCESS AREA OF UMC.** Clean, clothe drapes can be found at the primary entrance into both the Guyton Building and the 8<sup>th</sup> floor LAF. Two important factors are responsible for this policy. First, laboratory animals pose a significant zoonotic threat. Allergens, pathogenic bacteria and viruses, and physical injuries are potential human hazards and may be minimized by covering all animals in transport. Secondly, we must consider the publics perception of laboratory animals. Covering animals in transport through public areas (departmental areas, elevators, corridors) can reduce the exposure to these animals. Drapes/covers are provided at the entrance of the lab animal facilities.

### **Closed Door Policy**

A considerable amount of animal-based research takes place in investigator-maintained laboratories. The corridors serving these laboratories also serve students, outside contractors, patients/guests, etc. Discretion should be exercised while working with animals in these locations. People often make incorrect assumptions about animals in research and may create a public relations/regulatory problem. We can prevent this potential problem by keeping laboratory doors CLOSED when experimental animals are present. Animals are sensitive to environmental stimuli and respond more consistently to controlled surroundings.

### **Carcass Disposal in Walk-In Coolers**

The LAF maintains two walk-in coolers for disposal of animal carcasses (G-044, and 8<sup>th</sup> floor R820-03,). Each cooler has barrels for the placement of these carcasses. All animal carcasses should be contained within heavy plastic bags and placed within the barrels or on the shelves. Additionally, the LAF requests that all bags containing carcasses be labeled with the investigator's name and the date of animal euthanasia. The LAF will manage the waste stream from this point, including incineration of the waste and sanitation of the barrels and cooler.

### **Observation of Expiration Dates on Medical Supplies**

Medical supplies often have an expiration date stamped or imprinted on the product package. Drugs, suture materials, nutritional supplements, and fluids are common examples found throughout the LAF and associated laboratories. The use of these materials in biomedical research dictates that these dates be observed and respected. Ideally, materials should not be out-of-date when used in conjunction with animal-based research programs. Laboratories should check supplies on a monthly basis to prevent holding these expired materials. The IACUC has adopted a specific policy regarding the use of outdated/expired supplies. Consult the IACUC Policy Statements at ([http://iacuc.umc.edu/policies/Expired\\_MedicalMaterials6.doc](http://iacuc.umc.edu/policies/Expired_MedicalMaterials6.doc)).

### **Use of Supplemental Heat Sources for Laboratory Animals**

The addition of supplemental heat often is warranted for the care and support of laboratory animals. Hypothermia can be a devastating condition in animals, adversely affecting the metabolic status of the animal and having negative consequences on the science. High risk cases include neonates, sick/moribund animals, and animals recovering from anesthesia and surgery.

Circulating hot water and/or warm air heating blankets (such as BAIR Huggers) may provide an excellent means of maintaining core body temperatures. Never use electric coil heating pads as the potential for thermal burns is too great with these units. Circulating water pads may also burn animals; however, the chances are greatly reduced. To ensure against this, animals should be placed on a blanket or drape that covers the heating pad. Also, this will ease

the cleaning of the pad. It is recommended that these blankets not be left on recovered animals that may chew and destroy the circulating units!

Supplemental heat sources may be in other forms. Animals receiving fluid therapy should have the sterile fluids warmed prior to infusion. Microwave heating, soaking the fluid bags in a hot water bath or the use of warmed air (BAIR Hugger units) will achieve this warming effect. Take precautions to ensure that the temperature of the fluids does not exceed 100°F. The use of heat lamps can supply a tremendous amount of heat. Direct this energy into the cage to achieve a warming effect. Again, take the necessary precautions to ensure that the lamp is at a safe distance from the animal(s). It is advisable to check the temperature of the environment (inside cage) at frequent intervals while the heat lamp is in use. A final supplemental heat source may be found in placing warmed fluid bags around the animal(s). This method resembles a hot water bottle and may have a positive influence on the animal's core body temperature.

Investigators are reminded that surgical cases typically require the use of supplemental heat sources. While all of the above may be used, minimizing the duration of the animal's body cavity exposure will conserve significant quantities of heat. Finally, any animal receiving supplemental heat should have their core body temperature monitored frequently and documented for the duration of supplementation.

### **Use of LAF Equipment**

The LAF has numerous equipment items available for use by UMC researchers. Special animal restraint devices, monitoring equipment, anesthetic machines, and animal transport cages are utilized by numerous programs. Investigators needing such items should contact the LAF office (**4-1385**) to inquire/reserve these equipment items. Those laboratories utilizing the equipment are asked to assist the LAF by using the items correctly and returning the items in the same condition as they were issued. Problems that develop with equipment due to carelessness or negligence cost the LAF both in lost time and repair parts. Furthermore, the cost extends into various studies that have a future need for the damaged item.

### **Microbial Monitoring Program**

The LAF utilizes the RODAC (Replicate Organism Detection and Counting) microbial monitoring program to validate sanitation measures. Regulatory agencies and accrediting bodies request that institutions develop methods to ensure that the sanitation program is effective. This system uses an agar medium to quantitate bacterial contamination.

RODAC microbial monitoring is routinely used to verify sanitation measures of the automated cagewashers, LAF surgery suites, and bacterial burdens of restraint devices. Also, animal caging/equipment that is sanitized in a non-standard fashion (hand washed) will be checked to ensure that the sanitation is effective. Colony counts exceeding the manufacturers recommendations will be re-cultured, and corrective actions will be taken (by the IACUC, LAF, and investigator's laboratory) to address the ineffective sanitation issue.

### **Transmission of Respiratory Ailments to Laboratory Animals**

Common respiratory problems experienced by personnel may create significant health

problems for laboratory animals. A principle concern involves the transmission of influenza and measles to nonhuman primates. Primates are not a reservoir host; therefore, the reverse situation does not occur. Personnel experiencing upper respiratory ailments should minimize their contact with nonhuman primates. Bacterial and viral pathogens are known to infect nonhuman primates and are quite difficult to manage clinically. As well, rodents, ferrets, birds, and swine are susceptible to many human respiratory pathogens. It is advised that all personnel experiencing upper respiratory symptoms minimize their exposure to these species of laboratory animals.



# Security Concerns

## **Rationale**

Negative attitudes concerning animal research and animal rights activism may translate into critical reviews and actions directed toward researchers using animal models. It is advised that all Principal Investigators with animal-based research programs take precautionary measures to address any questions raised by animal rights activists. The institution, IACUC, LAF, and investigator are responsible for being prepared to defend against allegations of animal abuse or improprieties related to animal research. For maximum effectiveness, strong collaboration is required between Public Affairs, the investigator, the IACUC, and the LAF to enhance communication and to assure proper care and use of laboratory animals in accordance with federal, state, and institutional regulations.

## **Freedom of Information Act**

The Freedom of Information Act (FOIA) was mandated in 1976. The Act is based on the principle that every person should have clear access to identifiable records without having to state a reason for wanting the information. Only certain types of information may be withheld from the requestor. Components of Federal grants and IACUC records, including Animal Activity Protocols, may become subjects of the FOIA. Animal activists/rights organizations frequently use this tactic to gain information related to a research project. The requestor may solicit information directly from the institution, the USDA, or through the granting agency. Requests taken directly to Federal agencies will be forwarded to the institution and any specifically identified individuals.

## **Suggested Precautions for Investigators**

Investigators are encouraged to take a “pro-active” approach and prepare for possible problems before the work is questioned. It is recommended that an animal care and use file be developed and included in this section of the manual and maintained in the Principal Investigator’s laboratory. This file should contain:

- Approved research grant documents.
- IACUC-approved Animal Activity Protocols and correspondence.
- Curriculum vitae of each individual involved in the project.
- Brief descriptions (nontechnical) of your research goals and accomplishments.  
see: Research Summary
- Representative list of citations to your research.
- References supporting that no alternative methods exist.
- The UMC Administrative Action Plan.

The UMC Animal Activity Protocol form (question #14) is designed to partially address some aspects of this pro-active approach. Question #14 states, “In nontechnical / lay terminology, what is the objective of the experiments proposed in this Animal Activity Protocol?”. Since information contained in the UMC Animal Activity Protocol may be exposed through the FOIA, it is imperative that the information be complete and written in a nontechnical format.

### **Research Summary**

Principal Investigators may find it helpful to prepare a Research Summary that addresses several important aspects of their research program. This summary may include the following information:

- **The Problem**  
Specifically describe the problem your work is designed to address. Supportive statistics (number of people affected, incidence rates, sequelae of the problem) would be beneficial.
- **Questions We are Trying to Answer**  
What are the goals of the research? Identify specific questions that the research project will address.
- **What are the Benefits to Humans/Animals**  
Explain how the research will add value toward addressing the problem.
- **Why are Animals Required for the Study**  
Why is this animal model best suited for this research program? What are the possible alternatives to using animals?
- **How are Animals Utilized**  
In non-technical language, briefly describe how the animals are used in the research program (surgical manipulations, dietary management, drug administration, etc.).
- **What is the Progress of the Work**  
What are the major accomplishments of the research program?
- **What is Your Funding Source**  
Identify sources of financial support for the work.

## **Institutional Responsibilities**

The University of Mississippi Medical Center regards all questions relating to animal research with great respect. UMC has adopted an Administrative Action Plan to aid the institution and the targeted investigator(s). It is recognized that a consistent, methodical institutional response is required in these potential “crisis” situations. Investigators and their personnel should familiarize themselves with the Administrative Action Plan and be prepared to respond appropriately.

## **Administrative Action Plan**

Anticipating negative questions and attacks directed against individuals and the institution is very difficult. A reliable clue that your research is being questioned is notification from a federal funding agency that your grant application and reports have been requested under the Freedom of Information Act. **Whenever a funding agency informs you that your grant materials have been petitioned, you should treat this information with respect and prepare yourself and the institution for potential criticism.** Other forms of inquiry may include direct-mailed letters and packages sent to Principal Investigators, members of the IACUC, or to the LAF office. Yet another form of questioning may occur through telephones and electronic media. When questions arise via the telephone or in-person, note (if possible) the person’s name, distinguishing features, affiliation, and phone number/address.

All inquiries and questions should be taken seriously and handled through the proper administrative channels. **No contacts should be disregarded!** The following UMC personnel should be notified of all contacts by animal rights groups or anyone attempting to gather information about animal studies:

<b>UMC Public Affairs</b>	<b>4-1100</b>
<b>UMMC Office of Research</b>	<b>5-5000</b>
<b>LAF</b>	<b>4-1385</b>

**It is important for all inquiries to be directed to the appropriate personnel in Public Affairs. UMC Public Affairs will serve as the focal point for the University and will coordinate the action plan, including interaction of the Vice Chancellor, Associate Vice Chancellor for Research, IACUC Chair, Director of the Laboratory Animal Facilities, UMC Legal Counsel, and UMC Campus Police.**

Each inquiry and question should prompt the individual(s) and the institution to review the animal care and use issues related to the inquiry. Information should be current

and reflect ongoing activities. This file may contain the IACUC-approved Animal Activity Protocol form, any correspondence with the IACUC, information from funding sources, and copies of grant applications.

Furthermore, it is critically important for your funding source to know that your work is being questioned. Cases arise where the funding agency is not contacted via FOIA, thus you need to inform the project officer at your funding agency. As well, this officer should be contacted frequently to keep them abreast of all developments related to this inquiry.

A final note regarding contacts at professional societies. Intimidation is a characteristic tactic utilized by an animal rights organization making an attack on a research program. Numerous national societies and groups are available to support research programs. These societies can lend their support and assistance by providing public statements as to the appropriateness, the need, and the benefits for humans and animals of the work in question. Several societies and organizations are listed in Section V, Appendix A.

### **Laboratory Animal Facilities Security**

Security aspects of the LAF are of great importance to the institution. Only UMC personnel with animal-based research needs are granted access into the animal housing areas. UMC-issued identification badges must be worn when working in these areas. Access to each animal housing area is controlled via an electronic card reader. Personnel completing IACUC-mandated training and applicable occupational health questionnaires and risk assessments are granted access. Additionally, many animal rooms have a unique door locks. Investigators are assigned keys as needed, thus assuming responsibility for security to that room. The LAF office coordinates the issuance of all animal housing area keys.

Badge/card access is unique to each individual and ID badges must not be shared or exchanged. Security breaches are considered major institutional violations and may result in the loss of privileges to work in the LAF.

### **LAF Access**

Access into LAF environments is closely associated with IACUC study approval and occupational health and safety. Access is achieved via the following mechanisms:

1. Only personnel requiring LAF admittance will be granted access. Personnel must either be listed on an IACUC-approved protocol, be an employee of the LAF, or have work responsibilities within the area (Physical Facilities, Environmental Services, DIS, etc).
2. Personnel must complete the form "Training Requirements Registration (<http://iacuc.umc.edu/Forms/TrainingForm51507.doc>) including:
  - a. Attendance of an IACUC-sponsored orientation session
  - b. Completion of on-line training ([www.citiprogram.org](http://www.citiprogram.org))

- c. Complete an LAF tour
  - d. Complete occupational health and safety documents  
(<http://taws.umc.edu/EOH/AdminMenu.ctrl?action=Display>)
3. Completed forms are routed to the IACUC (Office of Research, U-020) and Student/Employee Health (N-128).
  4. Access via card reader is granted after completion of all documents.

## **VIDEO/IMAGING CONCERNS**

Video and still images conveying information about animal-based research must be created with great care and attention. Images may be captured for scientific presentations or educational/demonstrational purposes. High-ethical standards need to be used, resulting in professional-quality images.

Images and audio transmissions are particularly vulnerable to editing or mis-representation by animal rights groups. Taking special precautions prior to creating these forms of communication are essential. Telephones with camera capabilities are not secure and are inappropriate within the LAF. Camera phones should not be used in the LAF.

## **Animal Facilities Disaster Plan**

The LAF has taken proactive measures to prepare for potential emergency situations, including power failures and natural disasters. This disaster plan not only aids our efforts to provide for animal needs, it also is an AAALAC-required document. The plan has a twofold objective, 1) protecting personnel, and 2) providing appropriate veterinary medical and husbandry care to research animals.

The plan incorporates information about safe building egress, emergency coordinators, provisions for animal husbandry, and presents differing scenarios on how animals may be handled during an emergency. As well, the plan includes emergency telephone numbers (on-campus) and important numbers on a national level (USDA, AAALAC, CDC, OLAW).

## National & Governmental Agencies

**American Association for Accreditation of  
Laboratory Animal Care (AAALAC)**

5283 Corporate Drive, Suite 203  
Frederick, MD 21703  
(301)696-9626  
[www.aaalac.org](http://www.aaalac.org)

(301)504-6212

**Association for Research in Vision and  
Ophthalmology (ARVO)**

9650 Rockville Pike  
Bethesda, MD 20814-3928  
(301)571-1844

**American Association for Laboratory Animal  
Science (AALAS)**

70 Timber Creek Drive, Suite 5  
Cordova, TN 38018  
(901)754-8620  
[www.aalas.org](http://www.aalas.org)

**Association of American Medical Colleges  
(AAMC)**

2450 N Street NW  
Washington, DC 20037-1126  
(202)828-0400

**American Medical Association (AMA)**

353 North Dearborn Street  
Chicago, IL 60610  
(312)464-5000

**Foundation for Biomedical Research (FBR)**

818 Connecticut Avenue NW, Suite 303  
Washington, DC 20006  
(202)457-0654

**American Physiological Society (APS)**

9650 Rockville Pike  
Bethesda, MD 20814  
(301)530-7164

**incurably ill For Animal Research (iiFAR)**

PO Box 27454  
Lansing, MI 48909  
(517)887-1141

**American Psychological Association (APA)**

750 First Street NW  
Washington, DC 20001  
(202)336-6000

**Institute for Laboratory Animal Resources  
(ILAR)**

National Resources Council  
2101 Constitution Avenue NW  
Washington, DC 20418  
(202)334-2590

**American Veterinary Medical Association  
(AVMA)**

1930 North Meacham Road, Suite 100  
Schaumburg, IL 60173-4360  
(708)925-8070

**National Association for Biomedical Research  
(NABR)**

818 Connecticut Avenue NW, Suite 303  
Washington, DC 20006  
(202)857-0540

**Americans for Medical Progress (AMP)**

1735 Jefferson Davis Highway, Suite 907  
Arlington, VA 22202-3401  
(703)412-1411

**Office for Protection from Research Risks  
(OLAW)**

National Institutes of Health  
Building 31, Room 5B59  
9000 Rockville Pike  
Bethesda, MD 20892  
(301)496-7163

**USDA - Animal & Plant Health Inspection  
Service, Regulatory Enforcement and Animal  
Care (APHIS-REAC)**

6505 Belcrest Road  
Hyattsville, MD 20782  
(301)436-7833

**Society for Neuroscience**

11 Dupont Circle  
Washington, DC 20036  
(202)462-6688

**Animal Welfare Information Center (AWIC)**

National Agriculture Library  
USDA  
10301 Baltimore Blvd., Room 205  
Beltsville, MD 20705

# Laboratory Animal Formulary & Technical Information

## General

This section of the LAF Training & Procedural Manual is designed to provide technical assistance to investigators on matters related to drug dosages in laboratory animals and minor technical manipulations. Please consult this section for preparation of the Animal Activity Protocol form. Principal Investigators and their laboratory personnel are reminded that the LAF veterinary staff will supply additional, supportive information to this formulary, as well as hands-on technical assistance. Direct all related questions to the LAF veterinary staff at **4-1385** or pager **601-881-7693**.

## Animal Handling & Manipulations

All techniques and manipulations on live animals must be detailed in the IACUC-approved Animal Activity Protocol form. Handling and manipulative techniques are (must be) based on the species of animal, the technical expertise of the personnel, scientific needs, and temperament of the animal. Members of the LAF veterinary staff are prepared to assist in training investigators and their staff in the use of many techniques or suggest colleagues at UMC to serve as mentors. As well, the LAF library (G-201) has numerous reference books that may assist investigators and their personnel lacking practical experience with these commonly used techniques. Additionally, a number of reference resources can be found at <http://oacu.od.nih.gov/ARAC/>

## Plasma & Blood Volume

<u>Species</u>	<u>Plasma Volume</u> mean (range)	<u>Blood Volume</u> mean (range)
Cat	41 (35-52)%	55 (47-66) ml/kg
Dog	50	86 (79-90)
Rabbit	39 (28-51)	56 (44-70)
Ferret	--	75
Frog	80	95
Gerbil	43 – 49% **	67
Guinea Pig	39 (35-48)	75 (67-92)
Hamster	36- 55% **	78
Mouse	39-49% **	79
Pig	--	65 (61-68)
Rat	40 (36-45)	64 (58-70)
Rhesus monkey	36 (30-48)	54 (44-67)

\*Removal of Blood from Laboratory Mammals and Birds. *Laboratory Animals* (1993) **27**, 1-22.

\*\* from "Clinical Procedures" *The Biology and medicine of Rabbits and Rodents* (4<sup>th</sup> edition) John E. Harkness and Joseph E Wagner, 1995 Williams and Wilkins pp 75-96.

## Blood Sampling Volumes

Blood samples are routinely collected from laboratory animals in the research setting. Guidelines are provided to ensure that significant, adverse biologic effects are not created due to this sampling volume or frequency. Obviously, safe volumes will depend on the species of animal, the hydration and nutritional status, and the body weight. As a general reference, the following table is provided:

<u>Species</u>	<u>Blood volume (ml/kg)</u>	<u>Single sample collection(ml/kg)</u>
Cat	56	5.6
Dog	86	8.6
Hamster	78	7.8
Macaque	54	5.4
Mouse	78	7.8
Pig	65	6.5
Rabbit	56	5.6
Rat	64	6.4

### Examples

30 gm mouse X 7.8ml/kg X kg/1000 gm=0.234 ml = about 200ul

4.5 kg rabbit X 5.6 ml/kg=25ml

Species differences can be significant, but the safe volumes are based on a 10% blood loss. Research notes that removal of 10% volume will initiate homeostatic cholinergic mechanisms. Removal of greater volumes produces changes in cardiac output, blood pressure, and may eventually lead to hemorrhagic shock.

## Needle Sizes, Sites, and Recommended Volumes for Injection

<u>Species</u>	<u>SC</u>	<u>IM</u>	<u>IP</u>	<u>IV</u>
<b>Cat</b>	scruff, back, 50-100 ml, 21,23,25G	quadriceps/caudal thigh, 1 ml, 21,23,25G	50-100 ml 21,23,25G	cephalic vn, 2-5 ml (slow) 21,23,25G
<b>Dog</b>	scruff, back, 100-200 ml, 21,23,25G	quadriceps/caudal thigh, 2-5 ml, 21,23,25G	200-500 ml 21,23,25G 10-15ml (slow)	cephalic vn, saphenous vn, 21,23,25G
<b>Ferret</b>	scruff, 20-30 ml 21,23,25G	quadriceps/caudal thigh, 0.5-1ml,21,	50-100 ml 21,23,25G 23,25g	cephalic vn, jugular vn,2-5ml
<b>Guinea Pig</b>	scruff, back,	quadriceps/caudal	10-15 ml	ear vn,

	5-10 ml, 21,23,25G	thigh, 0.3 ml, 21,23,25G	21,23,25G	saphenous vn
<b>Hamster</b>	scruff, 3-4 ml 21,23,25G	quadriceps/caudal thigh, 0.1 ml, 21 23,25G	3-4 ml, 21, 23,25G	femoral vn, jugular vn, 0.3
<b>Mouse</b>	scruff, 2-3 ml 21,23,25G	quadriceps/caudal thigh, 0.05 ml, 23,25g	2-3 ml, 21,23,25G	lat tail vn, 0.2 ml, <25G
<b>Macaque</b>	scruff, 10-30 ml 21,23,25G	quadriceps/caudal thigh, triceps, 1-3 ml 21,23,25G	50-100 ml 21,23,25G	cephalic, tarsal, jugular vn, 10-20 ml (slow) 21,23,25G
<b>Rabbit</b>	scruff, flank, 30-50 ml, 21,23,25G	quadriceps/caudal thigh, lumbar muscles 0.5-1 ml, 21,23,25G	50-100 ml 21,23,25G	marginal ear vn 1-5 ml, (slow) 21,23,25G
<b>Rat</b>	scruff, 5-10 ml 21,23,25G	quadriceps/caudal thigh, 0.3 ml, 21,23,25G	5-10 ml 21,23,25G	lat ear vn 0.5 ml, <23G
<b>Bird</b>	pectoral, interscapular or inguinal fold, 1-3% BW bid, <21G	pectoral/per site 0.2 ml/100 g BW	NA	cutaneous ulnar <25G short bevel

\*Flecknell, PA. *Laboratory Animal Anesthesia*. Academic Press, 1987.

## Components of Fluid Therapy

**Maintenance Requirement**      50 ml / kg / day  
(Dog, Cat, Primate)

EXAMPLES:      \*22 kg dog x 50 ml/kg = 1,100 ml/day  
                         \*4.6 kg cat x 50 ml/kg = 230 ml/day  
                         \*6.9 kg macaque x 50 ml/kg= 345  
                         ml/day

**Maintenance Requirement**

Rabbit	≥ 10 ml/100g/day
Guinea pig	10 ml/100g/day
Hamster	> 20 ml/100g/day
Gerbil	4-7 ml/100g/day
Rat	10-12 ml/100g/day
Mouse	15 ml/100g/day

Dehydration in laboratory animals is evident by a variety of clinical signs. Animals that are known to be dehydrated or animals exhibiting any veterinary health abnormalities/concerns that may signal early hydration difficulties, should receive prompt veterinary medical attention.

The LAF veterinary staff will assess the animal's hydration status and clinical problems and institute the appropriate therapy.

### **Recommended Antibody Production Protocols**

Antibody Production methods may be broadly categorized as *in vitro* or *in vivo*. Research interests requiring antibody production methods must evaluate both forms to make an educated choice in the quality and quantity of antibodies.

*In vitro* methods have refined significantly over the last decade. These methods are readily available from commercial sources.

*In vivo* methods remain a popular choice, yet do require careful planning and participation by the investigative team, IACUC, and veterinarian. Sources of information and details of methods involved in *in vivo* antibody production may be found at:

<http://oacu.od.nih.gov/ARAC/freunds.pdf>

<http://oacu.od.nih.gov/ARAC/ascites.pdf>

### **Intraperitoneal injections- (IP)**

Caution must be exercised to avoid penetrating various organs within the abdominal cavity. Typically, the intestines retract away from the touch of a sharp needle point, however, this is not the case when the tract is full, or with the bladder or liver. The optimum location for the IP injection is the lower right quadrant of the abdomen (high enough to avoid the bladder and cecum and not so deep to puncture the kidneys or major vessels). Restrain the animal (upside down) with the head down at a 30<sup>0</sup> to 45<sup>0</sup> angle. Needle sizes and injection volumes may be found on page 2 of this section. It is important to pull back slightly on the plunger of the syringe prior to injection. If fluid is withdrawn (yellow/brown/green), the needle is probably in the bladder or intestinal tract. Withdraw the needle and re-direct to avoid that area.

### **Subcutaneous Injections - (SC)**

It is important to avoid major blood vessels with subcutaneous injections. Raising a tent of skin creates a large area of subcutaneous space for an injection. Grasp a fold of skin and pull away from the underlying musculature. Enter the injection site with the needle held at a right angle to the elevated skin surface. Needle sizes and injection volumes are found on page 2 of this section.

### **Intramuscular Injections - (IM)**

Intramuscular injections usually are given in the hindlimbs; although, other sites may be utilized. It is important to limit the volumes injected into muscle masses, as significant discomfort may be associated with large volumes. Caution should be exercised to avoid major vessels and nerves in the area. It is optimal to enter the biceps femoris muscle mass from the lateral aspect of the limb. Needle sizes and injection volumes may be found on page 2 of this section. It is important to pull back slightly on the plunger of the syringe prior to injection and check for the presence of blood. If blood is withdrawn, re-direct the needle and gently aspirate. If multiple injections must be made (either during a single procedure or with multiple doses over the course of days), it is best to alternate (left vs. right) limbs that receive the injection.

### **Rabbit Restraint**

Proper restraint of rabbits is necessary to avoid injury to personnel and severe musculo-skeletal problems in the rabbit. Grasping the loose skin over the neck and shoulder is the initial step in successful restraint. When lifting the rabbit, always support the rump and keep the animal from kicking its rear limbs. Rabbits should **never** be restrained by their ears. The LAF veterinary staff recommends restraint boxes for more than momentary work. Contact the LAF (4-1385) for use of rabbit restraint devices.

### **Rabbit Blood Withdrawal**

Blood sampling from rabbits is accomplished most successfully in a sedated, well-restrained animal. Animals should be sedated with Acepromazine @ 1 mg/kg IM approximately 30 minutes prior to blood collection. The sedative calms the animal, vasodilates the peripheral vessels, and minimizes the potential of post-procedural complications. Remove the sedated rabbit from the caging and place in a rabbit restraint device. Clip the hair from the outer surface of the ear. Wipe the surface with alcohol. Collect baseline sera from the central auricular artery or lateral auricular vein using a 21 gauge sterile needle. The LAF veterinary staff can assist with the anatomy of the rabbit ear. Insert the needle (no syringe attached) from the distal end of the ear and allow the blood to drip into the sterile collection tube. Volumes up to 7.7 ml/kg can be withdrawn safely during a single collection. When the appropriate volume is collected, gently remove the needle and apply pressure (hemostasis) as required.

### **Formulary-Anesthetic, Analgesics & Tranquilizers**

There are numerous chemical agents available that will provide appropriate anesthesia, analgesia and tranquilization to laboratory animals. Many laboratories have developed techniques and regimes that adequately address the needs of the research animal. The proper use of anesthetics and analgesics in research animals is an ethical and scientific imperative. The selection of the most appropriate anesthetic or analgesic should reflect professional judgement as to most appropriately meet clinical and humane requirements without compromising the scientific aspects of the research protocol. The specific details of anesthesia and analgesia, including drug names and dosages, must be provided in the IACUC Animal Activity Protocol

form. It is recommended that investigators consult with the LAF veterinary staff during preparation of the Animal Activity Protocol to ensure the most appropriate agents for their research needs.

The following compendium lists numerous anesthetics, analgesics, and tranquilizers and their known effective dosages. This list is not intended to be exhaustive. Special notations are provided where applicable (controlled substances, adverse effects, LAF preferred). The compendium is organized according to species, with drug combinations or “cocktails” noted first, followed by selected individual drugs and analgesic medications.

### **Swine**

	<u>Drug Combination</u>	<u>Dose</u>	<u>Route</u>	
	Telazol *	4-6 mg/kg	IM	
	Xylazine	2.2 mg/kg	IM	
	Ketamine*	20 mg/kg	IM	
	Xylazine	2 mg/kg	IM	
Λ	Ketamine*	10 mg/kg	IM	
	Butorphanol *	0.2 mg/kg	IM	
	Medetomidine	0.08mg/kg	IM	
	<u>Individual Drug</u> ⊥	<u>Dose</u>	<u>Route</u>	
v	Atropine	0.02-0.05 mg/kg	IM	
	Acepromazine	0.2-1.1 mg/kg	IM	
v	Isoflurane		inhalation	
	<u>Analgesic Drug</u>	<u>Dose</u>	<u>Route</u>	<u>Duration</u>
v	Buprenorphine *	0.005-0.05 mg/kg	IM,IV	8-10 hr
	Butorphanol	0.1-0.3 mg/kg	IM	4-6 hr
	Flunixin meglumine	2.2 mg/kg	IM,SC	12 hr
	Bupivacaine	(0.25% solution)	IM,SC	6-10 hr
v	LAF preferred agents			
*	Controlled substances			
⊥	Dosages reflect use as the sole agent, premedicants typically reduce the necessary dose of anesthetics.			

### **Rabbits**

<u>Drug Combination</u>	<u>Dose</u>	<u>Route</u>
Ketamine *	35 mg/kg	IM
Xylazine	5 mg/kg	IM
Butorphanol *	0.1mg/kg	IM
Ketamine *	25 mg/kg	IM
Medetomidine	0.5 mg/kg	IM

	<u>Individual Drug</u> †	<u>Dose</u>	<u>Route</u>
v	Atropine	0.05 mg/kg	IM
T	Acepromazine	1 mg/kg	IM
	Ketamine *	25-50 mg/kg	IM
	Xylazine	2-5 mg/kg	IM
v	Isoflurane		inhalation
	Medetomidine	0.25 mg/kg	IM

	<u>Analgesic Drug</u>	<u>Dose</u>	<u>Route</u>	<u>Duration</u>
v	Buprenorphine *	0.01-0.05 mg/kg	IM,SC	8-10 hr
	Butorphanol	0.1-0.5 mg/kg	IM,SC	4-6 hr
	Bupivacaine	(0.25% solution)	incision site	6-10 hr
	Carprofen	4 mg/kg	SC	daily

- v LAF preferred agents  
 \* Controlled substances  
 T excellent sedation for blood collection, adjuvant injection, minor procedures  
 † Dosages reflect use as the sole agent, premedicants typically reduce the necessary dose of anesthetics.

## Cats

<u>Drug Combination</u>	<u>Dose</u>	<u>Route</u>
Ketamine *	22 mg/kg	IM
Xylazine	1.1 mg/kg	IM
Ketamine *	20 mg/kg	IM
Acepromazine	0.11 mg/kg	IM
Ketamine *	7 mg/kg	IM
Medetomidine	0.08 mg/kg	IV

	<u>Individual Drug</u> ⊥	<u>Dose</u>	<u>Route</u>	
v	Atropine	0.05 mg/kg	IM	
	Acepromazine	0.05-0.2 mg/kg	IM	
	Ketamine *	5-20 mg/kg	IM	
	Xylazine	0.5-1 mg/kg	IM	
v	Isoflurane		inhalation	
	<u>Analgesic Drug</u>	<u>Dose</u>	<u>Route</u>	<u>Duration</u>
	Carprofen	2 mg/kg	PO	Once
v	Buprenorphine *	0.005-0.02 mg/kg	IM,SC	6-12 hr
	Butorphanol	0.2-0.8 mg/kg	IM,SC	2-4 hr
	Bupivacaine (0.25% solution)		incision site	6-10 hr
	(avoid acetaminophen, aspirin, and ibuprofen)			
v	LAF preferred agents			
*	Controlled substances			
⊥	Dosages reflect use as the sole agent, premedicants typically reduce the necessary dose of anesthetics.			

## Dogs

	<u>Drug Combination</u>	<u>Dose</u>	<u>Route</u>	
	Ketamine *	5 mg/kg	IV	
	Xylazine	1.0 mg/kg	IV	
	Ketamine *	5 mg/kg	IV (slow)	
	Medetomidine	0.04 mg/kg	IV (slow)	
	<u>Individual Drug</u> ⊥	<u>Dose</u>	<u>Route</u>	
v	Atropine	0.05 mg/kg	IM	
T	Acepromazine	0.1-0.25 mg/kg	IM	
	Xylazine	0.5 mg/kg	IM	
	Thiopental *	10 mg/kg	IV	
	Pentobarbital *	30 mg/kg	IV (to effect)	
v	Isoflurane		inhalation	
	Medetomidine	0.1-0.8 mg/kg	IM	
	<u>Analgesic Drug</u>	<u>Dose</u>	<u>Route</u>	<u>Duration</u>
v	Buprenorphine *	0.005-0.02 mg/kg	IM,SC	8-10 hr
	Butorphanol *	0.2-0.6 mg/kg	IM,SC	2-4 hr
	Flunixin meglumine	1.0 mg/kg	IM	daily
	Bupivacaine (0.25% solution)		incision site	6-10 hr

Carprofen	4 mg/kg	PO	12 hr
Fentanyl*	75 mcg	transdermal	72 hr

v LAF preferred agents

\* Controlled substances

T Very effective pre-medication

⊥ Dosages reflect use as the sole agent, premedicants typically reduce the necessary dose of anesthetics.

### **Rats**

<u>Drug Combination</u>	<u>Dose</u>	<u>Route</u>
-------------------------	-------------	--------------

Ketamine *	75 mg/kg	IP
Xylazine	10 mg/kg	IP

Ketamine *	75 mg/kg	IP
Medetomidine	0.5 mg/kg	IP

<u>Individual Drug</u> ⊥	<u>Dose</u>	<u>Route</u>
--------------------------	-------------	--------------

v Atropine	0.05-0.1 mg/kg	IM,SC,IP
Pentobarbital *	40-60 mg/kg	IP (to effect)
Isoflurane		inhalation

<u>Analgesic Drug</u>	<u>Dose</u>	<u>Route</u>	<u>Duration</u>
-----------------------	-------------	--------------	-----------------

T Buprenorphine *	0.01-0.05 mg/kg	SC,IP	8-10 hr
Butorphanol *	1.0-2.0 mg/kg	SC	2-4 hr
Bupivacaine	(0.25% solution)	incision site	6-10 hr
Ketoprofen	5 mg/kg	SC	once
Carprofen	5 mg/kg	SC	daily

v LAF preferred agents

\* Controlled substances

⊥ Dosages reflect use as the sole agent, premedicants typically reduce the necessary dose of anesthetics.

### **Mice**

<u>Drug Combination</u>	<u>Dose</u>	<u>Route</u>
-------------------------	-------------	--------------

	Ketamine *	80-100 mg/kg	IP	
	Xylazine	10 mg/kg		
	Ketamine *	75 mg/kg	IP	
	Medetomidine	1 mg/kg		
	<b><u>Individual Drug</u></b> †	<u>Dose</u>	<u>Route</u>	
	Atropine	0.04 mg/kg	IM,SC,IP	
	Pentobarbital *	50 mg/kg	IP (to effect)	
	Diazepam *	5 mg/kg	IP	
v	Isoflurane		inhalation	
	<b><u>Analgesic Drug</u></b>	<u>Dose</u>	<u>Route</u>	<u>Duration</u>
T	Buprenorphine *	0.05-0.1 mg/kg	SC,IP	8-10 hr
	Butorphanol *	1-2 mg/kg	SC	2-4 hr
	Bupivacaine	(0.25% solution)	incision site	6-10 hr
	Carprofen	5mg/kg	SC	daily
v	LAF preferred agents			
*	Controlled substances			
†	Dosages reflect use as the sole agent, premedicants typically reduce the necessary dose of anesthetics.			

### **Nonhuman Primates**

	<b><u>Drug Combination</u></b>	<u>Dose</u>	<u>Route</u>	
	Ketamine *	10 mg/kg	IM	
	Diazepam *	1 mg/kg	IM	
	<b><u>Individual Drug</u></b> †	<u>Dose</u>	<u>Route</u>	
	Atropine	0.05 mg/kg	IM,SC	
v	Ketamine *	10 mg/kg	IM	
	Telazol *	2-6 mg/kg	IM	
	Diazepam *	1 mg/kg	IM	
v	Isoflurane		inhalation	
	<b><u>Analgesic Drug</u></b>	<u>Dose</u>	<u>Route</u>	<u>Duration</u>
v	Buprenorphine *	0.005-0.01 mg/kg	IM,IV	8-10 hr
	Butorphanol *	0.01 mg/kg	IV	2-4 hr
	Bupivacaine	(0.25% solution)	incision site	6-10 hr
	Ibuprofen	10 mg/kg	PO	6-8 hr

Acetaminophen	5-10 mg/kg	PO	?
Flunixin meglumine	0.5-4.0 mg/kg	IM	24 hr
Carprofen	3-4 mg/kg	SC	daily

v LAF preferred agents

\* Controlled substances

⊥ Dosages reflect use as the sole agent, premedicants typically reduce the necessary dose of anesthetics.

### **Hamsters**

<u>Drug Combination</u>	<u>Dose</u>	<u>Route</u>
Ketamine *	200 mg/kg	IP
Xylazine	10 mg/kg	IP
Ketamine *	150 mg/kg	IP
Acepromazine	5 mg/kg	IP
Ketamine *	100 mg/kg	IP
Medetomidine	0.25 mg/kg	IP

<u>Individual Drug</u> ⊥	<u>Dose</u>	<u>Route</u>
Atropine	0.04 mg/kg	IM,SC,IP
Pentobarbital *	50-90 mg/kg	IP
v Isoflurane		inhalation

	<u>Analgesic Drug</u>	<u>Dose</u>	<u>Route</u>	<u>Duration</u>
T	Buprenorphine *	0.05-0.1 mg/kg	SC,IP	8-10 hr
	Butorphanol *	1-2 mg/kg	SC	2-4 hr
	Bupivacaine	(0.25% solution)	incision site	6-10 hr
	Carprofen	5 mg/kg	SC	daily

v LAF preferred agents

\* Controlled substances

⊥ Dosages reflect use as the sole agent, premedicants typically reduce the necessary dose of anesthetics.

### **Birds**

<u>Drug Combination</u>	<u>Dose</u>	<u>Route</u>
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	Ketamine *	10-30 mg/kg	IM	
	Xylazine	2-6 mg/kg	IM	
	Ketamine *	20-40 mg/kg	IM	
	Diazepam *	1-1.5 mg/kg	IM	
	<b><u>Individual Drug</u></b> †	<b><u>Dose</u></b>	<b><u>Route</u></b>	
	Atropine	0.01-0.04 mg/kg	IM,SC,IP	
	Telazol *	3 mg/kg	IM	
	Diazepam *	0.5-1.5 mg/kg	IM	
v	Isoflurane		inhalation	
	<b><u>Analgesic Drug</u></b>	<b><u>Dose</u></b>	<b><u>Route</u></b>	<b><u>Duration</u></b>
	Flunixin	1-10 mg/kg	IM	
	Buprenorphine *	0.01-0.05 mg/kg	IM	8-10 hr
	Butorphanol *	1-4 mg/kg	IM	2-4 hr
	Bupivacaine	(0.25% solution)	incision site	6-10 hr
	Carprofen	1-4mg/kg	IM	
v	LAF preferred agents			
*	Controlled substances			
†	Dosages reflect use as the sole agent, premedicants typically reduce the necessary dose of anesthetics.			

## Ferrets

	<b><u>Drug Combination</u></b>	<b><u>Dose</u></b>	<b><u>Route</u></b>	
	Ketamine *	25 mg/kg	IM	
	Xylazine	2 mg/kg	IM	
	Ketamine *	4-8 mg/kg	IM	
	Medetomidine	0.05-0.1 mg/kg	IM	
	<b><u>Individual Drug</u></b> †	<b><u>Dose</u></b>	<b><u>Route</u></b>	
	Atropine	0.2 mg/kg	IM,SC	
	Telazol *	12-22 mg/kg	IM	
	Pentobarbital *	36 mg/kg	IP	
v	Isoflurane		inhalation	
	<b><u>Analgesic Drug</u></b>	<b><u>Dose</u></b>	<b><u>Route</u></b>	<b><u>Duration</u></b>
	Buprenorphine *	0.01-0.03 mg/kg	SC,IP,IM	8-10 hr

Butorphanol *	0.4 mg/kg	IM	4-6 hr
Bupivacaine	(0.25% solution)	incision site	6-10 hr
Flunixin	0.5-2.0mg/kg	SC	daily

v LAF preferred agents

\* Controlled substances

⊥ Dosages reflect use as the sole agent, premedicants typically reduce the necessary dose of anesthetics.