HANDBOOK
FOR PERSONNEL WORKING WITH
LABORATORY ANIMALS

OFFICE OF LABORATORY ANIMAL MEDICINE
UNIVERSITY OF DELAWARE

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DEFINITIONS

Throughout this Handbook, the following acronyms and abbreviations will be applied:

**AF** – AF refers to the Animal Facilities in which OLAM staff has direct oversight of the care and maintenance of the animals.

**AHT** – Animal Health Technician

**AUP** – Animal Use Protocol

**AV** – Attending Veterinarian

**AVMA** – American Veterinary Medical Association

**CDC** – Center for Disease Control & Prevention

**FM** – Facility Manager

“**the Guide**” – refers to the Guide for the Care and Use of Laboratory Animals.

**IACUC** – IACUC refers to the Institutional Animal Care and Use Committee. This committee provides oversight of the program of animal care and use, and is responsible for review of all proposals to use animals in research.

**ILAR** – Institute for Laboratory Animal Resources

**NIH** – National Institutes of Health

**OHS** – Occupational Health and Safety

**OLAM** – OLAM refers to the Office of Laboratory Animal Medicine. OLAM provides veterinary and husbandry services to the University of Delaware animal facilities. Administration of the facilities is centralized in OLAM.

**PHS** – Public Health Service

**PI** – Principal Investigator

**SOPs** – SOPs refers to Standard Operating Procedures. SOPs at the University of Delaware are detailed operating procedures, which provide a step-by-step approach for accomplishing a given task.

**USDA** – United States Department of Agriculture
FOREWORD

This Handbook has been prepared to provide information and guidelines to personnel who are or will be using research animals at the University of Delaware. All Principal Investigators (PIs) and staff working with research animals at UD should be familiar with the contents of this handbook.

OLAM is committed to providing PIs with Animal Facilities (AF), which combine optimum research conditions with supportive service oriented staff, while at the same time keeping costs to a minimum. Under the current organizational structure, OLAM includes facility management and administrative support to the IACUC.

Accommodations are available at the OLAM AF for the housing and maintenance of common laboratory animals. Fees for these accommodations are included in the Per Diem charges. OLAM staff members are available to assist PIs and technicians with routine procedures including inoculations, bleeding, euthanasia or monitoring breeding colonies. An aseptic rodent survival surgery area is available in the AF.

Any questions regarding the health of laboratory animals in research may be addressed to the Attending Veterinarian (AV).

The well being of the laboratory animals being used in research at UD is the responsibility of the investigator. The OLAM staff regularly checks animal health, census, food, water and cleanliness, and the investigator’s staff should make similar checks. The OLAM Facility Manager (FM) is always available to investigators who feel they have encountered any problem related to the animal portion of their research and animal care.

At any time, anyone working with laboratory animals in a research setting may develop an animal welfare concern. The AV, as well as the IACUC, is always available to discuss such concerns with any member of the faculty or staff. Concerns regarding animal welfare may be sent to any IACUC member or the AV. All such concerns are considered confidential and are addressed by the IACUC in convened session.
INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE

If you need to contact the IACUC, send an e-mail to lam-iacuc@udel.edu.
INTRODUCTION

This section provides an outline for PIs to follow when activating a research program, which will involve laboratory animals at the University of Delaware. If you are already conducting such research, the outline should still be useful to you in understanding certain aspects of the program of animal care and use.

Responsibilities of Laboratory Animal Users:

1. If you are a new PI, you must contact OLAM before making arrangements to conduct animal research.

2. The OLAM office will arrange for you to participate in the Animal Facility Training Program, designed to familiarize personnel with the program of animal care and use at UD.

3. It is the PI’s responsibility to ensure that all members of his/her staff who are working with laboratory animals participate in the training program. Security access to the AF will not be granted to any individual who has not participated in the training program.

4. All PIs must submit to the IACUC, on an annual basis, an Animal Use Protocol (AUP) for each project, describing in detail the proposed or ongoing use of animals.

5. PIs must agree to advise the IACUC of any change in any of the technical procedures described in approved AUPs, when those changes can affect animal health or welfare. Members of their staff who will be participating in the proposed work with laboratory animals must be trained in the proper care and use of the animal species involved.
REGULATIONS GOVERNING THE USE OF ANIMALS IN RESEARCH

INTRODUCTION

Since the ultimate responsibility for compliance with regulations that affect the care and use of animals lies with the PI, it is important that he/she have a working knowledge of the basic regulatory requirements.

REGULATIONS

Animal Welfare Act

The Animal Welfare Act (AWA) was first passed August 24, 1966, as PL-89-544. It was entitled the “Laboratory Animal Welfare Act” and authorized, “The Secretary of Agriculture to promulgate such rules and regulations, and orders as he/she may deem necessary to effectuate the purposes of this Act”.

In charging the Secretary, Congress specifically prohibited the promulgation of rules, regulations, or orders, which would interfere with the conduct of actual research. Determination of what constituted actual research was left to the discretion of the research facility.

The Secretary established regulations and standards for the implementation of unannounced facility inspections and for the maintenance of specific records by dealers and research institutions.

In 1970, the original Act was amended (PL-91-579) and renamed the Animal Welfare Act. The amended Act covered broader classes of animals. The definition of an animal was expanded to include all warm-blooded animals. The definition of a research facility was expanded to include those institutions using covered live animals and not just dogs and cats. These facilities were required to file an annual report. Civil penalties were also added for refusing to obey a valid cease and desist order from the Secretary. The term “handling” was added to the basic categories for which standards were to be created and the phrase “adequate veterinary care” was broadened to include the appropriate use of anesthetics, analgesics and tranquilizers.

The intent of the original Act to prohibit interference with research was clarified and the Secretary was enjoined from directly or indirectly interfering with, or harassing in any manner, research facilities during the conduct of actual research or experimentation. The determination of when actual research was being done was still left to the discretion of the research facility itself.
In 1985, the Act was further amended with the passage of the Food Security Act of 1895 (PL-99-198), which contained an amendment entitled the “Improved Standards for Laboratory Animals Act.” This amendment strengthened the standards for providing laboratory animal care, increased enforcement of the Act, provided for collection and dissemination of information to reduce unintended duplication of experiments using animals and mandated training for those who handle animals.

The most recent amendment to the AWA also includes development of standards for the “exercise of dogs,” for “provision of a physical environment which promotes the psychological well-being of primates,” for limitation of multiple survival surgeries, and to require the investigator to consult with a veterinarian in the design of experiments which have the potential for causing more than minimal or slight pain or distress to ensure the proper use of anesthetics, analgesics and tranquilizers. Each research facility will have to show upon inspection, and include in their annual report, assurances that professionally acceptable standards for the care, treatment and use of animals are being used during the actual research or experimentation. As part of these standards, the investigator is required to consider alternative techniques to those which might cause pain or distress in the experimental animal.

The 1985 amendment requires the Chief Executive Officer of each research facility to appoint an Institutional Animal Committee consisting of at least three members including a doctor of veterinary medicine and one member who is not affiliated with the institution. The regulations promulgated to implement the amendment designate this committee as the Institutional Animal Care and Use Committee (IACUC) and charge it to act as an agent of the research facility in assuring compliance with the Act. The IACUC is required to inspect all animal facilities and study areas at least once every six months, and to review the condition of the animals and practices involving pain to the animals to ensure compliance with the regulations and standards promulgated under the Act. The IACUC is required to review once every six months the research facility’s program to assure that the care and use of the animals conforms to the regulations and standards. The IACUC must file a report of its inspection with the Institutional Official of the research facility. If significant deficiencies or deviations are not corrected in accordance with the specific plan approved by the IACUC, the USDA and any Federal funding agencies must be notified in writing.

The IACUC must review and approve all proposed activities involving the care and use of animals in research, testing or teaching procedures and all subsequent significant changes of ongoing activities.
As part of this review, the IACUC must evaluate procedures to determine if discomfort, distress and pain are minimized, and to determine that when an activity is likely to cause pain, a veterinarian has been consulted in planning for the administration of anesthetics, analgesics and tranquilizers.

Research is also evaluated to determine that paralytic agents are not employed except in the anesthetized animal. The IACUC must also determine that animals which experience severe or chronic pain are euthanized consistent with the design of study, that the living conditions meet the species needs, that necessary medical care will be provided, that all procedures will be performed by qualified individuals, that survival surgery will be performed aseptically and that no animal will undergo more than one operative procedure that is not justified and approved. Methods of euthanasia must be consistent with the definition contained in the regulations.

The IACUC must assure on behalf of the research facility that the principal investigator considered alternatives to painful procedures and that the work being proposed does not unnecessarily duplicate previous experiments. To provide this assurance, the IACUC must review the written narrative description provided by the investigator. This description must include the methods and sources used in determining that alternatives were not available.

In reviewing proposed activities and modifications, the IACUC can grant exceptions to the regulations and standards, if they have been justified in writing by the principal investigator.

In addition to the above requirements, the research facility is required to provide training in the following areas to scientists, animal technicians and other personnel involved with animal care and treatment:

1. Humane practice of animal maintenance and experimentation.
2. Research of testing methods that minimize or eliminate the use of animals or limit pain or distress.
3. Utilization of the information service of the National Agriculture Library.
4. Methods whereby deficiencies in animal care and treatment should be reported.
Public Health Service Policy (PHS Policy)

The Public Health Service Policy on Humane Care and Use of Laboratory Animals can be found in Chapter 4206 of the NIH Manual and Chapter 1-43 of the PHS Manual. The NIH originally initiated the Policy in 1971. It was extended to all PHS activities January 1, 1979, and was revised in the spring of 1985 with implementation to be effective January 1, 1986. With the passage of the Health Research Extension Act of 1985 (PL-99-158), the Policy was further revised and the Director of the NIH was required by law to establish guidelines, which heretofore had only been a matter of PHS policy. An additional revision was released in September 1986, which reflected the changes required by this Act.

Under the PHS policy, each institution using animals in PHS-sponsored projects must provide acceptable written assurance of its compliance with the Policy. In this Letter of Assurance the institutions must describe:

1. The Institutional Program for the Care and Use of Animals

2. The Institutional Status

3. The Institutional Animal Care and Use Committee (IACUC)

The Institutional Program must include a list of every branch and major component, the lines of authority for administering the program; the qualifications, authority and responsibility of the veterinarian(s), the membership of the IACUC and the procedures, which they follow, must be stated. The employee health program must be described for those who have frequent animal contact. A training or instruction program in the humane practices of animal care and use must be available to scientists, animal technicians and other personnel involved in animal care, treatment and use. The gross square footage, average daily census and annual usage of each animal facility must be listed.

The Institutional Status must be stated as either Category one (1) (AAALAC accredited) or Category two (2) (non-accredited). Institutions in Category two (2) must establish a reasonable plan with a specific timetable for correcting any departures from the recommendations in the “Guide for the Care and Use of Laboratory Animals”

The IACUC must be appointed by the Chief Executive Officer and consist of at least five members; one of whom is a veterinarian, a practicing scientist, an individual whose expertise is in a non-biological science and an individual who is not affiliated with the institution. This IACUC must use the Guide to review the animal facilities and the institutional program for humane care and use of animals at least once every six months and prepare reports of these evaluations for the responsible institutional official. The IACUC must review and approve animal-related components of proposals and significant modifications made in ongoing activities involving the care and use of animals.
The IACUC is responsible for reviewing concerns involving the care and use of animals and making recommendations to the Institutional Official regarding any aspect of the animal program, the facilities, or the personnel training. They are also authorized to suspend activity involving the care and use of animals as set forth in the PHS Policy. In reviewing the animal care and use component of a proposal, the IACUC must confirm that the project will be conducted in accordance with the AWA and consistent with the recommendations in the *Guide*. In addition, all procedures are reviewed to assure that pain or distress will be minimized and that (when necessary) appropriate anesthetics, analgesics and tranquilizers will be used. The living conditions and medical care available must be appropriate for the species used, and personnel conducting the procedures must be appropriately trained and qualified. Methods of euthanasia should be consistent with the recommendations of the American Veterinary Medical Association Panel (AVMA) on Euthanasia.

The PI is responsible for completing a proposal in accordance with recommendations in the PHS Policy and the instructions contained in the PHS 398 application packet.

The institution is responsible for maintaining all necessary records to document compliance with the PHS Policy and for filing annual reports which detail any changes in the program and indicate the dates of the semi-annual inspections and program reviews.

The PHS Policy described above is intended to implement and supplement the “U.S. Government Principles for the Utilization and Care of Vertebrate Animals in Testing.” The nine principles are published in the PHS Policy and the Appendix of the *Guide*. All those responsible for the design, supervision and review of the animal care and use component of a proposal should be familiar with this document.
COMMUNICATION

COMMUNICATING ANIMAL WELFARE CONCERNS

There are many animal welfare and animal rights organizations active in the United States and internationally. These organizations, to varying degrees, disapprove of the use of animals in research. They make every effort to halt, through legal and sometimes illegal means, any research program involving laboratory animals, which they feel, makes unnecessary or cruel use of laboratory animals. It is likely that the controversy surrounding the use of animals in research will remain a prevalent issue for many years to come.

The policies and procedures in place at the University of Delaware are designed to ensure that research animals are used humanely. When an animal welfare or animal rights organization expresses concern with a research program being conducted at the University of Delaware, the administration works with the IACUC to address that concern, while at the same time protecting the PI’s confidential and/or proprietary information.

Whenever animal research is ongoing at an institution, concerns may arise regarding whether or not the use of laboratory animals complies with all applicable Federal and State regulations, and institutional policies. All members of the faculty and staff are urged to communicate any animal welfare concerns that may arise. Such concerns should be communicated directly to the IACUC as a whole, any member of IACUC, or a member of the OLAM staff. All correspondence shall be held in the strictest confidence, and under no circumstances is any form of disciplinary action taken against members of the faculty or staff as a result of reporting an animal welfare concern.

This is not in any way intended to deter members of the faculty or staff from bringing any concerns that might arise directly to their supervisors, department chairpersons, or the OLAM staff.

COMMUNICATION BETWEEN FACILITY STAFF AND INVESTIGATORS

The OLAM staff contacts PIs in person, by telephone, or e-mail to convey information regarding animals that become sick, have died, or have been newly received.

When the facility staff finds overcrowded cages, the PI is informed by telephone or e-mail that the PI must remove animals from the overcrowded cage(s), or they will be removed and placed in new cages by the facility staff. When sick animals are discovered by the facility staff, the PI is contacted by the AV to discuss and plan a treatment program for the affected animal.
COMMUNICATION BETWEEN INVESTIGATORS AND FACILITY STAFF

It is often necessary for PIs to communicate special handling information regarding certain animals to the AV or the facility staff. To do so, PIs should contact the FM to discuss the special handling requirements. The FM, or staff, will then prepare special cage cards with the pertinent information.

Cards that indicate “DO NOT WATER”, “DO NOT FEED”, “FEED SPECIAL DIET”, “AUTOCLAVED CAGE ONLY” etc., can be prepared by the OLAM staff to ensure that the AV and husbandry staff handle these animals in the appropriate fashion.

ANIMAL CARE AND USE PROTOCOLS

Questions regarding Animal Use Protocols (AUPs) should be directed to either the IACUC Coordinator or the FM depending upon the nature of the question. Investigators with scientific questions regarding animal models, drugs, or procedures, should contact the AV. Questions concerning use of the AUPs, IACUC policies, IACUC meeting schedules, or the approval status of a particular study, should be directed to the IACUC Coordinator.
TRAINING

Participation in the animal facility-training program is a prerequisite for the activation of a protocol for the use of laboratory animals in research, and for access into the AF at the University of Delaware.

The training program consists of 2 components:

General orientation

Tour of the Animal Facility

Arrangements for participating in a training session may be made by contacting the FM at extension 2400. The general orientation includes a brief overview of the facility, the laws and regulations pertaining to animal research, AUP forms, Occupational Health and Safety (OHS) issues, information on animal procurement, husbandry services, veterinary services and per diem charges. Any questions pertinent to specific animal research programs in the PI’s laboratory are addressed at this time.

After completing the general orientation, the personnel must tour the facility in order to be granted security access. The tour includes instruction in proper handling of the species being used, emergency information needed and instruction on rodent euthanasia.

Following the tour, the training form will be signed and access granted.

Training in Animal Handling and Experimental Techniques

OLAM staff is available to provide more extensive instruction in proper animal handling and various experimental techniques than those which are demonstrated on the tour. Many of the animals used in research require handling and restraint that is peculiar to a particular species. If anyone plans to use an animal which they are not familiar with, they must schedule an animal handling training session with a member of OLAM before conducting animal work.
THE IACUC AND THE ANIMAL USE PROTOCOL FORM

OBTAINING AUP APPROVAL

Each study involving laboratory animals must be submitted for review by the IACUC on the current Animal Use Protocol (AUP) form.

The AUP New/3-Year Renewal form is used for any new project, whether departmental, or funded by external sources. This form covers three (3) consecutive years. An AUP Annual Review form is required by the USDA for the 2\textsuperscript{nd} and 3\textsuperscript{rd} year. For any major changes in the study design, animal procedures, increase in animals or to add or delete personnel, an AUP Amendment form is required. After the third year, the PI must submit a New/3-Year Renewal form.

When a PI submits an Amendment Form, the changes will be incorporated into the approved protocol after the IACUC has approved the amendment.

IACUC PROCEDURES AND RESPONSIBILITIES

The primary responsibility of the IACUC is the review of PI’s proposals to use laboratory animals in research. To facilitate this review and expedite activation of the study, the IACUC AUP Form has been carefully designed to request all the information required for review by IACUC.

It is extremely important that each PI’s AUP(s) accurately and completely describe the animal work being conducted. These forms are reviewed not only by the IACUC, but also by inspectors from the USDA. In conjunction with the health of the animals and condition of the physical plant, the quality of the IACUC approved AUPs reflects the overall quality of the University of Delaware program of Animal Care and Use.

The IACUC meets twelve (12) times during the year. The meeting date is normally either the first or second Monday of each month. The meeting schedule can be found on the Research Calendar on the website.

AUPs should be submitted by PIs at least 90 days in advance of the intended start date to allow ample time for IACUC review and approval.

ANIMAL USE PROTOCOL FORMS

The AUP forms can be downloaded from the IACUC website.
ANIMAL USE PROTOCOL APPROVALS

When submitting an application to any branch of the Public Health Service, or other funding biomedical research, the IACUC approval date will be required.

Both PHS and the USDA require that all research involving animals receive review by an IACUC. PHS policy requires that this review be performed at least once every three years. USDA regulations require that this review be performed on an annual basis. The University of Delaware complies with both PHS and USDA policy by requiring an annual review and 3-year renewal.

Every AUP must be submitted for approval by the IACUC. Each AUP is assigned an AUP 4-digit number. Once the AUP is approved, it is then signed and dated by the IACUC Chair. The next review for this AUP will be one year from the date of signed approval.
OLAM POLICIES FOR FACILITY USE AND SAFETY

All PIs should be familiar with OLAM use and safety policies and procedures for their own protection, and the protection of the research animals.

OFFICE HOURS

The OLAM Office is staffed from 7:00 a.m. to 4:30 p.m. Monday through Friday. After 4:30 p.m., or weekends and holidays, PIs may leave voice mail messages for any staff member.

In the event of an emergency, the FM may be reached during off hours by contacting the University Police/Public Safety at 302-831-2222.

FACILITY SECURITY

For faculty and staff to gain access to the AF, they must have ID cards that have been approved to be scanned by the card reader at the facility entrance.

Individual animal rooms are kept locked at all times. Keys are distributed to faculty and research staff who have participated in the training program.

ENTERING THE FACILITY

Anyone entering the AF must wear a lab coat, shoe covers, bouffant cap, gloves, mask and safety glasses.

REPORTING PROBLEMS

Should a PI or staff member detect apparent problems in the AF such as an animal room where the temperature control appears to be malfunctioning, the FM should be contacted immediately.

Should a problem occur after hours, or on weekends or holidays, contact Public Safety (302-831-2222). Public Safety will coordinate with Plant Maintenance and the FM to ensure that the problem is corrected in a timely fashion.

STORING EQUIPMENT IN ANIMAL ROOMS

No equipment may be stored in any animal rooms without the prior permission of OLAM’s FM. OLAM is not responsible for the loss of any supplies, research notes, or
equipment left in animal rooms. Any equipment brought into the AF needs to be wiped with a disinfectant prior to entering the AF.

REMOVAL OF OLAM EQUIPMENT

Equipment belonging to OLAM, with the exception of cages and water bottles, should not be removed from the AF for any reason. PIs who take animals from the AF may maintain those animals for no longer than 12 hours outside of the AF. If a PI’s research program requires that animals be housed outside of the AF for a period in excess of 12 hours, a justification for the special housing requirements must be included in the PI’s AUP, and must be approved by the IACUC.

CAGE POPULATION

Different species have different requirements for cage size and the number of animals that can be housed together in a cage of a given size. These caging requirements are summarized in and based upon the USDA regulations and the ILAR Guide recommendations.

DISPOSAL OF NEEDLES, SYRINGES, AND OTHER SHARPS

Each procedure room contains a specially constructed box for the safe disposal of sharp objects. Full sharps boxes are disposed of by facility staff.

All used needles, syringes and scalpel blades are considered contaminated and should be disposed of immediately after use. Needles should never be recapped, bent, broken or cut before disposal.

RESEARCH ANIMAL TRANSPORTATION POLICY

The OLAM policy on transportation has been designed to standardize animal transportation practices and to minimize contact between research animals, visitors and employees. All animal transportation throughout the building is accomplished in a safe, clean manner and in a manner that minimizes visibility.

All users should keep in mind that USDA regulations prohibit keeping animals outside the AF for periods in excess of 12 hours. A proposal to maintain animals outside of the AF for a period in excess of 12 hours must be approved by IACUC. Such approval shall not be granted until the IACUC has inspected the temporary housing area, and found it to meet all of the provisions of the ILAR GUIDE and USDA regulations.
CONTAINMENT DURING ANIMAL TRANSPORT

Containment must provide adequate ventilation for the animals, while minimizing visualization.

Types of acceptable containment are:

1. **Rodents:** Commercially available ventilated cardboard rodent transport boxes or opaque shoebox type cages with filter tops.

2. **RABBITS:** Commercially available ventilated heavy plastic (cat) carriers. Approved carriers are available by purchase or loan from OLAM. Carriers should be returned to the animal facility for sanitation after each use.

TRANSPORTATION TO LABORATORIES

When moving animals from the AF in which they are housed to on-campus laboratories outside the AF, the sensitivities and safety of others not engaged in animal research should be kept in mind at all times. **AVOID PUBLIC AREAS** such as classrooms, elevators external to the AF and lobbies. During transportation of animals, PIs must abide by the following procedures:

1. All methods of transporting animals must provide for the health and welfare of the animals.
2. The animals must be adequately restrained or caged to prevent escapes. Transport enclosures must be escape proof, adequately labeled, provide adequate ventilation, and able to be sanitized or disposed of to prevent the spread of pathogenic microorganisms, chemicals or radioactive materials where indicated. The enclosures should be opaque or shielded in such a way as to be non-stressful to the animals. See above instructions for proper enclosures for each species.
3. Care shall be exercised in handling enclosures to ensure that they are not tossed, dropped, needlessly tilted, stacked in a manner which may reasonably be expected to result in their falling, or handled in any manner which may cause physical trauma or stress to the animals.
4. Temperature extremes are to be avoided when animals are transported. Special precautions or postponements are required when temperatures are below 45 degrees Fahrenheit or above 85 degrees Fahrenheit.
5. Water bottles are to be removed or inverted on the cage to prevent leakage of water into the cage in transit.
6. The separation of the sexes must be maintained in transit.
7. Laboratory work areas are to be disinfected before and after working with animals, to prevent cross-contamination to or from the other animal rooms.
TRANSPORT OF ANIMALS TREATED WITH HUMAN PATHOGENS OR HAZARDOUS CHEMICALS

Warning labels are required on enclosures used to transport live or dead animals that have been exposed to biohazards or chemical hazards. The specific hazard must be identified and carcasses must be transported in accordance with OHS hazardous material policies.

TRANSPORT OF ANIMALS TO LOCATIONS OUTSIDE THE ANIMAL FACILITY

OLAM arranges for the preparation of necessary shipping boxes, health certificates, and common carrier transportation. A written note that includes the number of animals, the strain, the destination, the sex, and the experimental/health status must be received prior to OLAM receipt of the animals for shipping.

EXCEPTION AUTHORIZATION

Temporary exceptions to this policy are to be proposed in the AUP submitted to the IACUC. The Committee, in consultation with the AV, will determine whether or not an exception to this policy may be granted.

REGULATIONS AFFECTING POLICY

NIH Publication #85-23 (revised 1985); NIH Guide for the Care and Use of Laboratory Animals

Department of Agriculture Animal Welfare Regulation (9 CFR Parts 1,2,3)
CDC/NIH Biosafety Guidelines

Copies of these publications are available in the OLAM office.

HEALTH AND HAZARDS IN THE USE OF LABORATORY ANIMALS

BIOHAZARD CONTAINMENT

Occasionally, it is necessary for a PI to conduct an animal experiment which involves hazardous materials. Hazardous materials include, but not limited to, toxic chemicals, microbial pathogens and other infectious agents, radioisotopes, and carcinogens.
When preparing to submit a study that will involve hazardous materials, the PI should seek the assistance of the AV, and the Department of OHS.

Arrangements for special housing requirements may be made with the Facility Manager. Special housing includes the selection of appropriate animal caging systems and ventilated cabinets and hoods.

The PI must coordinate with Environmental Services or Radiation Safety regarding the decontamination of work areas, and the safe handling of these materials to prevent exposure to laboratory or facility staff.

**DISPOSAL OF RADIOACTIVE MATERIALS**

Disposal of radioactive animal waste is highly restricted and regulated by the Department of OHS. Arrangements must be made for the storage of radioactive materials. AUPs proposing the use of radioisotopes, where these materials are being used in sufficient concentration to present a potential hazard to humans, require special review by the Radiation Safety Committee.

**OCCUPATIONAL HEALTH PROGRAM FOR PERSONNEL WORKING WITH LABORATORY ANIMALS**

The NIH Guide states that an occupational health program is mandatory for anyone working in an AF or having substantial animal contact. The OLAM, in conjunction with Employee Health Services and the OHS, has designed the occupational health program to comply with the recommendations in the NIH Guide. There is a brochure and guideline for Occupational Health Policy for Personnel Working with Laboratory Animals, which describe the program in detail. This policy brochure and guideline is available from the OLAM office.

PIs should ensure that all members of their staff working with laboratory animals are familiar with the information contained in the employee health brochure.

**LABORATORY ANIMAL ALLERGY**

Individuals who have frequent contact with laboratory animals often develop hypersensitivity or allergy to animal dander. Such reactions occur in approximately 30% of those with frequent exposure to animals. Individuals already allergic to other environmental substances are at greater risk. Such allergies can progress to serious conditions such as asthma, which can be fatal. Animal users who are sensitive to such allergens should wear tight-fitting masks. At the first sign of hypersensitivity, the user should reduce animal contact and go to Christiana Care Occupational Health Services or contact the Department of OHS.
AVAILABLE SERVICES

The OLAM Staff is available for consultation on animal models, strain physiology, veterinary medicine, availability and sources of animals, techniques for animal research or diagnostic tests.

All questions concerning services and supplies offered by OLAM should be directed to the FM.

SERVICES

Animals Found Dead: Animals found dead in animal rooms are removed and placed in plastic bags, and identification is affixed to the outside of the bags. For a cage that houses several animals, the date and number of animals found dead are recorded on the cage card. PIs are notified of animal deaths by telephone or e-mail.

Care of Sick Animals: The technical staff provide for nail trimmings, teeth trimmings, and other minor procedures. If the staff detects a sick animal, the appropriate person is contacted before treatment is begun, if at all possible. The nature of the intervention to be undertaken is determined in consultation with the PI. All treatments are recorded in the individual Animal Health Record.

SUPPLIES

OLAM can provide animal users with the following:

- Restraint devices for rabbits, rats, mice
- Extra cages for rodents
- Certain types of Personnel Protective Equipment

Anesthetic and analgesic drugs are available by contacting the FM, AV or AHT.

Extra rodent cages and water bottles are available for use in animal rooms. Extra cages and bottles are kept in the clean cage storage room. Those anticipating a need for a large number of cages and water bottles for procedures such as weaning or separating groups of animals, should contact the FM at least 24 hours in advance to ensure their availability.

DIAGNOSTIC SERVICES

There is a laboratory within OLAM in which necropsy and parasitology on rodents can be performed. OLAM can also arrange for an outside laboratory to perform histopathology evaluation, testing for murine viruses and animal pathogens not screened for in-house, and hematology, clinical chemistry, microbiology and slide preparation.
SURGERY

OLAM has a full service accredited Surgical Suite available to the PIs. Please contact the FM or AHT to reserve the Suite.

No animal may be used in any surgical procedure until the applicable quarantine period has elapsed. PIs should take the required quarantine periods into consideration when scheduling surgery.

SURVIVAL SURGERY PROCEDURES

Survival surgery procedures are those invasive procedures in which the animal recovers consciousness before euthanasia. All survival surgery, regardless of the animal species involved, must be done using aseptic technique.

Rodent

A dedicated portable rodent surgery table is available in the AF. If use of this table is required, please call the FM or AHT to reserve.

Survival surgery procedures in rodent species may be performed in an area of the PI’s laboratory that has been specially designated for this purpose. The IACUC, as part of its semi-annual review of the program of animal care and use, makes visits to the laboratories of PIs conducting rodent survival surgery. Additionally, the AV must visit the laboratory to observe the surgery technique of the research staff and to ensure that aseptic practices are being followed.

MULTIPLE SURVIVAL SURGERIES

Performance of multiple major survival surgical procedures on one animal is strongly discouraged by OLAM and IACUC.

INSTRUMENT PREPARATION

The USDA regulations and the Guide require that all instruments used in survival surgery be sterilized. In general, packs of instruments or other materials that have been sterilized and are to be stored for long periods should be double-wrapped.
EUTHANASIA AND OTHER PROCEDURES

COLLECTION FROM ANIMALS

The OLAM technicians are available to assist PIs with phlebotomy or exsanguination. PIs may request this assistance by e-mail or telephone.

Animals must be anesthetized prior to exsanguination. Exsanguination of a properly anesthetized animal can yield up to 50% of the animal’s blood volume.

For bleeding of animals, a period of at least two weeks should be allowed between routine bleedings. This period allows the animals to recover lost blood volume and replace lost blood components. If a PI desires a more intensive schedule of blood drawings, a justification must be included in the AUP submitted to the IACUC for review.

ACCEPTABLE IMMUNOLOGICAL PROCEDURES INVOLVING COMPLETE FREUND’S ADJUVANT

The choice of a correct adjuvant is an important consideration when designing a protocol that includes immunization procedures. Complete Freund’s Adjuvant (CFA) may be used only when small amounts of soluble immunogens are available. CFA is typically administered as an emulsion including equal volumes of CFA to antigen (1 part CFA or less to 1 part antigen). If large amounts of particulate, or highly immunogenic immunogens are available, other adjuvants should be considered. CFA should be used only for the most problematic immunization situations. It must never be given in repeated doses.

Sound scientific evidence and justification must be presented in the research protocol if the intradermal route of injection of CFA is to be used because of the frequent ulcerations that occur at the site of such injections. The use of the intradermal route may be justified only when the purpose is to induce cell-mediated response. This route is inappropriate in the mouse or other rodents.

Rabbits

In rabbits, volumes of inoculum in excess of 0.05mls (50 microliters) per intradermal site should not be used. The location of the site(s) should be carefully selected so as to prevent mutilation. A minimal number of sites should be selected and the distance between each site maximized.

In rabbits, the site of choice for subcutaneous immunization is the inter-scapular region (between the shoulder blades) on the dorsum (back), administering up to 0.25ml of inoculum (250 microliters) per site, to a maximum of four sites. The distance between sites should be maximized. In rabbits, intramuscular injections of CFA may be administered in the thigh muscle: up to 0.5ml (500 microliters), preferable in one site.

CFA should not be injected into the footpad of a rabbit.
**Mouse**

The *intraperitoneal* route for injection of CFA is permitted in small rodents only. CFA should be administered only once, and be limited to minimal volumes of up to 0.1ml (100 microliters).

IM injection of CFA is not recommended for small laboratory animals such as rats or mice.

Footpad injection of CFA in rodents is not permissible in the absence of compelling scientific justification. Only one footpad may be used in any case. Rodents receiving footpad injection must be maintained on soft bedding and not on wire-bottomed cages.

**CFA should never be injected intravenously.**

The injection sites must be observed by the PI or his/her designate, a minimum of three times per week, for four weeks after each injection. If any animal exhibits any discomfort from an injection, it must be reported through established channels, e.g., the FM or the AV, and must receive appropriate veterinary treatment.

**INDUCTION OF ASCITES FLUID IN ANIMALS**

Pristine or other recognized priming agents (excluding CFA) may be used. The dose of pristine should not exceed 0.1ml. In no case should more than 0.2ml of pristine be injected. Ascites may be collected only for as long as the animal is not experiencing pain or distress, is in good body condition, and does not show signs of debilitation, dehydration, or other complications from the procedure. Daily observation for abdominal distension and poor general condition (rough hair coat, dyspnea, and lack of mobility) should be performed. Upon recognition of loss of condition, pain or distress, the animal must be euthanized according to the method described in the PI’s approved AUP.

**EUTHANASIA AND ANIMAL DISPOSAL**

All AUPs reviewed by IACUC must include a description of the method of euthanasia that will be used. The method of euthanasia selected must be consistent with the recommendations of the AVMA Panel on Euthanasia (March 2000). A copy of the *Journal of the American Veterinary Medical Association* article, which presents the AVMA Panel’s proceedings and findings, is available for perusal in the OLAM office. Should a PI’s research require that a method of euthanasia be employed which is not consistent with the AVMA Panel recommendations, a compelling justification must be provided to IACUC for review.

The use of dry ice as a method of Euthanasia is not approved by the AVMA.
The OLAM AV is available to consult with investigators on the appropriate method of euthanasia best suited to the particular species. The OLAM technicians will euthanize animals for PIs if requested to do so. To obtain the assistance of the OLAM technicians, PIs should write “SAC” on the appropriate cage card(s).

Together, these two required procedures ensure that the proper animals will be killed, the carcasses disposed of, and the appropriate number of animals subtracted from the PI’s inventory sheet.

The University employs a “Double Kill” policy for euthanasia. PIs who choose to euthanize animals themselves must be certain that they do so in the manner described in the PI’s IACUC approved AUP.
ANIMAL PROCUREMENT

Animal orders must be placed by sending an e-mail to Julie Mls at pugsley@udel.edu and copy Frank Warren at fwarren@udel.edu. Completed orders should include vendor, species, strain, sex, age, amount, PI, AUP number, and the date of delivery. These orders should be sent out by 12 noon on Fridays. All animal orders are posted on a board in the AF after they have been placed, so the expected arrival is known.

If an arrival delay is expected, the AUP is notified of the expected shipping date and also notified if problems arise concerning availability and source of animals. If no one is available to authorize a change in the order, it will be held until a change is approved.

The availability, strains, source cost, delivery dates, etc. can be confirmed with OLAM before an order is placed. If a particular vendor is desired, this must be indicated. OLAM will only place orders with approved commercial vendors. If a PI has any concerns about a vendor, he/she should check with the OLAM staff before completing the purchase form.

Animal Sources/Health Conditioning

Most animals used in experimental research are purpose bred and conditioned to the laboratory environment. Health, genetics, and clinical status reports of purpose-bred animals generally are available from the supplier.

Non-vendor Animal Sources

If a PI intends to receive animals from a non-vendor, such as another University, this information must be provided to the OLAM office. Prior to receipt of the animals, the OLAM staff must be provided with health profile information for the incoming animals. Animals will be quarantined in a room outside of the AF until a clean serology report comes back on the animals.

Reassignment of Unused Animals

PIs who find they have excess animals should contact the FM to discuss making arrangements to transfer the animals to another PI. The FM, in consultation with the AV, will endeavor to find another PI who can make use of the animals. When both PIs have agreed to the transfer, the FM will update the OLAM records to reflect the transfer.

PIs wishing to make advance arrangements for the transfer of animals as an alternative to euthanasia must include these arrangements in the AUP submitted to the IACUC for approval.
RECEIVING ANIMALS

Standard procedures for receipt and quarantine of animals in the AF vary according to species. The current procedures, presented by species, are:

Rodents: 75% of purchased rodents arrive from a single approved vendor. Almost 100% of commercially obtained rodents derive from four major suppliers. The AV reviews health surveillance reports from all approved vendors on a regular basis.

Available housing at the AF are conventional, micro isolator and ventilated rack. Incoming animals from approved commercial sources are housed for 6 days in the quarantine room before being incorporated into an appropriate existing room. Non-approved animals arriving from an academic institution or other non-commercial source are placed in a non-approved quarantine room with sentinel animals for five weeks. The AV directs the transfer from quarantine to permanent housing space based on the analysis of the sentinel data.

Rabbits: All rabbits are incorporated directly into an existing rabbit room.

PIs will be notified by phone or email if OLAM staff detects any problems when animals arrive at the AF. In order to protect the health of the animal colonies, it is essential that animals or equipment not be transferred from one room to another without authorization from the OLAM FM.

Since very specific types of research are conducted at the satellite animal facilities, each satellite facility has its own procedure for quarantine of newly arrived animals.

CAGE CARDS

Cage cards are produced in the OLAM office in advance of the receipt of animals, and are used to identify every animal in the AF. Cage card information includes: species, strain, sex and number of the animals in that cage, and PI. The animal’s date of birth, arrival date into the AF and AUP number is also included on the cage card.

EXTRA CAGE CARDS ARE AVAILABLE UPON REQUEST.
DELIERY OF ANIMALS

All research animals delivered by courier into the AF are received by OLAM staff. All shipping boxes are sprayed with a disinfectant prior to entering the AF. Special arrangements must be made with the OLAM FM for after hour deliveries.

IDENTIFICATION OF ANIMALS

It is often important to identify specific animals in a colony. Acceptable methods are available for permanently identifying each animal in an experiment. Suggested methods of identification are listed below:

- Rats and mice: ear notch, ear tag, tattoo, cage ID or ink marker
- Rabbits: ear tag or tattoo

SEPARATION OF ANIMALS BY SPECIES AND PRINCIPAL INVESTIGATOR

The OLAM FM coordinates the distribution of animals to various housing rooms. Each room houses only one species. If a PI has enough animals of one species to occupy a room to its full capacity, only that PI’s animals are assigned to that room. In some cases, however, PIs share animal rooms.

Each room has an inventory sheet for every PI who has animals housed in that room. When animal room assignments are changed, the OLAM FM will contact PIs and inform them of the new room location.
ANIMAL CARE

VETERINARY CARE

The OLAM staff and AV provide health surveillance on an ongoing basis, and veterinary care as indicated. The AV communicates any health problems that are detected to the responsible PI. If the PI does not respond to the AV, the AV then uses judgment in determining how best to treat the diseased animal. Every effort is made to contact the PI before sick animals are euthanized.

The PI and his/her research staff play an important role in maintaining the success of the OLAM animal health program. PIs may contribute to the health program in the following ways:

1. Contact OLAM staff whenever unexpected morbidity or mortality is observed.
2. Work with only one group of animals at a time. Sterilize all equipment before working with a different group of animals.
3. Animals, cell lines, and other biological materials brought to the university from other facilities or institutions may carry potentially infectious adventitious viruses. Arrangements should be made with the FM or AV to review the health status of any animal coming from a source other than an approved vendor. Cell lines and other biological materials must be screened for potentially infectious organisms before the materials are brought into the AF.

ROUTINE ANIMAL HEALTH CARE

Animals are observed daily by the animal technicians. If an animal appears to be sick, a health record is initiated for the animal in which the clinical observations, possible cause of the problem and proposed treatment plan are documented. The PI is consulted before treatment is administered. PIs are also contacted via phone or email to be informed of over-crowded cages. The PI is expected to separate the cage within 2 days after which the cage will be separated by OLAM staff.
MAINTENANCE OF ANIMAL ROOMS

Animal husbandry staff inspects each animal daily.

PIs who work in animal rooms and work areas are required to clean the area upon completion of their work.

WEEKEND AND HOLIDAY STAFFING

The AF is staffed every day of the year. Technicians enter each animal room on weekends and holidays to check for problems. Any cages that have become wet, or otherwise require immediate changing are changed.

Should a PI require the assistance of the AV or OLAM staff on a weekend or holiday, arrangements should be made in advance by contacting the FM.

CLEANING SCHEDULES

Animal rooms are swept and mopped daily. Corridors are swept and mopped daily. All animal rooms are sanitized monthly and corridors are sanitized quarterly.

Animal cages and pans are cleaned according to the following schedule:

Mice: all cages are changed no less than 1x/week
Rats: all cages are changed no less than 1x/week
Rabbits: all cages are changed 1x/week and pans are cleaned 3x/week

Bedding materials are selected for their clean source, minimal dust, innocuous composition, and ease of sterilization.

All racks are washed and sanitized every two weeks and documented in the Rack Wash Log.
ESCAPED OR UNIDENTIFIED ANIMALS

If a wild or escaped animal is recovered in the AF, it is euthanized by the staff and a serology assessment is conducted. The following precautions can help prevent escape and subsequent identification problems:

1. A mouse can pass through a 1-centimeter space. Make sure all cage tops are properly closed.

2. Mouse tops are smaller than rat tops. Make sure the proper equipment is chosen when putting together caging supplies.

3. An escaped animal should never be placed in any cage other than an empty cage.

All rodents are fed ad libitum unless a PI’s IACUC approved AUP requires restricted feeding. Rabbits are fed regulated diets intended to prevent obesity. OLAM uses commercially formulated diets as its primary feed source. All food in the AF is dated and stamped to ensure freshness.

Feed composition and analysis sheets are available from the FM. PIs can request that supplements be fed in combination with the prepared feed.

WATER

All animals are supplied with water bottles. The staff checks the functioning of these bottles to ensure that animals are receiving adequate water and that leakage does not present a drowning threat to the animals.

OLAM can provide acidified, autoclaved, or otherwise treated water. Requests for such services should be directed to the FM.

OBTAINING HUSBANDRY SERVICES

Husbandry services, such as the provision of extra cages, water bottles, tops and/or cage cards, may be requested by calling the FM.
SECURITY ACCESS TO ANIMAL FACILITIES

In order to access the AF, PIs and their staff must participate in the Animal Care and Use Training Program, and arrange to have their ID card activated by the FM. An activated ID card is required to gain access to the AF.

ANIMAL FACILITY HOUSING ROOMS

Each animal room contains inventory sheets for all animals housed in that room. If multiple PIs share a room, individual inventory sheets are provided for each PI.

No animal may be housed in the facility without an appropriate cage card. Cage cards are produced by OLAM. PI’s name, approved AUP number, species, strain, sex of the animal, date of birth and date of arrival are noted on cage cards. The cage card also provides any information requested by the PI.

INVENTORY SHEETS

Each animal room contains an inventory sheet for each PI housing animals in that room. As cages are added or removed, the appropriate notation is to be made on the inventory sheet.

The inventory sheets are collected monthly by the OLAM staff, and used to calculate per diem charges for that month.

The technical staff performs an actual count of all animals weekly. Any discrepancies between the actual count and the inventory sheet total are indicated and corrected on the inventory sheet.

ENVIRONMENTAL CONTROLS IN THE ANIMAL ROOM

Temperature control in the animal room is regulated by the FM. A table describing the recommended relative humidity and dry bulb temperature for common laboratory animal species may be found in the ILAR Guide.

Any variation in temperature, or presence of excessive animal odors indicative of inadequate ventilation, should be reported to the FM.

Illumination in the animal rooms is provided by fluorescent ceiling lights. Animal circadian rhythms are maintained by a timer, which turns all animal rooms lights on at 6:00 a.m. and off at 6:00 p.m. Special arrangements can be made with the FM if a PI’s animals require an alternate light cycle.
BILLING FOR SERVICES

MONTHLY BILLING

Per diem charges and procurements are charged at the end of each month in the form of a Journal Voucher for internal billing and an Invoice for external billing. Monthly statements are sent to all PIs who are currently being charged per diems for their review of the charges.

Each monthly statement includes the name of the PI, dates of billing period, and charges for per diem and animal purchases.

Animal Orders: The animal purchase portion of the monthly statement shows the date the animal was received at the AF and amount of purchase. Attached to the monthly statements are copies of the invoices from animal vendors.

Per Diem: Per diem is the cost of caring for each animal per day. The total number of care days is determined by multiplying the number of days in the billing period by the number of cages. This number is then multiplied by the per diem rate for the cost center to yield the total amount charged. The per diem portion of the monthly statement shows the number of care days, per diem rate and cost.

DISCREPANCIES

If a PI reviews his/her monthly statement and detects a possible discrepancy in the charges, he/she should contact the OLAM office. Any changes or corrections in monthly charges will be adjusted on the following month’s billing.

PER DIEM CHARGES

Per diem rates apply to routine animal health care, housing, sanitation, feeding, watering, and daily monitoring of research animals housed in the AF.

Per diem charges are calculated to allow the AF to recover costs associated with:
   Animal feed
   Supplies including bedding, cleaning supplies and disposables
   Replacement of broken or worn out caging
RODENT HEALTH MONITORING

The purpose of this program is to establish surveillance for subclinical pathogens that may interfere with research and to attempt to detect clinical pathogens before a clinical problem occurs.

Sentinel Program

Health monitoring of the AF consists of placing at least 4 naïve sentinel animals in each rodent room. On a quarterly or as needed basis, blood is drawn from the animals, and the serum is sent to Charles River Laboratories. The test panel conducted at Charles River is the Mouse Assessment Profile and/or Rat Assessment Profile, which consist of testing for 12 murine viruses.

During this time, one animal is removed to have a complete necropsy conducted by the AV and tape test to monitor for pinworms.

Helicobacter is tested for all newly arrived animals into the AF.

Micro Monitoring Program

Monthly, all animal rooms and other randomly chosen parts of the AF are tested for growth of bacteria, molds or yeasts. This test consists of placing agar coated strips directly onto the surface, sealing the test vial after sampling, placing them into an incubator for 48 hours and then reading the results.

All records of sentinel animals and micro monitoring are maintained in the FM’s office.
EMERGENCY INFORMATION

OLAM works closely with the Department of OHS to ensure that work areas and conditions are as safe as possible for the users of the facility.

Below are contact numbers and information that should be referred to in the event of an emergency.

- University Public Safety/Police x2222
- University OHS x8475
- University Biosafety Officer x1433
- University Chemical Hygiene Officer x3123
- University Radiation Safety Officer x1434
- University Fire Marshall x6847

In the event of a power failure, the lights in the rooms will go OFF but a few light panels will remain lighted in the hallways to help with an exit.

Also there are a series of EXIT signs that will act as a guide in the event of an emergency. While in the AF, all personnel should become familiar with these signs and all other emergency items that have been described.