Office of Research Services
Facility Policies and Procedures

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(Revision 2)

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INTRODUCTION

This document is intended to be used as a supplement to the UML Institutional Animal Care and Use Committee Policies and Procedures for faculty, staff, and students who use the facility for animals in research, testing, and instruction. Activities involving animal use are regulated by the federal government. The UML Institutional Animal Care and Use Committee (IACUC) is appointed by the Institutional Official (IO) to ensure compliance with all regulations. This document outlines the policies and procedures that the IACUC and UML community will follow to meet these regulatory requirements. It is intended to communicate information necessary to make the process clear and easier for those who are involved in animal care and use at UML. The Public Health Service (PHS) Office of Laboratory Animal Welfare Institutional Animal Care and Use Committee Guidebook states that "Proper housing and management of animal facilities are essential to animal well-being, to the quality of research data and teaching or testing programs in which animals are used, and to the health and safety of personnel. A good management program provides the environment, housing, and care that permit animals to grow, mature, reproduce, and maintain good health; provides for their well-being; and minimizes variations that can affect research results. Specific operating practices depend on many factors that are peculiar to individual institutions and situations. Well-trained and motivated personnel can often ensure high quality animal care, even in institutions with less than optimal physical plants or equipment." The purpose of this policy and procedure manual is to ensure that all aspects of housing and management of animal facilities meet these guidelines.

While recognizing the importance of using live vertebrate animals for these purposes, UML, for both ethical and scientific reasons, insists upon the highest standards for the care and use of such animals. It is the responsibility of each individual using and/or caring for animals to be familiar with, and to ensure compliance with, these standards. The Institution is required to uphold and comply with the same standards as the PIs. This document is subject to changes and/or updates as rules, regulations, and/or policies change. The most current version will be available on the Institutional Compliance webpage at http://www.uml.edu/ora/institutionalcompliance.

UML has an **Assurance of Compliance with Public Health Service Policy on Humane Care and Use of Laboratory Animals** on file with the Office of Laboratory Animal Welfare, as required by law. This Assurance is signed by the Institutional Official and submitted to the Office of Laboratory Animal Welfare (OLAW). Although the IO has signatory authority and final responsibility to enforce and supervise the requirements of AWA and PHS policy, the IO cannot override an IACUC decision. The Assurance indicates that UML will comply with the Public Health Service Policy on Humane Care and Use of Laboratory Animals, hereinafter referred to as PHS Policy. The Assurance is valid for a period of five years and then a new Assurance must be submitted to OLAW. PHS-conducted or supported activities that involve animals at UML are only allowed to continue with an applicable PHS-approved Assurance in place. At this time, UML is a Category 2 Institution, which means the program and facilities are evaluated by the Institution.

INSTITUTIONAL POLICY

The OLAW Assurance states that UML will:

- Comply with all applicable provisions of the Animal Welfare Act and other Federal statutes and regulations relating to animals.
- Follow the "U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training."
- Acknowledge and accept responsibility for the care and use of animals involved in activities covered by the Assurance. UML will make a reasonable effort to ensure that all individuals involved in the care and use of laboratory animals understand their individual and collective responsibilities for compliance with this Assurance as well as all other applicable laws and regulations pertaining to animal care and use. Oversight is provided by an Institutional Animal Care and Use Committee appointed by the Institutional Official.
- Establish and maintain a program for activities involving animals in accordance with the "Guide for the Care and Use of Laboratory Animals".

Per Diem

Most research institutions charge per diem to cover the daily cost of running an animal facility. Per diem includes specified rates per animal or cage to cover bedding, food, caging, staff, and other incurred expenses. UML currently charges no per diem for animal care and use.

DEFINITIONS

Activities: Include, but are not limited to, research, research training, biological testing, and instruction of students.

Animal: PHS Policy defines an animal as "any live, vertebrate animal used or intended for use in research, research training, experimentation, or biological testing, or for related purposes". The Animal Welfare Act Regulations (AWAR) define an animal as "any live or dead dog, cat, nonhuman primate, guinea pig, hamster, rabbit, or any other warm-blooded animal, which is being used or is intended for use for research, teaching, testing, experimentation, or exhibition purposes, or as a pet. This term excludes birds, and rats and mice bred for use in research." The UML IACUC ensures the campus is in compliance with all regulations by applying the AWAR and PHS regulations to all vertebrate animal use on campus for teaching and research. Studies involving dead animals require reporting and justification to the IACUC but the IACUC does not require the PI to report the use of dead animals via a protocol unless the animals are euthanized for the purpose of the research or teaching activity. The UML IACUC considers embryos and fetuses as vertebrate animals if their central nervous system is sufficiently developed to feel pain.

Animal Facility: An animal facility is any and all areas, buildings, enclosures, rooms or vehicles, including satellite facilities used for: animal confinement, breeding, experiments including surgical manipulation, maintenance or transport. Animals may be held outside an animal holding facility for a period of less than 12 hours without IACUC approval except for survival surgery areas. Locations where animals are held for more than 12 hours become a satellite facility requiring justification, and prior approval by the IACUC as well as approval of husbandry plans and physical plant.

Animal Welfare Act (AWA): Public Law 89-544, 1966, as amended (P.L. 91-579, P.L. 94-279, and P.L. 99-198) 7 U.S.C. 2131 Et. Seq. Implementing regulations are published in the Code of Federal Regulations (CFR, Title 9, Chapter 1, Subchapter A, parts 1,2, and 3) and are administered by the U.S. Department of Agriculture. Only mice of the genus *Mus,* rats of genus *Rattus,* and birds are excluded.

Assurance: Assurance of Compliance with the U.S. Public Health Service Policy on Humane Care and Use of Laboratory Animals.

Attending Veterinarian (AV): A voting member of the IACUC with special expertise, who also reports directly to the Institutional Official. The AV provides advice about animals, animal handling, and proposed research activities and may offer training in specific procedures that involve animals. The AV also sits on the IACUC pre- and post-review subcommittees.

Biosecurity: Processes and procedures designed to minimize the likelihood that biological research will be misused for the production or enhancement of biological weapons.

Care and Use: Petting, feeding, watering, cleaning, manipulating, loading, crating, shifting, transferring, immobilizing, restraining, treating, training, working and moving, or any similar activity with respect to any animal.

Designated Representative: Someone appointed by the principal investigator to direct or oversee the project. Even though the PI may appoint someone to this role, the PI holds full responsibility for all aspects of the project.

Guide: The Guide for the Care and Use of Laboratory Animals, National Academy Press, 1996, Washington, D.C. or succeeding revised editions.

Institutional Animal Care and Use Committee (IACUC): The committee appointed to oversee the UML animal program, facilities, and procedures. The CEO (Chancellor) is charged with appointing an IACUC but has delegated this authority to the UML Provost. The Provost is the Institutional Officer (IO) and the IACUC reports to the IO. The IACUC is mandated under the Animal Welfare Act (AWA) and the Health Research Extension Act (HREA). The IACUC is charged under the AWA with representing "….society's concerns regarding the welfare of animal subjects …". The UML IACUC has adopted uniform policies that apply to all vertebrate animals used in research and teaching regardless of whether the species are covered by the USDA AWAR or PHS. The IACUC is required to perform semiannual program and facility evaluations as a means of overseeing the animal care and use program. The IACUC reviews and approves animal use protocols. Its decision to withhold approval may not be overruled by the IO. It is also authorized to investigate concerns involving the care and use of animals and has the authority to suspend an activity involving animals if it determines that the activity is not being conducted in accordance with what was described to and approved by the IACUC.

Institutional Official: An individual who signs, and has the authority to sign, the Institution's Assurance, making a commitment on behalf of the institution that the requirements of the PHS Policy will be met.

Morbidity: The state of being affected by disease, the relative incidence of disease.

Moribundity: In the state of dying, approaching death.

Noncompliance: Failure to follow federal, state, local, or institutional regulations or fulfill official requirements.

Principal Investigator (PI): Any full-time UML faculty members and qualified employees who may serve as project directors/leaders for activities that involve animals. The PI accepts full responsibility for all aspects of the project.

Public Health Service (PHS): The Public Health Service includes the Alcohol, Drug Abuse and Mental Health Administration; the Centers for Disease Control; the Food and Drug Administration; the Health Resources and Services Administration; the National Institutes of Health; and the Office of the Assistant Secretary for Health, Department of Health and Human Services.

Violation: Disregard for or infringement of the rules or regulations.

Zoonoses: A disease communicable from animals to humans under natural conditions.

APPLICABILITY

The Assurance, the UML Policy on the Care and Use of Animals, and the information in this document apply to all activities, regardless of funding source, involving animals that are:

- Sponsored by UML, Federal, State, or private funding
- Conducted by or under the direction of any employee, student, or agent of UML in connection with his or her individual UML responsibilities
- Conducted by or under the direction of any employee, student, or agent of UML involving the use of any UML property or facility, or
- Involving any collaborating, sub-granting, or sub-contracting individual or institution working with UML.

Activities involving animals covered by the Assurance and the UML Policies and Guidelines for the Care and Use of Animals must be conducted in facilities approved by the UML IACUC. The guidelines apply to all use of animals at UML, regardless of whether the activity is funded or not. The purpose is to ensure that humane care and use of animals in research, testing, and instruction is provided at all times and that all applicable laws, standards, and policies affecting such use are followed.

FEDERAL LAWS, REGULATIONS, AND GUIDELINES

The privilege of using animals in research and the common concern for the care and welfare of laboratory animals used in research and testing falls under the jurisdiction of three different government agencies and is subject to three Congressional Acts. The primary responsibility for the **Animal Welfare Act** (AWA) is assigned to the U.S. Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS). This act details requirements for the care and use of animals in research, testing and education. The AWA applies to all warm blooded animals used in biomedical research except for purpose-bred rats and mice, birds, and farm animals used in agricultural production research. Institutions are licensed and must report yearly their animal use and describe their animal care program. Implementing regulations of the AWA are established in the Code of Federal Regulations, Title 9, Chapter 1, Subchapter A, Parts 1,2,and 3. Unannounced inspections of facilities covered by the AWA are performed annually by the USDA APHIS Inspector. UML is licensed as a research institution by USDA and the Research Facility Registration number is RT-032-5820.

The U.S. Department of Health and Human Services, **Food and Drug Administration**, is also involved in ensuring proper procedures are followed for the care and use of laboratory animals. Regulations are implemented under the Federal Food, Drug, and Cosmetic Act as implemented by the Good Laboratory Practice Regulations (21 CFR Part 58). The U.S. Department of Health and Human Services, **National Institutes of Health**, is responsible for the implementation and general administration of the **Public Health Service Policy** on Humane Care and Use of Laboratory Animals (PHS Policy). The PHS Policy implements the **Health Research Extension Act of 1985**(Public Law 99-158), and is based on the U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training. UML applies each set of regulations equally to all vertebrate animal use for research and teaching. The PHS Policy and Health Research Extension Act apply to all institutions receiving animal research funds from NIH and NSF and include all vertebrate species. Institutions must either have AAALAC accreditation or an NIH Assurance Statement on file at OLAW/NIH. Animal care and use facilities must be built and operated in compliance with the recommendations of the "**Guide for the Care and Use of Laboratory Animals"**.

Institutions are required to submit yearly reports on the status of their animal care program. UML has a NIH Assurance Number (A3867-06). UML requires that the policies and procedures are followed for all vertebrate species used at the Institute, whether covered under USDA or PHS Policy and regardless of funding sources, to allow for uniform compliance and enforcement policies.

TRAINING REQUIREMENTS

All personnel involved in animal care, treatment, or use must be trained in accordance with the following guidelines established by the UML IACUC to insure that concepts related to responsible care and use of animals are fully understood and that UML is in compliance with federal regulatory requirements. These concepts include

- Humane animal care and use practices
- Research and/or test methods that minimize or eliminate animal use
- Research and/or test methods that limit animal pain and distress
- Using library databases to search for alternatives to research methods to reduce or eliminate pain and distress and to verify that the proposed experiment is not duplication of research
- Procedures to report deficiencies in animal care and use

The Animal Welfare Act Subpart C, Section 2.32, Personnel Qualification, requires that:

- It shall be the responsibility of the research facility to ensure that all scientists, research technicians, animal technicians, and other personnel involved in animal care, treatment and use are qualified to perform their duties. This responsibility shall be fulfilled in part by providing training and instruction to those personnel.
- Training and instruction shall be made available, and qualifications of personnel reviewed, with sufficient frequency to fulfill the research facility's responsibilities under this section.

The IACUC requires that all personnel listed in an animal use protocol that have contact with living vertebrate animals receive appropriate training for using animals. Users include faculty, post-doctoral candidates, research technicians and other staff, graduate and undergraduate students, and visiting scientists. The IACUC may accept a visiting scientist's training certification from another institution if that institution has AAALAC certification or an OLAW/NIH Assurance. Animal use protocols, annual reviews, and amendments will not be approved until the IACUC is satisfied that each person listed has a current animal users' training certification on file and is qualified to perform the procedures listed. Training and certification documents are kept on file with the Director of Institutional Compliance. Hands-on training records are documented by the ORS Manager and also reported to and kept on file with the Director of Institutional Compliance.

Training will include, but not be limited to, instruction on the following:

a) Regulations covering the humane practice of animal care and use; basic needs and proper handling and care for species used at UML; pre- and post-procedural care of the animals; and aseptic surgical methods and procedures;
b) Research or testing methods that minimize or eliminate the use of animals or limit animal pain and distress;
c) Sources of information for alternatives to the use of animal research models;
d) EHS lab safety training;
e) Health and Safety Training for Animal Workers
f) Reporting of deficiencies or concern for animals;
g) Instructions regarding animal ordering and receipt;
h) Instructions on IACUC policies and procedures.

Additional training will be offered to personnel on a regular basis from the ORS Manager, AV, or IACUC and include but not be limited to the following:

- Hands-on individual or group orientation sessions for newly employed personnel, in accordance with the Animal Handling and Training Protocol
- Review of ORS Facility Policies and Procedures, in addition to specific SOPs before training, to inform animal care personnel about new policies, regulations or methods pertinent to animal activities
- Individual instruction to scientists, technicians and students for specific techniques, including animal handling, surgery, anesthesia, and experimental manipulation
- Lectures from agency representatives or UML or invited scientists on ethical, philosophical, and/or technical aspects of animal research

Goals for training at UML are for all IACUC members, staff, students, and PIs to understand and become familiar with include but are not limited to:

- State, local, and federal regulations related to animal care and use
- UML Policies and Procedures regarding animal care and use and facility operations
- Occupational health and safety issues and zoonoses
- Proper use of anesthetics, analgesics, etc. to minimize pain and distress for the animals
- Instruction in aseptic surgical techniques
- Guidelines for endpoints and euthanasia
- Guidelines for alternatives to animal use, methods to reducing the number of animals used, and unnecessary duplication of studies

Online Training

Online training and a certificate of completion is required for IACUC members and anyone involved in animal care and use effective July 1, 2006. A Certificate of Completion is required to verify completion of "Working with the IACUC" from the Collaborative Institutional Training Initiative's (CITI) online training. This training provides a good overall review of care and use of animals and compliance regulations. This exam is provided free of charge and your results can be linked to University of Massachusetts Lowell from website. Certification must be updated every three years. Additional online training is available through CITI with additional curricula on other animal research topics. Any of these training modules may be required, depending on the type of activities being conducted and the expertise of the person conducting the procedure. Individuals that need to take one of these training modules will be notified by IACUC staff. Please check with the Institutional Compliance Office for more current information.

Laboratory Safety Training

All faculty, staff, graduate students, teaching assistants, and researchers that use chemicals and/or generate hazardous waste must attend the EHS Laboratory Safety Training on an annual basis. The training is offered monthly throughout the year and the certification must be kept current to work in any UML laboratory. The training provides information about the

EHS staff and responsibilities, right-to-know law, emergency spill response notification, blood borne pathogens/biohazards, personal protective equipment (PPE), hazardous waste management, fire response procedures, and laboratory practices and policies. It is the responsibility of the faculty member or laboratory manager that oversees the laboratory to ensure that all workers complete the EHS laboratory safety training and are certified. Training certificates are kept on file at the EHS Office.

PPE is provided at no cost to the employee. Animal care personnel shall wear appropriate protective clothing, which includes shoe covers, gloves, splash goggles, safety glasses, disposable garments and hair bonnets that are required to safely conduct the research activity. No personal protective equipment shall be worn beyond the boundary of the hazardous work area or the animal facility. PPE (minimum of eye protection and gloves) is also required for handling animals used in classroom and laboratory exercises that are conducted outside of the ORS facility.

Health and Safety Training for Animal Workers

Health and Safety Training for Animal Workers is provided annually. The training provides an overview of health and safety risks from working with animals and informs workers how to protect themselves from injuries, allergies, and diseases associated with animals. It also reviews general safety rules and personal protective equipment required for working with animals. Information is provided in regards to the use of the Occupational Health and Safety program, contracted out through EHS with experienced physicians, should a personal health care evaluation be necessary to determine any issues or problems from working with animals. Health Survey Questionnaires are available from the website.

Facility Overview and Record Keeping

The Office of Research Services Manager oversees daily animal inspections (including weekends and holidays) and maintains records regarding animal care, facility condition, and health status of animals in projects assigned to them. The ORS Manager tracks training events and reports the type of training offered and the participants that have successfully completed the training to the Director of Institutional Compliance. Records on procedure training are also maintained by the ORS Manager in the Animal Handling and Training Protocol logbook. Entries include the date of training, the procedure, and the individuals in attendance. The ORS Manager ensures all staff are using personal protective equipment as required by EHS policies and in accordance with all standard operating procedures used in the facility.

Procedures Using Animal Handling and Training Protocol

The ORS Manager also provides frequent hands-on training related to various laboratory procedures involving animal care and use. This training is required for anyone that will be conducting procedures in the animal care facility and is covered under an Animal Handling and Training Protocol. All individuals who will be actively involved in research must train on the animals that are assigned to this protocol, as opposed to training on animals intended for specific studies. PIs are held responsible to ensure their personnel are listed on the protocol(s) and have adequate training before conducting any procedures. Procedures that are covered by this protocol include, but are not limited to

blood draws, injections, and necropsy training. The ORS Manager and AV are also available for one-on-one or group training activities. Call the ORS Manager (ext. 2830) to inquire about or schedule a training event. Training records will be kept on file with the ORS Manager and the Director of Institutional Compliance. Individual investigators develop and provide their own staff training in techniques and practices used in their own laboratories.

Sufficiently detailed information on the experience and training of each individual involved must be included on the protocol review form and be officially approved in writing by the IACUC before any hands-on work may start.

NONCOMPLIANCE AND MISTREATMENT OF ANIMALS

Individuals who have concerns regarding mistreatment of research animals (complainants) at UML may contact the Director of Institutional Compliance in person, by email (Elaine_Major@uml.edu), or phone (ext. 3452). The IACUC Chair will be advised of the complaint and will review the concerns with the PI in charge of the project in question. **All animals** are covered under the UML IACUC Policies and Procedures and the UML Assurance. The Institution maintains this policy to assure eligibility for federal funding and meet the requirements of the Assurance. The PHS can decide to withhold funding to the Institution as a whole, depending on the nature and frequency of noncompliance.

Reporting Concerns
Any employee, student, or agent of UML reporting a concern will be protected against reprisal. Every effort will be made to protect the complainant's confidentiality, but UML is an agency of the Commonwealth of Massachusetts and is therefore subject to the Massachusetts Public Records law, G.L. c.66, § 10. This law states the general rule that any record made or received by an officer of the Commonwealth is presumed to be a public record and must be released to "any person" who requests it. If appropriate, concerns involving the care and use of animals may fall under the purview of the UML Policy on Misconduct in Science.

Initial information to be obtained from a complainant includes:

- Complainant's name (optional)
- Nature of the concern(s)
- Description of the event or charge and the observed date of the alleged violation(s)
- Copies of any written, photographic, or taped documentation to substantiate the complaint
- Names of other people who may corroborate the complainant's concerns

The Director of Institutional Compliance, IACUC Chair, IACUC Administrator, or ORS Manager will review the information and consult with other committee members to determine the seriousness of the complaint. If an investigation is necessary, the IACUC may obtain additional information through:

- Unannounced visits to the location of the concern (laboratory/facility)
- Review of laboratory procedures, IACUC protocols, lab/facility documents (including records pertaining to animal purchase, care, health records, or research records)
- Interview with the Principal Investigator (PI)
- Interviews with laboratory personnel, co-workers, etc.
- Letters or interviews with other individuals who might provide information for the investigation
- Assistance from other IACUC members in collection of information

IACUC Policy on Noncompliance
The IACUC must review and if warranted, investigate concerns involving the care and use of animals. All complaints must be reviewed but not all complaints may need to be investigated. Protocol noncompliance occurs when procedures or policies affecting animal care or use are not followed. When faced with protocol noncompliance, the IACUC will work to bring the protocol into compliance or take immediate action to stop any mistreatment

of animals. The IACUC is empowered to make a decision as to the type of violation and suspend any research or teaching activity if it finds violations that are a threat to the health or safety of animals or activities conducted that are not in accordance with provision of the AWA, the Guide, or the UML Assurance (PHS Policy IV,C,6 and IV,C,1,a-IV,1g). The IACUC as a full committee may suspend activity and/or make a decision as to the type of disciplinary action recommended and make such recommendations or consult with the IO to impose further sanctions. The AV also has the authority to suspend an activity to provide adequate veterinary care and the IACUC will be quickly notified to review the decision. The IACUC is empowered by the UML Chancellor, who has appointed the Provost as the IO. Frequent communication is encouraged between PIs, Director of Institutional Compliance, IACUC Chair and Administrator, and the ORS Manager to avoid compliance issues.

Deviations from IACUC policies are reported to the IACUC Chair, Director of Institutional Compliance, and the IO. If there is a deviation from the UML policies and procedures, an IACUC meeting will be convened, members informed of the complaint/investigation, and a decision about appropriate action will be made. If the IACUC determines that the violation is valid, the PI, department chair, college dean and/or IO will be notified of the IACUC's recommendations or action. If the individual reporting the concern is dissatisfied with the IACUC's decision, concerns may then be presented to the IO but the IO cannot override an IACUC decision. For Public Health Service funded research, the IO is required to report serious or continuing non-compliance with the PHS policy, any serious deviations from the provisions of the Guide, and any suspension of a research activity to the PHS Office of Laboratory Animal Welfare (OLAW). Regardless of the funding source, the IO must notify the USDA of any suspensions of activities involving USDA covered species. USDA typically communicates this information to PHS. Failure to comply with the Animal Welfare Act can carry penalties that range from a reprimand to the levy of a substantial fine, along with the immediate suspension of all activities associated with the use of animals by the individual investigator, or by the entire institution. These regulations are not subject to negotiation or individual interpretation by investigators.

Any and all violations require prompt response to resolve the problem that initiated the violation. All incidents are entered into the animal care log and reported to the IACUC Chair and IACUC Administrator. Specific information about minor and major violations and a guideline of typical IACUC responses are provided below. The IACUC has the authority to determine violations more serious than those outlined here and take necessary steps to meet the requirements of the Animal Welfare Act. Actions that may necessitate stronger levels of enforcement by the IACUC include transmission of infection or disease into the facility or compromising human health as a result of ignoring policies and procedures.

Minor Violations

Minor violations are situations in which the UML Policies and Procedures are not followed but there is no immediate harm to the animals. Warnings and minor violations will be entered into the animal care log, reported at the next IACUC meeting, and entered into the meeting minutes. The ORS Manager is held responsible to notify the IACUC Chair and Administrator about the incident and if possible recommend corrective action.

Examples of minor violations might include improper entry into animal quarters, failure to adhere to ORS SOPs, improper waste disposal, failure to clean or maintain an area, improper disposal of dead animals, improper maintenance, incomplete cage cards, using expired food, not wearing proper PPE, failure to maintain or falsifying daily records, or improper ordering procedures. Any member of the IACUC may call for full IACUC review of a minor violation and discussion of corrective actions at a meeting. Response to a minor violation is outlined as follows:

First Minor Violation:

- Written notification is sent to the PI
- Immediate action is taken to resolve the problem
- Follow-up review is conducted by the Director of Institutional Compliance

Second Minor Violation:

- Written notification is sent to the PI and Department Chair
- Immediate action is taken to resolve the problem
- PIs and staff are required to retrain on the procedure or review the SOP that was violated
- Follow-up review is conducted by the Director of Institutional Compliance

Third Minor Violation

- Written notification is sent to the PI and Department Chair
- Immediate action is taken to resolve the problem
- PI and staff are required to retrain on the procedure or review the SOP that was violated
- Follow-up review is conducted by the Director of Institutional Compliance
- PI is required to attend an IACUC meeting

Major Violations

Major violations are situations in which the UML Policies and Procedures are not followed and there is immediate harm to the animals. When it appears that procedures involving live animals are being conducted without prior IACUC approval, health and safety of personnel is threatened, or animals are used in violation of regulatory guidelines, the AV has the authority to suspend the activities and the IACUC must convene as soon as possible thereafter to vote on immediate cessation of the activity pending completion of the investigation. Any activities that are suspended are required to be reported to the IO and the PHS or USDA. Actions will be taken as expeditiously as possible to obtain an appropriate resolution.

Examples of major violations might include repeated minor violations, use of animals without an IACUC approved protocol or amendment, using non-approved anesthesia or euthanasia, disregard for animal suffering, having more than the accepted number of animals per cage, conducting research without the proper training, or knowingly providing false or inaccurate information to the ORS Manager or IACUC. Response to a major violation is outlined as follows:

First Major Violation:

- PI is informed, project activity is suspended, and the violation is corrected immediately
- Person committing the violation and the PI must be retrained from a second on-line course and submit certificates of completion to the Director of Institutional Compliance
- IO is informed and notifies PHS and/or USDA
- Further activity on study in question is suspended until above conditions are met
- Follow-up review is conducted by Director of Institutional Compliance to assure continued compliance

Second Major Violation:

- PI and Department Chair are informed, project activity is suspended, and violation is corrected immediately
- Person committing the violation and the PI must be retrained from a second on-line course and submit certificates of completion to the Director of Institutional Compliance
- IO is informed, notifies PHS and/or USDA, and determines whether the funding agency is notified of the violation
- All further activity involving animal use is suspended for 30 days.
- PI is required to meet with the IACUC
- After suspension requirement is met, a follow-up review with the Director of Institutional Compliance is conducted before any animal use can resume

Third Major Violation:

- PI and Department Chair are notified, project activity is suspended, and the violation is corrected immediately
- Person committing the violation and the PI are retrained from a second on-line course and must submit certificates of completion to the Director of Institutional Compliance
- IO is informed, notifies PHS and/or USDA, and determines whether the funding agency is notified of the violation
- PI is required to meet with the IACUC and the IO
- All further activity involving animal use is suspended for 90 days or longer and the University Ethics Committee (established under the Misconduct in Science Policy) is contacted to evaluate the situation as an ethics violation

Disciplinary Actions

Typical disciplinary actions are outlined above for minor and major violations. Depending on the severity of the violation, enforcement or disciplinary actions may also include but not be limited to termination of privileges, suspension of privileges, probation, a letter of reprimand, mandatory training, or other actions deemed necessary by the IACUC or IO.

ORS MANAGER ROLES AND RESPONSIBILITIES

The animal care facility is under the direction of the Office of Research Services Manager (ORS Manager). The ORS Manager reports to the Director of Institutional Compliance at UML. The ORS Manager, in general, oversees and coordinates the daily activities of the animal facility at UML and provides oversight for all of the animals housed there. The Manager is required to maintain performance levels consistent with and according to UML requirements, IACUC Policies and Procedures, and the ORS Facility Policies and Procedures.

The ORS Manager is responsible for ensuring animals receive proper care and housing and that all regulatory requirements are met. The ORS Manager oversees facility operations to control the environmental factors that are essential for animal well-being. Responsibilities of the ORS Manager include but are not limited to

- Conducting routine daily inspections of all animal holding and support facilities and equipment to maintain animal health, facility condition, sanitation, and environmental parameters
- Assisting in development and implementation of standard facility operating procedures for full compliance with all state, federal, and local regulatory compliance requirements
- Maintaining, generating, and submitting facility records and documentation necessary for reporting
- Coordinating maintenance of physical environment
- Ensuring all UML performance standards are met and that required duties are completed
- Participating as required in budget development for equipment, supplies, and personnel to ensure effective operations of the facility
- Coordinating research projects and scheduling space usage for the facility
- Providing training activities and appropriate supervision to build competence among those using the facility
- Ensuring UML safety policies and procedures are adhered to including those related to biological and radioactive materials
- Participating in meetings with UML staff, the IACUC, IACUC Chair, and IACUC Administrator to keep them informed of current and future projects, policies, and procedures
- Coordinating movement of animals throughout the facility and intake of new animals
- Assisting in other duties as assigned to complete required work

The Manager is required to be in frequent communication with the Director of Institutional Compliance, IACUC Chair, Attending Veterinarian (AV), and IACUC Administrator in regards to protocol submissions and amendments, animal care and use, and the general conditions of the facility environment. The ORS Manager must have a working knowledge of laboratory animal facility operations, be able to communicate effectively, and demonstrate the ability to adapt and respond in a timely and respectful manner to the needs of faculty, students, and staff.

ANIMAL MANAGEMENT

Animal Import, Receiving, Acclimation, and Quarantine

Acquisition of all animals will follow federal, state, and local regulations. All necessary permits and licenses will be obtained by the user. Animals purchased must be from a reputable vendor and of known health status. The ORS Manager is responsible to ensure compliance with the SOPs for animal ordering and receiving. All forms are on file at the facility. A Departmental Purchase Request/Change form must be completed and forwarded to the ORS Manager, along with an approved protocol number. The ORS Manager will review and approve the form based on space and cage availability. The approved form will then be forwarded to the Research Administration Purchasing Agent and the Agent will approve the order and supply the ORS Manager with the purchase order number. The order will be placed for the animals by the ORS Manager and the PI will be notified that the order has been placed.

The PI or project representative must notify the ORS Manager of the bedding preference before the animals are expected to arrive. Options include sani chips, Care Fresh, shavings, nestlets, or Kim Wipes. Prior to arrival, the clean cages will be set up with lids, filled water bottles, and cage card holders. No more than five adult mice or five adult hamsters are allowed per cage.

The transfer cages must be disinfected prior to entering the facility. Materials required include gloves, safety glasses, masks, clean cages and lids, water bottles with stoppers, bedding, cage card holders, Quatricide TB, and a sponge. The transfer cage(s) are placed on an animal room cart and brought to Olsen 617. Gloves, gowns, and shoe covers will be used by all personnel involved and are located inside 618 anti-room. To disinfect the cages, pour Quatricide TB on a new sponge (DO NOT SPRAY IT!), and wipe down all surfaces of the transfer cages. Once the disinfection process has been completed, the transfer cages may be moved into the facility. The used sponge and personal protective equipment is disposed inside the facility in appropriate waste bins. If skin is exposed to Quatricide TB, wash the area for 15 minutes with soap and water and refer to the Material Safety Data Sheet (MSDS) in Olsen 618G.

Upon arrival at the ORS facility, animals must be inspected by the ORS Manager or an assigned representative. If the animals are found to be unsatisfactory or diseased, the vendor, AV, IACUC Chair, and PI or project representative must be notified immediately. Contact the PI to confirm arrival. The animals must be acclimated for five to seven days after arrival to recover from shipment stress and to adjust to new environmental conditions.

When an animal is brought to campus from a non-approved source there is a chance the animal is harboring infectious disease(s) even though it may appear healthy. Non-approved sources of animals include wild-caught animals and animals from non-approved animal vendors or other institutions. Animals must have a recent documented health screening at the place of origin reviewed by the UML AV prior to being shipped. Animals will need to be quarantined in a room separate from the animal facility for at least eight weeks. (Only with IACUC approval and under certain conditions, will IACUC approve a third-party holding and testing facility.) The quarantine room must be open for inspection at any time and daily monitoring is required. Strict PPE is required to be used at all times and SOPs have been established to prevent cross-contamination to animals in other locations at UML. Access to the quarantine room is limited to those individuals with

no direct contact with animals in the ORS. Animals may not be used for research projects until they are cleared from quarantine. Breeding is not allowed for animals in quarantine. Sentinels will be sent to an outside company for diagnostic testing to ensure the incoming animals are free of specific pathogens being excluded by the ORS vivarium.

Colony Management

Breeding is allowed in the ORS facility, if covered by an IACUC approved protocol. However, a number of parameters must be considered before establishing a breeding colony. Technicians should work closely with the ORS Manager to ensure that the facility is capable of housing the amount of animals that a study requires. Information in regards to establishing a mouse breeding colony is provided below. If a PI is interested in breeding other species, please consult with the ORS Facility Manager and AV to discuss breeding details. Colony growth is dependent on caging availability and space. In the event of a water or steam shut down, the ORS needs to have a clean backup supply of the number of cages, lids, and bottles that are currently in use for proper operations.

Mouse Breeding

Breeding and colony expansion may proceed when the mice reach sexual maturity. A breeding protocol is dependent on an investigator's preferred breeding scheme and may be either monogamous or polygamous. A breeding pair (1 female x 1 male) is encouraged for strains that typically produce large litters to avoid cage overcrowding before the pups reach weaning age. A breeding trio (2 females x 1 male) is preferred for strains that produce smaller litters or if the goal is rapid colony expansion. Gestation periods typically last between 19 and 21 days. A post-partum estrus occurs within 14 to 28 hours after parturition in mice. Therefore, male and female mice may be separated after pregnancy confirmation to avoid post-partum insemination if overcrowding is a concern.

Weaning

Depending on strain, the number of neonates littered may vary from one to sixteen per litter. Ear flaps fully develop on day 4; a full coat of hair is grown and ears open on day 10; eyelids open on day 13 and pups are ready to eat adult food at two weeks of age. Around this time, supplements of breeder chow (high fat) and electrolyte gel may be placed on the floor of the cage to prepare them for weaning. Weaning typically occurs at 21 days of age, unless prior approval is obtained from the IACUC as a deviation to the protocol (i.e. weaning at 28 days of age).

Overcrowded Cages

Overcrowded mouse cages represent a significant animal welfare concern. Such cages are noncompliant with Public Health Service (PHS) Policy and UML's Assurance to PHS. The Guide for the Care and Use of Laboratory Animals states the PHS recommendations for housing densities. In order to standardize housing densities and prevent or eliminate the possibility of overcrowding within cages, ORS has established mouse breeding and cage density guidelines. (Refer to Space Guidelines included in the Facility Management section.)

Breeding Cage Card

A separate breeding cage card is completed once pups are born. Information includes the cage number, date of birth, number of pups, date removed, and date weaned. This card is placed behind the primary cage card and an example is displayed to the right.

B2
Bred with B2M: 2/3/06
Male Removed: 2/17/06

Pups: 2/27 C 2/28
3/2 6
Weaned 3/23/06
2F / 4M

Bred with B2M 3/31/06

Troubleshooting

Many factors can contribute to suboptimal animal reproductive performance or poor rearing behaviors and these range from improper environmental conditions to animal health status to genetic predisposition. Investigators are encouraged to contact the ORS Manager or the AV for troubleshooting, or to discuss rescue effort options if breeding problems are encountered.

Animal Identification

Cage Cards- Federal law requires that all animals or groups of animals be identified at all times. The SOP form is on file at the laboratory facility and all individuals working with animals are responsible for complying with it. It is the responsibility of the ORS Manager to ensure compliance. Each cage should have a card and the following information should be on each card: PI and phone number, protocol number, strain of animal, sex, and number of animals in each cage. See example to the right. Additional information may include the vendor, date of birth, date of arrival/weaning, department the animals are assigned to, the technician name, and cage or animal number.

C57 Control Mice
Cage # B2

1M/2F
DoB: 12/21/05
Mated 2/3/06

Protocol 04-07

Dr. Jones
Tech: M. Underwood
x2890

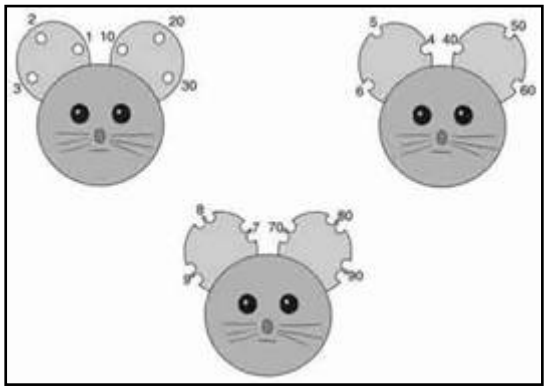
Marking Methods

Several systems are available for individually identifying laboratory rodents. Depending on the circumstances, either temporary or permanent methods may be used. Temporary marking methods are those that are typically groomed off, rubbed off, or shed by an animal. Several methods are particularly well suited for identifying cage mates. Methods for permanently identifying animals include ear punching (rodents), ear snipping (rodents), ear tagging (rodents and rabbits), tattooing, and subcutaneously implanting a numerically coded microchip. Marking methods must be included in the protocol or an amendment must be filed to add it. Certification of training to use marking methods is required.

<u>Temporary identification methods</u>

- A felt tip marker may be used for marking an ear or tail: such marks usually disappear in 1-2 days due to grooming, and regular re-marking is necessary.
- Food coloring may be used to dye a patch of fur: such marks generally last for 1-2 weeks but can be used only on albino and light colored animals.
- A patch of fur on the back or side of the animal may be shaved: such marks generally last 1-4 weeks (depending on stage of the hair cycle) and can be used on any color animals.

Permanent identification methods



- Ear Punch/Ear snip: this is a commonly used procedure which employs a special metal punch instrument to place a hole in the ear of the rodent, following a code. Unfortunately, there is not a universal ear punch/snip identification method, but one example of ear punch scheme is provided here. It is quick and easy, cheap, relatively atraumatic, no anesthesia is required, and punched tissue can be used for DNA (PCR) screening. This cannot be performed on pups under two weeks of age due to size and position of ears. If done incorrectly, there is the potential for ear damage or the punch may be difficult to read.
- Ear tag: numbered metal clips can be applied to the base of the pinna with special pliers. Various sized tags exist; the appropriate size must be selected for the species being identified. It is quick and easy to perform, cheap, relatively atraumatic, and no anesthesia is required. However, it cannot be performed on pups less than three weeks of age due to size and weight of tags. Note that it's been reported in the literature that granulomas may form at the site of tag application. If applied improperly, tags can fall out, or they can cause necrosis of the ear pinna. It is highly recommended that the tags be properly disinfected prior to use to minimize risk of infection.
- Tattooing: the preferred method for identifying neonatal rodents, and may also be used to mark weanling and older animals. The tattoo is placed on a toe or tail of neonates under manual restraint, or on the tail, toe, or ear of weanling and adults under sedation or in a restraining device. The animal's skin and the tattoo needles must be disinfected prior to application and only use pigments approved by the United States Food and Drug Administration.
- Microchips: microchip transponders are implanted via subcutaneous injection. A special recording instrument reads and displays the number on the scanner. Microchips are about the size of a grain of rice and transmit a unique alphanumeric code for each animal. The codes are easily distinguished from one another by a computer. Because the implants are relatively large, they are acceptable for identifying weanlings and adults only. Contact Office of Research Services for more information if you would like to use this method for identifying your animals.

Resources for Marking Instruments

Following are the names and addresses of some companies that sell animal identification tools (this list is not comprehensive).

Ear punches

- Roboz Surgical Instruments Company, Inc., 9210 Corporate Boulevard, Suite 220, Rockville, Maryland 20850, in 1 mm (RP-9901) or 2mm (RP-9902) sizes (http://www.roboz.com)
- Braintree Scientific, Inc., PO Box 850929, Braintree, MA 02185-0929, in 1mm (EP-901) or 2mm (EP-902 scissors style or EP900 thumb style) (http://www.braintreesci.com/ID-SYSTEMS.htm)

Ear tags (model 1005-1)

- National Band and Tag Company, 721 York St., PO Box 430, Newport, Kentucky, 41072-0430 (1-800-261-TAGS). (http://www.nationalband.com/) (This manufacturer can stamp up to four number-letter combinations on one side of a tag, or a total of six numbers that extend around the bend of the tag.)

Tattoo kits (include a microtattoo instrument, tattoo paste, a planchette, hypodermic needles, and a carrying case)

- Braintree Scientific, Inc., PO Box 850929, Braintree, MA 02185-0929 (MT-KIT) (http://www.braintreesci.com/ID-SYSTEMS.htm)
- Fine Scientific Tools (No. 24201-00) (http://www.finescience.com/fst/LabAcc/24201-00.html)
- Animal Identification and Marking Systems (AIMS*) 1-607-324-6752 (http://www.animalid.com/rats.html)

Microchips

- Bio Medic Data Systems, Inc., 255 West Spring Valley Avenue, Maywood, New Jersey 07607 (http://www.bmds.com/)
- AVID, 3179 Hammer Avenue, Suite 5, Norco, California 91760. (http://www.avidid.com/special/index.html)

Animal Screening and Equipment Monitoring

ORS staff must inspect all animals daily (including weekends and holidays) and report to the ORS Manager all concerns regarding animal care, facility condition, or health status of animals in projects assigned to them. The ORS Manager is responsible to report this information to the AV and IACUC. Appropriate records of veterinary care are required.

To monitor equipment function as research studies are initiated, a cage and water bottle will be set up as an equipment control as directed by the ORS Manager. Extra animals that are commonly provided with incoming shipments will be used and placed in this housing, with equipment set up identical to that for the research study. The purpose of this practice is to identify any equipment malfunctions and reduce animal distress by monitoring closely the equipment and watering devices. These animals will be placed on a normal diet and weighed daily or weekly to monitor weight and monitor hydration. Results are sent to the Director of Institutional Compliance on a biweekly basis.

Animal Monitoring Responsibilities
The PIs, their designated representative, or students listed on the protocol are responsible for regular monitoring of animals on a research study. Monitoring frequency should be outlined in the study protocol and conducted in accordance with it.

Pain and Distress: Anesthesia/Analgesia
Procedures that involve pain and/or discomfort must be designed to eliminate any unnecessary distress to the animal. Animals must be returned to a normal state as soon as possible, or euthanized immediately. Federal law requires that animals be rendered insensitive to distress or pain by the use of appropriate tranquilizing, analgesic, or anesthetizing drugs. The use of muscle relaxants or paralytic drugs alone (e.g., succinylcholine or other curariform drugs) as anesthetics is forbidden by the IACUC. The PI has the responsibility to assure the proper use of anesthetics, analgesics, and tranquilizing drugs and to educate personnel about the drugs' use.

Emergency Care
Provisions for emergency care will be made by the Attending Veterinarian or his /her designee. In the event of animal medical emergencies when the principal investigator/project representative cannot be reached, treatment consistent with good veterinary practice will be administered, after approval from the AV and/or the IACUC Chair.

Disposition of Animals
At the termination of a study, animals are euthanized and disposed of in an appropriate manner. After euthanasia, the carcasses are stored as biohazard waste in the freezer in 618B, until the container if filled. Upon request, the EHS Office (ext. 2543) will remove the full box and replace it with a new one. The carcasses are incinerated at a Biological Waste Incinerator off-site and all waste disposal must be in accordance with all Federal, State, and local regulations.

Animal euthanasia may be a necessary part of many animal activities. The quick and humane euthanizing of all animal species will be performed using methods approved by the American Veterinary Medical Association Panel on Euthanasia. (See 2000 Report of the AVMA Panel on Euthanasia, or online at http://www.avma.org/resources/euthanasia.pdf) Use of euthanized animals in a subsequent activity is not permitted unless specifically approved by the IACUC in the Application.

Sentinels
Sentinel animals are used to verify the health of an animal colony. The ORS mouse sentinel program works as follows:

- Each mouse rack has a cage containing two to three outbred (e.g. CD-1, SW) mice, placed on the bottom row.
- During cage change, the sentinel cage will receive dirty bedding from one row of PI animal cages (a handful of dirty, soiled bedding from each cage). About half of the sentinel cage bedding will be clean bedding and half soiled bedding.
- ORS staff will put the date and row used on the sentinel card each time cages are changed.
- A minimum of 1 animal from each rack or 1 animal for every 70 cages will be tested quarterly, and samples from a minimum of 2 sentinel animals from each room should be submitted if available.

- Every quarter, whole blood will be collected from sentinels and submitted to a 3rd party diagnostic laboratory for Serology Prevalent Profile testing. Once a year, sentinel mice will be submitted to a 3rd party diagnostic laboratory for complete health monitoring with Helicobacter PCR testing (pooled feces) unless the room is known positive for Helicobacter.
- Sentinel testing program for other animal species (e.g. hamsters, gerbils, rats) will be determined based on risk assessment and if the animal species occupy a room for longer than 3 months.

VETERINARY CARE

Veterinarian Role in Facility Management and IACUC
Federal mandate requires that any facility using animals for research, testing, and teaching must have an Attending Veterinarian (AV) to provide adequate veterinary care to the facilities' animals. The AV is chiefly responsible to provide for the health and welfare of the animals used at UML and to assure that UML is meeting professionally acceptable standards governing the care, treatment, and use of animals. The AV is a voting member of the IACUC, provides veterinary care for the research animals, makes recommendations to the IACUC and PIs regarding technical information about procedures and protocols, provides advice to minimize animal pain and distress, evaluates personnel qualifications for using animals, provides oversight of clinical and preventative veterinary medical programs, and provides oversight of animal husbandry programs. The AV is a member of the pre-review committee for all protocols and amendments. The AV is also available to PIs for consultation about alternative procedures to reduce pain and distress and offers guidance on quarantine and isolation of incoming animals, anesthetic and analgesic agents, euthanasia, surgical procedures, and post-operative care. The AV maintains close communication with the ORS Manager, the IACUC Administrator and the IACUC Chair. The AV may provide training related to specific procedures and offer guidance for medical intervention and emergency care.

Diagnostic Services
Arrangements for diagnostic services may be available on a fee for service basis. Fees generally will be the responsibility of the principal investigator/project representative. Where there are instances of suspected contagious diseases, the AV will work with the PI/designated representative to expedite disease diagnosis. Subsequent treatment and control measures will be determined by consultation between the department chairperson and the project representative. Costs for such treatment and control generally are the responsibility of the PI.

General Animal Physiology
Normal animals are neither thin nor fat, except for genetically modified animals that have an obese phenotype. They have well-groomed fur coats and should not have discharge from their eyes, ears, mouth, or nose. Their breathing should be quiet and regular, through their noses and with their mouths closed. If they are awake, animals should be alert, responsive, move freely around the cage and interact with their cage mates or handlers. Normal animal body condition is a "3" (see following body condition scoring system).

It is important to understand and recognize normal appearance and behavior in the animal species you work with. Any deviation from "normal" is a clinical sign, and such observations should be promptly reported to the veterinary care personnel in the Office of Research Services. Most of the time the clinical signs observed will be non-specific (i.e. weight loss, dehydration, ruffled fur coat, inactivity, etc.) and additional diagnostic work-up may be required in order to determine the cause of problem.

The following table contains normative physiologic data. For other animal species or particular animal models, contact the ORS Manager.

Normative Data for the Laboratory Mice (from LAM 2nd edition)

Adult Weight -Male	20-40 gm
-Female	18-35gm
Life Span - Usual	1-3 years
-Maximum reported	4 years
Surface Area	0.03 – 0.06 cm^2
Chromosome Number (diploid)	40
Water Consumption	6.7 ml/8 weeks age
Food Consumption	5.0 gm/8 weeks age
Body Temperature	98.8 – 99.3 ºF (37 – 37.2 ºC)
Puberty (both Male and Female)	28 – 49 days
Breeding Season	None
Gestation	19 – 21 days
Litter Size	4 – 12 pups
Birth Weight	1.0 – 1.5 gm
Eyes Open	12 – 13 days
Weaning	21 days
Heart Rate	310 – 840 beats/minute
Blood Pressure -Systolic	133 – 160 mm Hg
-Diastolic	102–110 mm Hg
Blood Volume -Plasma	3.15 ml/100 gm
-Whole Blood	5.85 ml/100gm
Respiration Frequency	163/min
Tidal Volume	0.18 (0.09 – 0.38) ml
Minute Volume	24 (11 – 36) ml/min
Stroke Volume	1.3 – 2.0 ml/beat
Plasma -pH	7.2 – 7.4
-CO_2	21.9 mEq/L
-CO_2 pressure	40 ± 5.4 mm Hg
Leukocyte Count -Total	8.4 (5.1 – 11.6) x 10^3/µl
-Neutrophils	17.9 (6.7 – 37.2) %
-Lymphocytes	69 (63 – 75) %
-Monocytes	1.2 (0.7 – 2.6)%
-Eosinophils	2.1 (0.09 – 3.8)%
-Basophils	0.5 (0 – 1.5) %
Platelets	600 (100 – 1000) x 10^3/µl
Packed Cell Volume	44 (42 – 44) %
Red Blood Cells	8.7 – 10.5 x $10^8/mm^3$
Hemoglobin	13.4 (12.2 – 16.2) mg/dl
Maximum volume of Single Bleeding	5 ml/kg
Clotting Time	2 -10 minutes
PTT	55 – 110 sec
Prothrombin Time	7 – 19 sec

Body Condition Scoring Description (from Ullman, Cullere and Foltz, 1999)

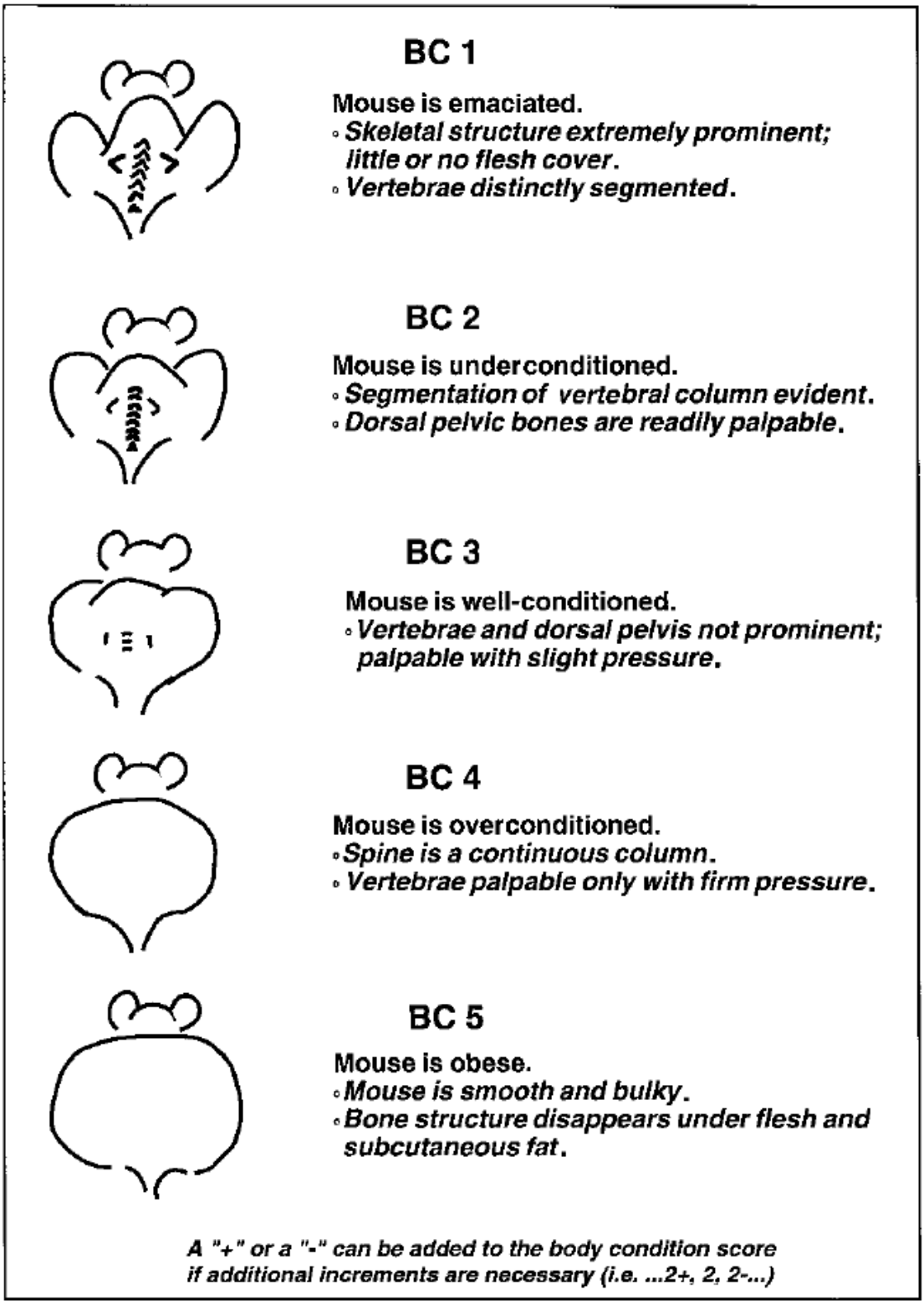


Figure 1. Line drawings and descriptions of body-condition (BC) scoring.

Veterinary Examination Record

Special cage cards are available for flagging and identifying animals with clinical signs. Pending clinical sign, a treatment plan or resolution action should be carried out at the earliest possible time to minimize potential animal pain or distress. If the Research Group has any questions or concerns, they should contact the Attending Veterinarian or the ORS Manager.

For USDA regulated species, individual record sheets have been developed to keep track of each animal to document specific problems and track the condition of the animal. Forms are on file with the ORS Facility Manager and are used by the attending veterinarian

SURGERY

Surgery may be performed only in facilities intended for that purpose and must include an area for the proper post-surgical management of the animal. PIs must provide evidence of experience, training, and/or other qualifications for personnel who are to perform the surgeries. Survival surgery on rodents does not require a special facility, but should be performed in a dedicated area using sterile instruments, surgical gloves, and general aseptic techniques to prevent the occurrence of post-surgical clinical infection.

Aseptic Surgical Technique

The federal Animal Welfare Act and the NIH Guide for the Care and Use of Laboratory Animals both set standards that are obligatory for biomedical research involving live, vertebrate animals. These documents have been adopted by virtually all public and private funding sources, and are therefore pertinent to all research projects, regardless of funding source.

The following guidelines for rodent surgery are recommended from the "Guide":

- Major surgery in rodents does not require a surgical facility but should be performed in a dedicated space that is appropriately managed to minimize contamination from other activities in the room during surgery
- Major survival surgery penetrates and exposes a body cavity or produces substantial impairment of physical or physiologic functions
- Minor procedures such as wound suturing and peripheral-vessel cannulation are often performed under less-stringent conditions but still require aseptic technique and instruments and appropriate anesthesia

The goal of aseptic technique is to reduce the possibility of microbial contamination to the lowest practical level. No single technique, practice, germicide, or piece of equipment will achieve this objective. Rather, proper aseptic technique is dependent on numerous practices that require input and cooperation of all personnel within the operating area.

Definitions

Aseptic technique: Practices and procedures implemented to reduce microbial contamination to the lowest practical level.

Survival surgery: A surgical procedure from which an animal is expected to recover from anesthesia. Aseptic surgical technique must be used.

Non-survival (Terminal) surgery: A surgical procedure from which an animal is euthanized before recovery from anesthesia. Clean surgical technique may be used.

Major survival surgery: A surgical procedure that penetrates and exposes a body cavity or produces substantial impairment of physical or physiologic functions. Examples include but not limited to laparotomy, thoracotomy, craniotomy, orthopedic procedures, limb amputation, and enucleation.

Minor survival surgery: A surgical procedure that does not expose a body cavity and

causes little or no physical impairment. Examples include but are not limited to wound suturing, peripheral vessel cannulation, and placement of subcutaneous implants.

Disinfectant: Disinfectants are substances that destroy or inhibit the growth of microorganisms but do not sterilize the area to which they are applied.

Sterilization: Is the process of killing all microorganisms present, including spores, by the use of chemical or physical methods.

Surgical Facilities

A surgical area for small rodents can be any room or portion of a room that is easily sanitized. The immediate surgical area should not be used for other purposes during the time of surgery. Surgery may be conducted on a clean, uncluttered lab bench or table, in a laminar flow HEPA filtered hood, or in a glove box or other type of isolator.

Prior to and between surgeries, clean and disinfect the surface upon which surgery will be performed. Use soap and water, rinse thoroughly, and follow with a Quatricide TB or equivalent chlorine based disinfectant such as 10% sodium hypochlorite (household bleach) solution (Table 1). Disinfectants must be prepared and used according to the manufacturer's recommendations.

Table 1. Disinfectants for Equipment and Surface Decontamination

Name	Example	Comments
Chlorine	Quatricide TB Sodium Hypochlorite (Household Bleach 10% solution	Corrosive. Can be used as a disinfectant on previously cleaned surfaces. Fast acting and broad spectrum. Use a 1/:10 dilution of bleach with a contact time of 3 minutes to kill vegetative organisms. Follow manufactures label for chlorine dioxide compounds

Preparation of the Animal

Prior to taking the animal to the surgery area, hair should be removed for at least a centimeter on either side of the surgical site. Hair can be removed by clipping with a #40 clipper blade, shaving with a razor, plucking (in anesthetized mice or similar-sized rodents), or by using a depilatory cream. Vacuum or otherwise remove loose hair. Remember to be careful about burns or lacerations caused by clippers in animal species with delicate skin (i.e. rabbits, mice).

Clean and aseptically prepare the surgical site. Use an effective antiseptic surgical scrub solution (see Table 2). Carefully scrub the area with a new clean surgical sponge or sterile cotton swab. Scrub in a gradually enlarging circular pattern from the center of the proposed incision to the periphery. The sponge or swab should not be brought back from the contaminated periphery to the clean central area.

Table 2. Disinfectants for Use on the Skin

Name	*Example*	*Comments*
Alcohol	70% Ethyl alcohol 70% Isopropyl alcohol	Evaporation can contribute to hypothermia in animals. Not a high level disinfectant.
Iodophors	Betadine®, use of individual swabs is recommended.	Activity is reduced in the presence of organic matter and hard water. Wide range of microbicidal action

Dininfect the area that has been scrubbed using 70% alcohol and repeat the scrub/rinse cycle for a total of 3 times, each time beginning at the center and proceeding to the periphery.

To prevent hypothermia, try not to wet the animal any more than necessary. Care should be taken to prevent contamination of the sterile surgical field during subsequent handling and positioning of the animal. Place the animal on a clean absorbent surface and maintain body temperature using a circulating water blanket, warm water bottle, or equivalent external heat source, taking care to not cause thermal burns to the animal's skin.

Place lubricating ophthalmic ointment (such as Paralube) in the anesthetized animal's eyes to prevent drying. Once the animal has been positioned for the procedure, spray or paint the prepared surgical site with a surgical prep solution that is compatible with the surgical scrub solution you used (i.e. Betadine prep after Betadine scrub, etc.). Avoid using unrelated products as they are frequently incompatible.

Preparation of Surgical Instruments

Surgical instruments must be sterilized for use in survival rodent surgery. Several techniques (steam, dry heat, or chemical agents) can be used to sterilize instruments and other materials that will come in contact with the animal's tissues (see Table 3). Steam is the preferred method to sterilize surgical instruments at the UML ORS Facility.

Table 3. Instrument Sterilants

Method	Example	Properties
Steam sterilization	Autoclave	Time, pressure, and temperature determine effectiveness. Items should be autoclaved for at least 15 minutes at 121ºC and a pressure of 15 pounds per square inch.

Where only the tips of instruments have contacted the animals, instrument tips may be wiped with 70-90% alcohol and maintained in a sterile environment between animals. In between animals, instruments must be properly disinfected with 70% isopropyl alcohol.

Preparation of the Surgeon

Surgeons should wash their hands with an appropriate surgical scrub (e.g. Betadine Scrub) and wear a mask, sterile gloves, and clean scrub shirt or lab coat. New sterile surgical gloves should be used for each animal. Alternatively, surgeons may wipe their gloves for 30 seconds with sterile gauze pads soaked in 70-90% alcohol or alcohol foam. Latex exam gloves may be used if taken from a freshly opened box or if previously sterilized.

Intra-Operative Conduct

The sterile surgical field must be kept sterile throughout the procedure. Sterile instruments must be prevented from contacting non-sterile surfaces. Avoid touching the wound or tissues with your gloved hands. Only the sterilized tips of the surgical instruments should be in contact with animal tissues. Place instruments on a sterile surface when not in use. Sterile surgeon's gloves are required. In most cases, the use of sterile drapes is also required for maintenance of the sterile field. Monitor the animal carefully during the surgical procedure. Surgeons should pay close attention to the animal's heart rate, respiratory rate, and body temperature. Surgical incisions must be closed with appropriate materials (see Table 4). Check the expiration date of

suture packages, as expired sutures may not be used for survival surgeries.

Table 4. Suture Materials

Suture	Properties
Vicryl®, Dexon®	Absorbable 60-90 days
PDS®, Maxon®	Absorbable 6 months
Prolene®	Inert material, nonabsorbable
Silk	Nonabsorbable but may wick bacteria into the wound
Stainless Steel Wound Clips and Staples	Nonabsorbable

*Suture material used for skin closure, in general, must be removed in 10-14 days post surgery. Stainless steel wound clips and staples require a special instrument to remove.

Post-Operative Care

Prevent hypothermia by placing the animals in a warm room or cage. If necessary, the cage may be placed on a bedded or padded surface and supplied with supplemental heat as required. Be cautious with supplement heat sources; hyperthermia can be as detrimental as hypothermia. Dehydration can be ameliorated by the administration of appropriate fluid therapy. Initially, this may be done by giving 1 to 2 ml of warm fluids (0.9% NaCl or equivalent) per 100 gm of body weight by subcutaneous injection. If blood loss occurred during the surgical procedure, or if the animal is slow to recover from anesthesia, provide additional fluids.

In general, antibiotics should not be needed for short procedures if proper aseptic technique is followed throughout the surgery and the surgeon is well trained or experienced. Antibiotics should not be used in place of surgical asepsis and good tissue handling techniques. Allow animals to recover in a clean cage with no bedding, or place a paper towel between the animal and the bedding material to prevent aspiration of bedding during recovery. Animals should not be returned to the vivarium until they are stable and clearly beginning to wake up. Rodents should be housed individually until they are awake and ambulating on their own to prevent cannibalism.

Post-surgical animals should be seen every day by a member of the PI's staff or other individual to whom post-operative care has been delegated. Animals should be observed daily until all wounds have been healed and sutures or wound clips are removed (10 to14 days post surgery).

Surgery Records

A postoperative record should be kept in the room where the animals are housed. Having the record in the room accomplishes several functions:

- It explains the condition of the animals to animal care staff (a sedated animal may otherwise be thought to be ill).
- It assures animal care staff and USDA Animal Welfare inspectors that the animal is being cared for.
- It informs animal care staff how recently the investigator has seen the animal; this knowledge helps them decide whether or not there is a need to contact the investigator to inform him or her of the present condition of the animal.

Although individual records are desirable, USDA allows a composite post-operative record to be used for a group of rodents. Such a record would have a list of the animal numbers down the side and columns indicating dates. The column entries would include a notation that the animal had

been checked, any abnormal observations, and a list of any therapeutics given including drugs, doses, and routes of administration.

Records must be kept until sutures or wound clips have been removed. The post-operative record requires no further entries, but should continue to be kept in the area where the animals are housed. When the study is completed and the animals are euthanized, the records are stored for a minimum of three years.

ENDPOINTS

The IACUC must consider the selection of the most appropriate endpoint(s). Each protocol must address the expected endpoint of the animals used in each study. This requires careful consideration of the scientific requirements of the study, the expected and possible adverse effects the research animals may experience (pain, distress, illness, etc.), the most likely time course and progression of those adverse effects, and the earliest most predictive indicators of present or impending adverse effects. The effective use of endpoints requires that properly qualified individuals perform both general and study-specific observations of the research animals at appropriate time points. Optimally, studies are terminated when animals begin to exhibit clinical signs of disease if this endpoint is compatible with meeting the research objectives. Such endpoints are preferable to death or moribundity since they minimize pain and distress. Efforts must be made to minimize pain and distress experienced by animals used in research. Benefits to new and better endpoints include less per diem expenses, shorter testing times, enhanced search data, and publishable data.

PIs or their designated representative will be notified if an animal is showing signs of pain and/or distress. If the responsible designated representative cannot respond within 24 hours and animals show evidence of illness, pain, or distress, emergency care including euthanasia may be administered by the ORS Manager after consultation and approval from the AV or the IACUC Chair.

Exceptions to these euthanasia guidelines are permitted only if the clinical signs listed below are expected as part of the experiment and appropriate measures are taken to minimize pain or discomfort in the animals. Such exceptions must be approved by the IACUC as part of the protocol review process.

Protocols with death or moribundity as an endpoint should contain the following information to assist the IACUC review;

- Scientific rationale for the endpoint
- Can the pain be alleviated without compromising the study
- What alternatives were considered
- Why morbidity cannot be used as an endpoint
- How alternatives will be used whenever possible
- Why pain relieving measures cannot be utilized
- Number of animals to be used and why it is the minimum number required
- Whether animals will be euthanized when moribund and if not, what information is to be gained during the time between moribundity and death
- What is the shortest duration of pain necessary to meet research goals

Criteria for consideration of euthanasia are based on clinical signs any one of which may constitute an endpoint but are not limited to include:

Weight loss: Loss of more than 20% of body weight (depending on attitude, weight recorded at time of arrival, and age; growing animals may not lose weight, but may not

gain normally). If weight is not measured, cachexia and muscle wasting are alternative indicators.

Change in appetite: Complete anorexia for 24 hours in small rodents, or up to 5 days in large animals. Partial anorexia (less than 50% of caloric requirement) for 3 days in rodents, 7 days in large animals.

Weakness: Inability or extreme reluctance to stand which persists for 24 hours (assuming that the animal has recovered from anesthesia).

Moribund state: Depression, complete anorexia and hypothermia with little likelihood to recover (assuming that the animal has fully recovered from anesthesia). Examples of research proposals that may have death or moribundity as an endpoint include infectious disease studies, drug and toxicity studies, and cancer research.

Infection: Infection involving any organ system (either overt, or indicated by increased body temperature or WBC parameters) that fails to respond to antibiotic therapy within an appropriate time, and is accompanied by systemic signs of illness.

Organ dysfunction/failure: Signs of severe organ system dysfunction non-responsive to treatment, or with a poor prognosis as determined by a veterinarian.

Respiratory: Dyspnea and cyanosis unresponsive to appropriate medical therapy.
Cardiovascular: Acute blood loss resulting in hematocrit below 20% or severe chronic anemia (Hct < 15%).
Gastrointestinal: Severe vomiting or diarrhea (duration greater than 24 hours, unresponsive to medical therapy), obstruction, or intussusception.
Urogenital: Renal failure characterized by elevated BUN, creatinine or uroperitoneum.
Nervous: CNS depression, seizures, paralysis of one or more extremities; pain unresponsive to analgesic therapy.
Musculoskeletal: Muscle damage or fracture resulting in inability to use the limb, unless anticipated as part of the study.
Integumentary: Non-healing wounds, repeated self-trauma, second or third degree heating pad burns.

Tumor growth: Solid tumors that exceed 10 percent of normal body weight in rodents (assume 1 cm^3 = 1 gm), or tumor growth that impedes an animal's ability to ingest food, water or ability to move about its cage and remain clean and dry. A recommended overall endpoint for tumor burden is >10% of body weight. For an adult mouse, a mean tumor diameter exceeding 20mm or for an adult rat, a mean tumor diameter exceeding 40mm is considered an endpoint. See Table 5 for what to look for in cancer and toxicological studies.

Uncontrollable pain/distress: Animals showing signs of pain and/or distress that is not responsive to analgesics or anesthetics, or as determined by a veterinarian.

Table 5. Selected Clinical Observations Used in Cancer Research and Toxicological Studies*

Parameter	What to Look For
General Appearance	Dehydration, decreased body weight, missing anatomy, abnormal posture, hypothermia, fractured appendage, swelling, tissue masses, prolapse, paraphimosis
Skin and Fur	Discoloration, urine stain, pallor, redness, cyanosis, icterus, wound, sore, abscess, ulcer, alopecia, ruffled fur
Eyes	Exophthalmos, microphthalmia, ptosis, reddened eye, lacrimation, discharge opacity
Nose, Mouth, and Head	Head tilted, nasal discharge, malocclusion, salivation
Respiration	Sneezing, dyspnea, tachypnea, rales
Urine	Discoloration, blood in urine, polyuria, anuria
Feces	Discoloration, blood in the feces, softness/diarrhea
Locomotor	Hyperactivity, coma, ataxia, circling, muscle, tremors,

*Montgomery, C.A. Jr. (1990), Cancer Bulletin 42:230-237 and appeared in AWIC Newsletter, Spring 1995 6:4

FACILITY OPERATIONS

UML Policy and federal guidelines require that living conditions for research animals are appropriate for their species and contribute to their health and comfort. Accurate records must be kept regarding all aspects of animal management. Animal care and related standard operating procedures (SOPs) are provided in the UML Animal Care and Use Policies and Procedures. Procedures are posted in the animal care facility and also available in all IACUC-approved facilities. General oversight of all animals is provided by the ORS Manager who routinely consults with the AV. Specific oversight is required by the PI to whom the animals are assigned and the PI, students, or staff assigned to that research project are required to monitor animals on protocols on a regular basis. All parties must be trained in animal care and use.

Facility Access and Security

Facilities shall have security and biosecurity measures in place. Such measures will vary depending on the status or type of animals housed and the types of materials used in research projects but might include security fences, locks, or entry alarm systems, signs posted that indicate restricted entry, or limiting visitors. Access to the ORS Facility is via a card reader with a valid staff/faculty ID card only. Individuals are allowed access by contacting the ORS Manager and providing necessary UML personal identification information. The IACUC will determine the access hours granted to each individual. Access options include Monday through Friday from 6am to 6pm or twenty-four hours/day, 7 days/week. Only ORS personnel will have 24 hour access or those with IACUC-approved protocols that specifically request after-hours access. This information is forwarded to the Director of Institutional Compliance and then enters the personal information into the UML database and activates card access. Access may be denied to anyone who does not comply with UML policies and procedures as set forth by IACUC. In the case of a power outage or computer database problem, the ORS Manager and Campus Police can be contacted for entry into the facility. Anyone entering Olsen 618 is required to sign-in using the check-in log on top of the black file cabinet in the anti-room. Information collected includes name, date, time, room(s) visited, study or protocol number, animals checked (yes or no), any animals requiring special attention, and ORS Manager notified (yes or no). The door to the facility is not to be propped open at any time for security reasons, unless it is temporary to move equipment or animals.

Personal Protective Equipment

Procedures are in place to protect the research animals and the facility from personnel that could bring in contagious disease agents as a result of contact from their own or other animals that may harbor diseases. PPE is also required to protect personnel from contracting anything from the animals. Anyone entering the facility must wear personal protective equipment (PPE) and it is the responsibility of the ORS Manager to ensure compliance. An SOP is on file to describe the PPE necessary to enter the facility. Entrance to all animal rooms and the working procedures room is allowed only after individuals are wearing a disposable laboratory coat, shoe covers, and gloves. Shoe covers protect the animals and gloves protect both the animals and people. Face masks and laboratory coats protect people. All PPE is located in the Olsen 618 anti-room and must be worn prior to entering 0S618A, OS618B, OS618C, OS618D, and OS618F. PPE (a minimum of gloves and eye protection) is mandatory for handling and using animals in any UML teaching laboratories and is provided upon request.

Facility Inspections

Animal Care Facilities are inspected by a subcommittee of the IACUC at six-month intervals. The NIH Guide for the Care and Use of Laboratory Animals, Animal Welfare Regulations, and Office of Laboratory Animal Welfare (OLAW) guidelines are the principal guides on which the IACUC bases its evaluations. All surgical areas in animal care facilities, survival surgery areas in investigator's laboratory, and de-centralized or satellite quarantine facilities are included in the inspections. This includes areas in laboratories where survival surgery on rodents is practiced in order to maintain compliance with, and meet the spirit of, the AWAR, PHS Policy and Guide (both the AWAR and the Guide detail facility and procedural requirements for conducting survival surgery on rodents or APHIS/AC covered species). The IACUC attempts to inspect sites that include housing enclosures. When review of such sites is not be feasible, the IACUC may request that photographs, videos and husbandry SOPs be submitted for review.

As well as the animal use facilities, drugs, materials intended for in vivo use, surgical logs, and animal care records are inspected. At the conclusion of the inspections, the IACUC Administrator prepares a Semiannual Inspection Report. The report includes minor/and/or significant findings, a correction plan and is reviewed by the inspection team, including the ORS Manager and the AV. The final Report is then submitted to the full IACUC for approval. Depending on the findings in the report, the IACUC Chair may assign non-compliant items listed to one or more responsible persons or units, such as the study PI, the ORS Manager, Department Head, and/or the IACUC. Following the date of completion, the Director of Institutional Compliance will inspect to verify that the corrective action plan is in place and working. The results of the correction plan are reported at subsequent IACUC meetings.

The ORS Facility is also inspected on a yearly basis by the USDA. This inspection is unannounced. The USDA is allowed to inspect any and all rooms except for those that house mice and rats. They pay close attention to the condition of all covered species, facility record keeping, food expiration dates, cage wash temperatures, and overall cleanliness and condition of the facility. If the ORS Manager is unable to attend this inspection, the Life Sciences Technician II (ext. 2865) is contacted to respond. If the Life Sciences Technician is not available, the Animal Care Technician II individuals are capable of assisting with the inspection. The IACUC Administrator and AV should be notified immediately when the USDA Inspector has arrived.

The Animal Welfare Act (9CFR part 2.38b) allows the USDA APHIS Inspector to access and inspect the records, facilities, property, and covered species in animal research facilities. APHIS officials conduct unannounced inspections as necessary to enforce the provisions of the Animal Welfare Act. At the end of an inspection, the USDA inspector details his/her findings via a report. The report gives a deadline for addressing areas of non-compliance. The IACUC Administrator distributes the inspection report as soon as possible after receipt to the IO, IACUC Chair, IACUC members, and the Director of Institutional Compliance. The IACUC Administrator reviews the report, discusses next steps with the IACUC Chair, and develops a plan for corrective action if necessary. Specific issues are identified and sent

to the appropriate person and requested to be resolved by a specific date. Documentation that the corrections have been made are kept on file with the IACUC Administrator and reported at subsequent IACUC meetings.

Following the date of completion for any and all corrections, the IACUC Administrator or an IACUC member will inspect to verify that the corrective action plan is in place and working. The report is distributed to the IACUC. The Director of Institutional Compliance may also make unannounced visits to the laboratory facility.

Off-Hour and Emergency Care

All animals in the ORS Facility must be observed on a daily basis, including weekends and holidays. The ORS Manager and staff share this responsibility and a schedule is assigned by the ORS Manager. Weekend coverage includes daily observations of all animals, feeding and watering as necessary, changing cages that have water bottle dumps, applying treatment to animals as requested by the PI, monitoring temperature and humidity levels, recording and signing daily maintenance logs, and checking "tin cat" traps. Animal room doors are to be locked at all times. If there are any temperature or security problems, Campus Police should be contacted (ext. 2911). If an animal appears sick or has died, the ORS Manager should be contacted who will then contact the AV, PI, and their designated representative. Snow emergencies are covered by the staff person that lives in closest proximity to the Facility.

Controlled Substances

The Office of Research Services has been issued a license to use controlled substances by the State of Massachusetts Department of Public Health and the U.S. Drug Enforcement Agency. Both licenses are held by the Dean of the School of Science with the ORS Manager serving as Power of Attorney. Copies are on file with the IACUC Administrator.

Controlled substances are used in animal care for anesthesia, euthanasia and analgesia. They are stored in a stainless steel, wall-mounted, double locked cabinet located in room 618H. Each controlled substance is accompanied by a log that is maintained by the ORS Manager. Information contained in the inventory includes drug name, supplier, date received, and amount received. It also tracks usage, including the solution was used, volume removed, volume remaining, and the purpose of use with the PI/protocol number. Please contact ORS Manager at least 24 hours in advance, who will log and sign out controlled substance for your study. Both the PI/technician using the controlled substance and ORS Manager/Professional Technician II must sign off each time a drug is dispensed. An example of the controlled substance log is attached as Appendix H.

Any controlled substances are purchased from commercial vendors and received into the hazardous material receiving area, recorded, and delivered unopened directly to ORS. It may be received by only two authorized persons, the ORS Manager or Professional Technician II, who will verify the contents and add it to the inventory. Disposal of DEA substances requires notification of the EHS Office.

Food, Water, and Bedding

Nutritional requirements are species-specific. Animal feed must be fresh, palatable, and nutritionally adequate. Attention must be given to those animals with special dietary needs or on

special diets. Pretreatment of feed (e.g., autoclaving) may alter nutrients and require supplementation. All feeds should be stored in a cool, dry place free of potential contamination. Water is to be clean, potable, and uncontaminated. Unless otherwise approved by the IACUC, animals will have unlimited access to water. If animals will be fasting or having water withheld, the IACUC requires close monitoring of such activities. Individual caging or housing of such animals must be clearly identified.

An SOP is on file at the laboratory facility for procedures related to food and bedding. All food and bedding must be disinfected before it enters the facility. An animal room cart is taken to room 617. PPE is used and is available in the Room 618 anti-room. Use a new sponge and pour (Do NOT Spray) Quatricide TB onto it. All surfaces of the food and bedding bags are to be wiped down with the sponge. The food and bedding bags are now safe to move into the facility. The used sponge and PPE should be disposed of inside the facility in the appropriate bins. If skin is exposed to Quatricide at any time, wash the exposed are for 15 minutes with soap and water and refer to the MSDS Sheet in 618G.

Food bags must be stored in Room 618G and bedding bags may be stored in either 618G or 617. All bags are stored on racks or pallets. Each time a new bag is opened, sign the food and bedding log located on the wall in 618G. Once the food is inside the animal room, place a sticker on the food barrel and label the sticker with the name of the food, mill date, and expiration date. Most food expires 6 months after the mill date. Special diet food is stored in the refrigerator, requires a protocol number, and expiration date. It is the responsibility of the PI to dispose of expired food in a timely manner.

Environmental Requirements for Animals

The optimum temperature for the ORS Facility animal quarters is 70º F. Minor deviations from this temperature are allowed but any large drop or increase in temperature can be detrimental to the animals. The optimum humidity level, as per the Guide is 30-70%. Air exchange requirements are 10-13 per hour, per room. Based on a study performed on 10/13/04, ORS falls within these guidelines. For the detailed report, see Appendix B, ORS Airflow Survey for Olsen 618.

Space Guidelines

The Guide for the Care and Use of Laboratory Animals provides recommended space for commonly used laboratory rodents that are housed in groups. If animals are housed individually or exceed the weights provided in Table 7 below, they may require more space. Specific guidelines for various stages of mice have been established by the IACUC and are more specific than those provided in the Guide. These are posted in the ORS Facility. Please see the Guide for additional information.

Table 7. Recommended weight and space limitations by animal species.

Animal	Weight, g	Floor Area/Animal, in^2	Height, in
Mice	<10	6	5
	Up to 15	8	5
	Up to 25	12	5
	>25	>15	5
Rats	<100	17	7
	Up to 200	23	7

	Up to 300	29	7
	Up to 400	40	7
	Up to 500	60	7
	>500	>70	7
Hamsters	<60	10	6
	Up to 80	13	6
	Up to 100	16	6
	>100	>19	6
Guinea Pigs	<350	60	7
	>350	>101	7

For mice, if multiple females are bred to one male in a small cage, the pregnant females need to be separated prior to parturition. Juveniles at 21 days of age need to be sexed, weaned, and separated. Any exceptions to this rule must be approved by IACUC. Conditions that generate overcrowded situations include litters that remain with the dam for longer than 21 days after birth, more than one litter in a small cage (67 or 75 sq. in.) or more than two litters in a large cage (153 sq. in.), an older litter still in a cage when a new litter is born, and/or metabolically abnormal or aggressive animals which require lower housing density. The UML ORS staff will separate cages into single-sex groups 7 days after tagging a cage, or sooner if necessary.

Escaped Animals

Animals may occasionally escape from their cages but the best practice is to avoid or eliminate all escapes. In the event that an animal is located outside of its cage, the ORS Manager should be notified immediately. A mortality/morbidity form will be completed if the animal has died. If the animal is alive, it will be placed in a separate cage until it can be identified. If the animal is in good condition, it can remain on study but should continue to be separated from its previous cage mates. If the animal is on a special diet study, the PI must be notified immediately and a decision made regarding the disposition of the animal. Unidentified animals found in the room or on the floor wandering for an unknown period of time should be euthanized.

Pest Control Management

Bain Pest Control maintains the program to monitor unwanted rodents in the interior of ORS. On a monthly basis, a Bain technician inspects all traps in the facility. Two live "tin cat" traps are placed on the floor of all rooms. Each room also has at least one snap trap above the ceiling that is inspected monthly. If a pest is sighted and/or captured in the ORS facility, information must be entered in the pest control log book, located in room 618G.

Housing and Equipment Control

All animals will be maintained in housing systems that meet the applicable regulations, laws, and/or policies of USDA, PHS, and/or State of Massachusetts. Space recommendations for animals will be in accordance with PHS policy and the AWA. Minimum space recommendations follow those recommended in the Guide and are also provided in the UML Animal Care and Use Policies and Procedures. In general, housing guidelines require

- All animals must be maintained in an animal facility approved by the IACUC
- Physical housing and maintenance of animal facilities must be in accordance with the most recent edition of the Guide
- IACUC approves facilities and requires environmental and physical parameters are maintained at a level appropriate for the species (including but not limited to temperature,

humidity, ventilation, lighting, and noise)
- All facilities are inspected and approved by the IACUC at least twice a year

Isoflurane Use
Isoflurane is available for anesthetizing rodents. The machine and gas should only be used after training to ensure the equipment is used appropriately and safely. The ORS Manager must be in the facility during use to assist should any problems be encountered. A Standard Operating Procedure is available in the ORS Facility and must be followed when the Isoflurane machine is used.

Electrical Problems
The ORS Facility occasionally experiences electrical problems. If any should occur, notify the ORS Manager and the Physical Plant (ext. 2601). If during off hours, notify the University Police (ext. 2911). Problems may include blown electrical circuits and non-functioning light timers. Some, but not all, of the facility is powered by an emergency back-up generator. For more specific information on these types of issues, contact John Belanger, Trades Manager (ext. 4893).

Equipment Failure
The ORS Manager will be notified immediately when an equipment failure is noticed in the facility.

Animal Room Sanitation
Sanitary practices are important to maintain animal health, protect the people working with the animals, and to assure appropriate scientific standards are followed. Sanitary conditions must be maintained for all animals at all times and a regular schedule of animal care must be followed. Animal rooms, storage areas, laboratories, and other support areas must be cleaned as often as necessary with appropriate detergents and disinfectants. Litter or bedding in animal cages must be changed as often as necessary to keep animals dry and clean, and to minimize offensive odors. Animal cages, feed, water devices, racks, and auxiliary equipment must be regularly inspected, cleaned, and sanitized. Intake and exhaust ducts, including filters, should be cleaned and kept free of dust. Trash and other waste from animal facilities must be removed and disposed of by animal care personnel in a safe and sanitary manner.

An SOP for cleaning the animal facility is on file at the facility. The ORS Manager is responsible for sanitation at the facility. Proper protective equipment is worn when conducting these activities. Cleaning equipment is not to be removed from the room it is stored in unless it is stored in the cage wash room. Each room has a color-coded mop, broom, brush, and dust pan. Equipment for the cage wash room, hallways, and room G and H are stored in the cage wash room. The water in the mop bucket must be dumped and re-filled with Quatricide before cleaning the next room. All animal rooms and floors must be cleaned, swept, and mopped once per week. Animal room walls and ceilings are washed using Quatricide once per month. Cage wash room floors are hosed with Quatricide and scrubbed with a 3M Doodlebug once per week. Hallways, anti-room, storage, and office areas are swept and mopped once per week. The Procedures Room is swept and mopped after each use. If skin is exposed to Quatricide at any time, wash the exposed area for 15

minutes with soap and water and refer to the MSDS Sheet in 618G. Alcohol is NOT considered a disinfectant.

Cage Changing and Washing

All cages are changed once per week. Wire bars and micro-isolator tops are changed are changed once every two weeks. The cage washing machine must first be filled before it is used. Close the drain valve at the bottom of each door opening. Lift the door up slightly from the J-hook and slide it closed. Verify the toggle switch is set at the correct setting for the types of cages you are washing:

- DETERGENT for mouse cages, all lids, and all water bottles
- ACID for the hamster cages

Push the POWER button from off to on. The machine will fill – this takes about 7 minutes. (Tyvek suits are to be worn when the acid cycle of the cage wash is being run.)

Once the machine is full of water, turn the MOTOR button from off to on to begin running. Fill the green trays with cages or bottles (three cages can fit into the trays with the prongs and water bottles, lids, cage card holders, etc. go on the mesh trays). Slide the tray into the washer so that it connects with the conveyer belt. This will allow the tray to be pulled into the machine. Remove the tray at the right side of the cage washer. If the trays back up at the end of the right counter, they will trigger the motor to stop. Once a tray is removed, the machine will start again. Move all items to Room F for drying.

To drain, verify the type of setting that was used for washing. If you are draining the ACID cycle, push the NEUTRALIZE ACID TANK switch and let the pH Control dial spin until it stops. Let the machine run for approximately one minute. If the ACID POWER dial spins, press the NEUTRALIZE button again. Turn the POWER button off. Lift the doors up and rest them in the J-hook. Let the steam rise. Lift up the drain valve at the bottom of each door opening.

Waste Management

The staff of the ORS is responsible for their own waste removal. Garbage cans are provided in every room, except for the storage room. When a garbage can is full, the bag is removed and placed in the large garbage barrel in the outer hallway. Any bags that are excessively heavy should be double-bagged. New garbage bags are stored in the anti-room.

All biological waste is placed in the freezer in 618B. When the box inside the freezer is full, please notify Hazardous Materials Stockroom (ext. 2543) to schedule a pick-up. The same procedure is to be followed for a full sharps container.

All potentially contaminated suits are placed inside the blue barrel in the anti-room. This barrel is checked weekly by Triumvirate Environmental, removed when full, and processed through the UML Tyvek recycling program.

HAZARDOUS MATERIALS

Facilities used for animal experimentation with hazardous agents shall be separated from animal housing and support areas. Access to hazardous agents shall be limited to authorized personnel, in accordance with the safe handling, storage and disposal practices of UML. The use of appropriate ventilation such as chemical fume hoods or biological safety cabinets must be utilized to separate personnel from exposure to hazardous agents. Hazardous agents include biological, radiological, and chemical materials that may be used during a research project. The EHS Department oversees procurement, use, and chemical inventory and provides several types of safety training related to the use of these materials. Biological agents (recombinant DNA) are required by NIH to have oversight by a sister committee to the IACUC, the Institutional Biosafety Committee (IBC). The IBC reviews proposed experimentation, facility capabilities, institutional procedures, and PI training and expertise to ensure that projects using biologically-based materials are conducted safely and that they follow the guidelines set forth by NIH. While the IACUC ensures the welfare of animals involved in research, the IBC reviews and oversees all r-DNA research as well as research with biologic or infectious agents and coordinates with the IACUC on projects that involve the use of animal models. Good communication between the IACUC and IBC is important for this process to work effectively. Similarly, the Radiation Safety Committee reviews and approves projects that involve the use of radioactive materials.

EHS Policies

Depending on the specific work activity, research protocol, and/or procedure being conducted in the animal facility, the use of personal protection equipment (such as gloves, eye protection, laboratory coats, shoe covers, respirators, etc.) is required to properly protect individuals. Workers are advised to review and familiarize themselves with the specific SOP that is available at the animal facility that provides specific references and information regarding what PPE is to be worn and utilized during specific work processes. All accidents and injuries (including animal bites and needle sticks) must be reported immediately to the ORS Manager. Emergency response personnel are available on campus and equipped to deal with medical emergencies. All personnel including staff, faculty, students, and contract employees are required to adhere to the University's Blood Borne Pathogen Program and Exposure Control Plan. The occupational health and safety program provides guidance for personnel to acquire Tetanus and Hepatitis B immunizations.

Hazardous agents shall be purchased and inventoried through the UML's EHS Hazardous Materials PeopleSoft purchasing program. All Material Safety Data Sheets (MSDS) and product safety information are available from the ORS Manager.

The disposal of hazardous materials including biological, chemical and physical agents shall be conducted in accordance with the UML's EHS Office program and in accordance with applicable federal, state, and municipal regulations. See Appendix C for Instructions on Working with Botox (Botulinum Toxin A) and Appendix D for Instructions on Working with Streptozotocin.

All accidents and injuries (including animal bites and needle sticks) must be reported immediately to the ORS Manager. An emergency phone (ext. 2911) has been established and is staffed 24 hours a day in the UML Police Office at 125 Ball Hall on the North Campus for medical emergency response by UML Police and Emergency Medical Technicians. Upon notification to University Police regarding an injury, the dispatcher answering the phone will call for medical assistance and an ambulance, if necessary. The injured person and ORS Manager are to reference the University's Blood Borne Pathogen Program and Exposure Control Plan to assure that appropriate "Post Exposure and Follow-Up" procedures are followed.

Biological Materials
The UML Institutional Biosafety Committee (IBC) reviews and oversees all research and teaching activities involving biological materials, biotoxins and human or mammalian cells, tissues or body fluids including:

- Pathogenic or infectious bacteria, viruses, fungi, parasites, nucleic acids (prions), or agents of unknown pathogenicity to humans, plants, or animals
- Drug resistant bacteria, including those with drug resistant plasmids
- Human and non-human primate materials that include
  - -All human blood, blood components, tissues and body fluids
  - -Cultured human or animal cells that are potentially infectious
- Recombinant DNA or transgenic plants, animals, and microbes
- Infected animals or animal tissues
- Select agents
- Biotoxins

Investigators must register all work done with biological materials as defined above. Based on the registration information it will be determined whether the work qualifies as "exempt" or whether review by the IBC will be required. See the IBC policies and procedures document on the UML Institutional Compliance webpage for more detailed information.

Radiological Materials
The procurement, use, and disposal of radiological materials is coordinated through the University Radiation Safety office in accordance with the applicable federal, state and municipal regulations. Anyone interested in performing animal experiments using radioactive materials must 1) register and undergo general radiation safety training with the Radiation Safety Office at UML and 2) have their laboratory registered with the Radiation Safety Office for compliance. The use of radiological materials must be approved by the Radiation Safety Office prior to IACUC approval and procurement. New hires are required to attend the Radiation Safety course, which includes safety procedures for using radioactive materials and animals. For more information regarding the use of radioactive material or radiation emitting devices in research, please either consult the UML Radiation Safety Manual, available through the Radiation Safety Office, or contact a member of the Radiation Safety Office at ext. 3372 or 3373. See Appendix E for Radiation Safety Procedures for Animal Testing.

Chemical Materials
The EHS Office uses UML's PeopleSoft purchasing program to review, approve, accept delivery of, inventory, and distribute all chemical and biological products requested for purchase by

faculty and staff. The EHS office provides various safety and awareness training programs to safeguard individuals, support research initiatives and assure compliance with applicable federal, state, and municipal regulations.

APPENDICES

Appendix A. Reference Documents and Regulatory Information

Appendix B. ORS Air Flow Survey for Olsen 618

Appendix C. EHS Instructions for Working with Botox

Appendix D. EHS Instructions for Working with Streptozotocin

Appendix E. Radiation Safety Procedures for Animal Studies

Appendix F. Emergency Response Plan

Apprendix G. Level 3 Emergency Disaster Plan

Appendix H. Controlled Substance Usage Log

Appendix A. Reference Documents and Regulatory Information

General and Regulatory

Animal Welfare Act and Animal Welfare Regulations. August 2002. USDA and APHIS. Beltsville, MD.

Guide for the Care and Use of Laboratory Animals. National Research Council. 1996.

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http://cal.vet.upenn.edu/surgery/index.htm (surgery website from the University of Pennsylvania School of Veterinary Medicine – includes quick-time movies of suturing and knot tying)

NIH guidelines for survival rodent surgery at http://oacu.od.nih.gov/ARAC/surguide.htm

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Appendix B. ORS Air Flow Survey for Olsen 618

Provided by Dave Kiser, Director, dated September 13, 2004

Room/ AH		Design Supply CFM	Post Maint Supply CFM	Design Exh CFM	Post Maint Exh CFM
618 A AH1/EF11	Animal	450	332	500	370
618 B AH1/EF11	Procedures	300	218	325	209
618 C AH1/EF11	Animal	300	215	325	222
618 D AH1/EF11	Animal	600	478	650	457
618 E AH1/EF11	Cage Wash	600	505	650	464
618 F AH1/EF11	Animals	250	183	300	218
	Tot AH1/ EF 13	2500	1931	2750	1940
618 G NA EF12	Storage	None	None	250	270
			Total EF12	250	270
618 H AH2/EF13	Office	350	83	231	231
	Tot AH2/ EF 13	350	83	400	231

Overall the animal rooms, cage room, and procedures room (618 A-F) were designed to have approximately 13 air changes per hour provided by air handler 1 in the penthouse. This was intended to satisfy cooling during periods with full animal occupancy. Current air changes average about 80% and seem to be meeting the cooling/ventilating needs.

The exhaust for these rooms is provided by exhaust fan 11 on the roof. The entire area was intended to have slightly more exhaust than air supply to provide for odor control. The exhaust at this time is under performing and requires investigation. There is a moderate odor problem in the area. Even when the exhaust is functioning to design there may be a problem with heavier than air odor components. Many animal facilities are now splitting the exhaust between ceiling and floor or taking them entirely from the floor.

The storeroom (618G) on exhaust fan 12 was designed to have exhaust air only and is performing to standard.

The office (618H) was formerly a darkroom served by air handler 2 with 13 air changes per hour, 5 is sufficient for an office. The design short fall of air is overstated. The high exhaust, however, is contributing to the odor problem by pulling air form the corridor and eventually animal rooms. Need to slightly increase the air supply to 618H but more important reduce the exhaust to about 75 CFM. AH2 serves a large area and room 618G is the end of the line.

Appendix C. EHS Instructions for Working with Botox

1. Purpose

The purpose of this work instruction is to specify the procedures necessary to properly order, receive, store and use BOTOX Cosmetic (Botulinum Toxin A) Purified Neuorotoxin Complex (100 Units) "BOTOX" in protocols approved by the IACUC.

2. Scope

This procedure applies to the use of BOTOX at UML, Weed Hall, Lab 301A or The Office of Research Services, Olsen Hall.

3. Responsibility

a. It is the responsibility of the PI to authorize and train individuals who can perform this procedure.
b. It is the responsibility of the individuals authorized by the PI to read, understand, and abide by this procedure and receive certified Lab Safety Awareness training provided by EHS on an annual basis.

4. Definitions

"Properly Marked Bio-Hazardous Waste Container" – A container issued by the UML EHS used for collection of bio-hazardous wastes.

"Small Spill" – A release of 5 milliliters or less of liquid or fewer than 10 Units of BOTOX.

5. Ordering, Receiving, and Storage Procedures

a. To minimize the amount of BOTOX on hand, determine the quantity of BOTOX ordered by assessing the number of injections/transdermal applications.
-Determine the average weight (20 – 25 grams) of the animal at the time the injection will be given.
-The dosage for IM injection of BOTOX is (1.0, 5.0, or 10.0 U /5 uL of saline/kg of body weight.) The dosage for transdermal application of BOTOX is (1.0, 5.0, 10.0, 25.0, or 50.0 U /100uL of NanoEmulsions/kg of body weight.)
b. BOTOX should be ordered using the UML chemical purchase ordering system in PeopleSoft. The product is sold by Allergan.
c. Packages of BOTOX must be directed to the UML Hazardous Materials Receiving Stockroom located at Olney Building, Riverside Street, Lowell, MA 01854.
-Upon receipt, packages shall be inspected by UML EHS Staff. Damaged or leaking packages shall not be accepted.
-UML EHS staff shall assign an inventory bar code label to the container and deliver the BOTOX product to Weed Hall, Lab 301A.
-BOTOX shall be stored in Weed Hall, 3rd floor, 301A Cold Room.

6. Personal Protective Equipment

a. Before handling containers of BOTOX, wear talc free nitrile gloves.
-Torn or punctured gloves should be discarded and not used.
- If wearing double gloves, one glove should be under the gown cuff and the other one should be placed over it so no skin of the wrist or forearm is exposed.

-If clothes become contaminated do not wash them as this could potentially contaminate others.

-Dispose of contaminated clothing in a properly marked bio hazardous waste container.

b. Wear safety glasses when handling chemical containers and splash goggles when preparing solutions of BOTOX.

c. Personal protective equipment can be obtained in Weed Hall, Lab 313 Preparation Laboratory area and Olsen Building, Room 618 Anti Room.

7. Botox Preparation

a. Minimize handling of BOTOX whenever possible to avoid exposure. No eating, drinking, or smoking in or around the use area. Refer to product MSDS for additional information.

b. BOTOX will be re-constituted in 5ml of deionized and distilled water.

c. BOTOX administrated via injection will be a fixed volume of 5µl using a 30-gauge needle attached to a sterile 250µl syringe.

d. BOTOX administrated transdermally will be prepared in Weed Hall, Lab 313 preparation laboratory area. 20µl – 1ml of BOTOX will be pipetted out of the BOTOX vial into a 200ml beaker. Oil, emulsifier, and deionized/distilled water will be added to the beaker. This solution will then be passed through the microfluidizer unit. The final end product will be formulated into a cream and applied to the mice.

e. All vials, including empty and expired vials, glassware, equipment, and materials contaminated with BOTOX must be disposed of in a properly marked bio-hazardous waste container or autoclaved. Autoclaving may be applied to BOTOX contaminated material which is in solution or to which the autoclave steam has access. Autoclaving at 121 degrees Celcius for 30 minutes or greater will render the product safe.

8. Botox Administration

a. Weigh all mice to determine the dosage a day before injections/transdermal applications. Mice shall weigh 20-25 grams.

i. Determine the volume of injectable BOTOX (1.0, 5.0, or 10.0 U /5 uL of saline/kg of body weight.)

b. All treatment applications shall be performed on the right hind leg, gastrocnemius muscle, of all mice.

-Swab the mouse right quadrant with an alcohol swab. Let air dry.

-Hold the needle straight up in the air and inject into alcohol moistened cotton ball to safely eliminate air bubbles that are present.

-Insert needle at less than a 15 degree angle into the mouse right hind leg, gastrocnemius muscle.

-Draw back slightly on the syringe making sure that you have not entered a blood vessel.

-Administer the injection.

9. Cleanup Procedure

a. Never recap syringe needles.
-Discard syringe and needle into an appropriate puncture proof, bio-hazardous waste sharps container.

b. Discard unused BOTOX solution into a properly marked bio-hazardous waste container.
-Discard any additional solids, including bedding, padding and cotton balls contaminated with BOTOX, in a properly marked bio-hazardous waste container.

c. Clean the preparation area by discarding the plastic backed absorbable paper liner into a properly marked bio-hazardous waste container and thoroughly spray the work surface with a 0.5% sodium hypochlorite solution. Let stand for 5 minutes.

d. The inner surface area of cages should be assumed to contain some BOTOX contamination from incidental contact to mice with transdermal applications. The inner surface of the cages must be sprayed with a 0.5% sodium hypochlorite solution prior to routine handling and cage washing.

i. Let stand for 5 minutes. Use paper towels to dry the surface area and discard wetted paper towels into a properly marked bio-hazardous waste container.

e. All contaminated clothing and PPE, such as contaminated gloves, must be removed and discarded into a properly marked bio-hazardous waste container before leaving the work area.

f. Thoroughly wash hands with soap and water to remove any possible residue.

g. Autoclaving may be applied to BOTOX contaminated material which is in solution or to which the autoclave steam has access. Autoclaving at 121 degrees Celsius for 30 minutes or greater will render the product safe.

10. Emergency Response Spill Procedure

a. If a spill occurs that is greater than 5 mL of BOTOX solution, immediately evacuate and restrict access to the area. EHS will respond to the concerned area and clean the spill.

b. Notify University Police (ext. 2911) and the EHS Office (ext. 2618 or 2543) as soon as possible.

c. For skin contact, wash the skin with soap and water.

d. Contaminated eyes should be flushed with an eyewash for a minimum of 15 minutes. Consult a physician immediately.

e. Contaminated clothing must be removed and discarded with all other contaminated waste in a properly marked bio-hazardous waste container.

f. For additional information refer to the product MSDS sheet.

11. Reference Documents

a. 310 CMR 30, Massachusetts Hazardous Waste Regulations

b. Allergan, Material Safety Data Sheet for BOTOX, December 29, 2003

c. UMass Lowell Spill Response Policy

Appendix D. EHS Instructions for Working with Streptozotocin

1. Purpose

The purpose of this work instruction is to specify the procedures necessary to properly order, receive, store and use streptozotocin in protocols approved by the Institutional Animal Care and Use Committee (IACUC).

2. Scope

This procedure applies to streptozotocin used in the Office of Research Services (Olsen 618) at UML.

3. Responsibility

a. It is the responsibility of the PI to authorize and train individuals who can perform this procedure.
b. It is the responsibility of the individuals authorized by the PI to read, understand, and abide by this procedure and receive certified Lab Safety Awareness training provided by EHS on an annual basis.

4. Definitions

"Properly Marked Waste Container" – A container issued by UML EHS Department that has a completed UML hazardous waste label affixed to it.

"Small Spill" – A release of less than 10 milliliters of liquid or fewer than 5 grams of streptozotocin powder.

5. Ordering, Receiving, and Storage Procedures

a. To minimize the amount of streptozotocin on hand, determine the quantity of streptozotocin ordered by the number of injections that will be given.
    -Determine the average weight of the animal at the time the injection will be given. Rats between 8 and 10 weeks old average 250 grams.
    -The dosage is 40mg/kg or 4 mg/100g given in 1 intraperitoneal injection.
b. Streptozotocin should be ordered through Sigma Aldrich, product S0130 in 100mg or 500mg containers using the UML Chemical Ordering System in PeopleSoft.
c. Packages of streptozotocin must be directed to the UML Hazardous Materials Receiving Stockroom located at Olney Building, Riverside Street, Lowell, MA 01854.
    -Upon receipt packages shall be inspected by UML EHS Staff. Damaged or leaking packages shall not be accepted.
    -UML EHS Staff shall assign an inventory bar code label to the container and deliver the streptozotocin product to Olsen Building where it shall be stored in a properly marked zipper closure plastic bag or in a bin designed to contain accidental leaks.
    -Streptozotocin shall be stored in the Olsen Building 6th floor cold room.

6. Personal Protective Equipment

a. Before handling containers of streptozotocin, wear talc free nitrile gloves.

-Torn or punctured gloves should be discarded and not used.
-If wearing double gloves, one glove should be under the gown cuff and the other one should be placed over it so no skin of the wrist or forearm is exposed.
-If clothes become contaminated do not wash them as this could potentially contaminate others.
-Dispose of contaminated clothing in a properly marked waste container.

b. Wear a disposable face mask when handling streptozotocin powder.
c. Wear a pair of safety glasses or splash goggles.
d. Personal protective equipment can be obtained in the 618 Anti-Room.

7. Streptozotocin Preparation

a. Preparation of streptozotocin must take place in a properly calibrated chemical fume hood.
b. Minimize handling of streptozotocin to avoid creating dust. Refer to product MSDS for additional information.
c. Weigh all rats to determine dosage the day before injections.
d. Make up 0.1M citric acid (19.2 g/L) and 0.1M sodium citrate (29.4 g/L)
-Mix the above solutions approximately 1:1 until the final pH = 4.5.
-Filter the final buffer in the hood with a 0.2 micro millimeter syringe filter (acrodisc) into a sterile bottle and leave at room temperature.
-Sterilize two small glass bottles with rubber stoppers for needle insertion.
e. Add buffer to sterile small glass syringe bottle(s).
-Add 20 mg of streptozotocin per mL of buffer and swirl to mix.
-Make up only as much as you need plus an extra mL.
-The final injection should not be greater than 500 mL.
-At 20 mg/mL the injection volume will be 200 micro liters for a 100 gram animal.
-Diluting the streptozotocin to 20 mg/mL makes it easy to calculate the final volume for a dosage of 4 mg/100g

8. Streptozotocin Administration

a. Group rats according to weight i.e., 200 – 225g, 225 – 250g, 250 – 275g.
-Determine the volume of injectable streptozotocin solution needed for 4 mg/100g dosage of each group.
-Make up and label 1mL tuberculin syringes with the correct volume of streptocotocin solution for the rats in each weight group.
b. To administer injection have technician hold the rat by the scruff of their neck with one hand and their rear feet with other.
-With the animals back in the palm of your hand, hold the animal so that the head is slightly lower than the back feet. This will allow the internal organs to fall away from the injection site.
-Swab the rat's right quadrant with an alcohol swab. Let air dry.
-Hold the needle straight up in the air and inject into alcohol moistened cotton ball to safely eliminate air bubbles that are present.
-Insert needle at less than a 15 degree angle into the rat's lower right quadrant.

-Draw back slightly on the syringe making sure that you have not entered a blood vessel.
-Administer the injection.

9. Cleanup Procedure

a. Discard the syringe and needle into an appropriate puncture proof waste container.
   -Do not recap the needle.
b. Discard unused streptocotocin solution into a properly marked waste container.
   -Discard any additional solids contaminated with streptozotocin in a properly marked waste container. i.e., cotton balls.
c. Clean the preparation area by discarding the plastic-backed absorbable paper liner and then wash the surface with Quatricde TB.
   -Use paper towels to dry the surface area.
d. All contaminated clothing should be removed and discarded into a properly marked waste container before leaving the work area.
e. Thoroughly wash hands with soap and water to remove any possible residue.

10. Emergency Response Spill Procedure

a. If a spill occurs which is greater than 10mL of streptozcotocin solution or 5 grams of streptozotocin powder, immediately evacuate and restrict access to the area. EHS will respond to clean spill and concerned area.
   i. Notify University Police (ext. 2911) or EHS Office (ext. 2618 or 2543) as soon as possible.
   ii. If contaminated by the spill, the contaminated skin should be washed with soap and water.
   iii. Contaminated eyes should be flushed with an eyewash for a minimum of 15 minutes.
   iv. Contaminated clothing must be removed and discarded with all other contaminated waste in a properly marked waste container.
   v. For additional information refer to the product MSDS sheet.

11. Reference Documents

a. 310 CMR 30, Massachusetts Hazardous Waste Regulations
b. Sigma-Aldrich, Material Safety Data Sheet, Product S0130, Version 1.3, Dated 4/11/2004
c. UMass Lowell Spill Response Policy

Appendix E. General Radiation Safety Procedures for Animal Studies

Provided by Dr. David Medich, Director Radiation Safety, October 6, 2008

The following is a list of established radiation safety procedures for use with radiation tracer/use animal studies.

1. All animals are to be housed on racks in closed bottom cages containing absorbent bedding. The animals are to be handled cautiously and with respect.

2. The doors to the animal room entrance shall be kept locked at all times.

3. Smoking and Eating are strictly prohibited inside the animal care room.

4. Each research project must have written approval from the Radiation Safety Office and the IACUC

5. Animals in which radioactive materials are injected or incorporated are to be maintained in separate areas from untreated animals.

6. Splash guards shall be hung on the front of each cage.

7. Each animal cage is to be labeled with the name of the researcher, date, experiment number, isotope, and quantity of the radionuclide present within the animal.

8. Floor surfaces near the controlled area are to be clean and free of clutter and debris.

9. The Radiation Safety Office shall be notified immediately in the event of a radiation related accident (ext. 3372 or 3373). After Hours, call UML Police (ext. 2911).

10. Personnel dosimetry and additional requirements may be necessary depending on the particular experiment.

11. Radioactive waste, including animal carcass waste, shall be disposed of as per Procedure HPP-5. NOTE: Animal carcasses containing less than 0.05 μCi of C-14 or H-3 per gram of animal tissue, averaged over the weight of the entire animal, may be treated as *non-radioactive*.

12. Changes or release from the above controls may only be granted by the Director of Radiation Safety.

Appendix F. Emergency Response Plan

Purpose

This plan outlines actions to be implemented in the event of a disaster or emergency before any such unexpected disaster happens. The plan is designed to

- Provide a framework in responding to weather or staffing emergencies
- Minimize injury, damage, and loss to people and animals
- Protect research that is in progress, if possible
- Resume operations as soon as possible after the emergency

The plan will be communicated to all personnel; practice drills will be conducted once a year to ensure all personnel understand the appropriate steps to take in the event of such an emergency.

Definitions

Abnormal Situation: Anything that deviates from the standard operating procedures.

Assessment: A study to estimate or determine the significance and effects of factors or events.

Biosafety: A complete program of administrative controls, medical surveillance, facility design, vaccination, and containment strategies for promoting safe laboratory practices, procedures, and containment equipment to reduce the risk of disease or transmission of biologic agents to employees from potential occupational exposure to infectious agents or other biologically derived molecules.

Disaster: A natural or man-made event that results in loss of life and property or that is ruinous to an undertaking.

Emergency: An unexpected occurrence or set of circumstances demanding immediate action. Any emergency can become a disaster if not properly identified and correctly handled.

Responsible Official: An official who has been designated to ensure emergency actions are carried out.

Risk: The probability of loss or injury from a hazard.

Threat: An expression of intention to inflict evil, injury, or damage; an indication of something impending.

Threat Assessment: An evaluation that is made based on available information of the actual or potential threats of malevolent actions.

Vulnerability: Susceptibility to damage from adverse factors or influences; open to attack or damage; capable of being physically or emotionally damaged or wounded

Vulnerability Assessment: A systematic evaluation process to determine how susceptible something is to attack or damage and the information is then used to evaluate control mechanisms in place and make recommendations about increasing control mechanisms to reduce vulnerabilities.

Potential Threats
The vulnerability of the facility is evaluated to determine potential threats and identify those that pose the highest risk. The facility has limited access and is secured at all times. The following events have the potential to affect operations at the ORS facility:

- threats from animal activists
- weather-related events (e.g., floods, earthquakes, hurricanes, blizzards, or tornadoes)
- fires
- pandemic influenza outbreaks
- contamination of air and water

Extended loss of power and the inability of support staff to reach the facility would create the highest need for action.

Emergency Response Categories
In all cases, protection of human life is to be considered the highest priority at all times. Response to any emergency is based on the level of concern and the duration of the event. Emergencies are categorized by level.

Level 1= event of short duration with minor implications to the animals such as:

- power outage < 2 hours,
- HVAC shutdown for any time,
- elevators stopped and corridors closed off,
- water or steam out < 4 hours
- escaped animals

Level 2 = scheduled event of longer duration or weather advisory such as:

- Power outage >2 hours,
- HVAC shutdown > 4 hours,
- Damaging noise for several days (potential for substantial physiological and metabolic effects on rodents)
- Water or steam out > 4 hours (or any unscheduled outage),

Level 3 = sudden unplanned event or long-term planned shut down with potentially hazardous circumstances for personnel or animals such as:

- Riots
- Extended closure due to pandemic event
- Facility damage – fire, earthquake structural damage, etc.
- Massive catastrophe
- Weather that prevents workers from reaching facility for several days

The time of year the event occurs will influence the response action. If a Level 1 or 2 shutdown occurs during the winter, portable heaters could be used to keep temperatures from dropping too low. More serious problems may occur during summer as room temperatures rise quickly when power is out for extended times. The first floor or basement of Olsen could be used temporarily as a site to hold the animals if temperature considerations are an issue for a short time period because these areas are not appropriate for long-term animal care, but only after approval from

the appropriate vice chancellors. There is one elevator on emergency back-up power if animals need to be relocated.

Level 3 emergencies that are anticipated require a disaster plan (see Appendix G). That plan will be posted in the anteroom at the ORS Facility. In the event of a Level 3 emergency that requires shutting down for an extended period of time, it is likely that animals would need to be euthanized. There should be enough drugs on hand at the facility to euthanize all of the animals, if necessary. For animals already on studies, the PI or their designated representative would be required to have directions on file in the ORS Facility with their authorization for such emergency actions. In the event all animals had to be euthanized, carcasses would be placed in biohazard bags and placed in the freezer and locked if there is not time for normal procedures for pick up to be followed. When early detection of potential threat is possible, the freezer would be emptied in advance to prepare for this alternative. Emergency supplies should always be available at the facility and include batteries, flashlights, first aid supplies, food, water, and bedding materials.

Facility Considerations

The type of and severity of the emergency that occurs will dictate the response. In addition, the time of the year that the emergency occurs will influence how quickly the response will need to be enacted. Temperature is an important consideration for maintaining the health and welfare of the animals. If the room temperature falls below 40°F or rises above 80 °F, emergency action plans will be implemented to care for the animals appropriately. It is anticipated that there would be between 12 and 24 hours to respond under worst case conditions (e.g., extreme hot or cold outside temperatures with high winds) before interior temperatures fall above or below the critical range identified. A critical component that would affect the temperature and the response time is related to the heat/air systems turning off but the air exchange system continuing to work. If this were to happen, the most significant impact could occur in the summer months and reducing the response time to approximately six hours. At other times of the year, when temperatures are more moderate, the animals could remain in the facility possibly indefinitely without power before they would need to be moved or sacrificed due to temperature.

Another important consideration with loss of power is air exchange. There is no backup air handling system and that may dictate how long the facility could be operated without power. Action response time will depend on the number of animals in the facility at the time of power loss; fewer animals could be maintained for a longer time period with out detrimental effects. There is also no backup cooling system for the animal facility if the primary system fails during the swing seasons (between April to May and September to October). Cooling is generally not required from mid-October to mid-April.

The average number of animals housed in the facility from April 2006 through March 2007 was 625 per month. The house mouse is the primary species used in the facility. Animal numbers presented are per calendar year. Exact numbers were available only for 2006 and those numbers were used to generate the estimates. Gerbils, hamsters, and rats are used occasionally. The table below displays an estimated total of the animals used by species at UML from 2004 through 2006. The average number of animals housed in the facility per month has increased from 382 in 2004 to 544 in 206.

Table 1. Numbers of animals use by species at UML.

Species	2004 (est.)	2005 (est.)	2006 (exact)
Mouse	4400	5485	5990
Hamster	175	368	500
Rat	5		21
Gerbil			14
Total	4580	5853	6525
% of Total	Mouse 96.1% Hamster 3.8% Rat <0.1% Gerbil	Mouse 94% Hamster 6% Rat Gerbil	Mouse 91.8% Hamster 7.7% Rat 0.3 Gerbil 0.2

There are approximately 250 pounds of food on hand at any one time, which should be enough to feed the animals for approximately 1.5 months, again depending on the number housed at the facility when the emergency occurs. When there is advance notice of a short term or predicted weather related emergency, water will be stored in extra bottles and placed in the cabinet. Normally, cages are changed and washed at least once per week. Extra bedding should always be stored at the facility to allow for cages to be dumped and refilled if there is no power to do cage washing. Enough cages are stored at the facility to allow for one cage change without power. If possible, hamsters and gerbils and other USDA covered species should be prioritized for cage changes. There are two first aid kits in the facility; there are no overnight accommodations are available.

Other Considerations

Equipment

Items of the highest expense (biosafety cabinets, anesthesia machine, etc.) need to be protected in the event of a Level 3 emergency and need to be restarted appropriately once power is restored.

Roles and Responsibilities

Contact information for critical staff is provided below in the event of any emergency. The ORS Manager schedules personnel to maintain weekend and off-hours coverage.

Emergency Contact List

Name	Title/Position	Address	Phone Number
Alex Cepeda	ORS Facility Manager	48 Royal Crest Dr., #4 N. Andover, MA 01845	W 978-934-2830 H 978-258-8921 C 978-397-5201
UML Police		118 Engineering Bldg.	Routine 978-934-2394 or 2398 Emergency x2911
Dave Kiser John Belanegr	Facilities Personnel	Update contact info University Police	Police 978 943 2394
Morton Ailing	Operations Specialist	251 Ballardvale St Wilmington, MA 01887	W 781-222-6780 H C 802-238-4901
Scout Chou	Attending Veterinarian		W 781-222-6166 H C 9617-840-2521
Facility Support Staff	Regular hours After hours	Facilities Office Cumnock C10 UML Police	Facilities 978 934 2604 Police 978 943 2394
Elaine Major	Inst. Compliance Director	55 Old Stage Rd Chelmsford, MA 01824	W 978-934-3452 H 978-455-5020 C 978-618-9542

Amy Finneral	IACUC Administrator	215 Wannalancit Bldg.	W 978-934-4698 H 978-937-9427 C 978-996-5041
Glenn MacDonald	EHS		W 978-934-2632 H 978-251-4407 C 978-804-5576
Rich Lemoine	EHS Director	115 Kitson Hall	W 978-934-2618 H C 978-265-2661
Susan Braunhut	Biology Dept Faculty		W 978-934-2876 H C
Garth Hall	Biology Dept Faculty		W 978-934-2888 or 2877 H C
Robert Nicolosi	Ctr for Health & Disease Res Faculty		W 978-934-4501 H C
Peter Gaines	Biology Dept Faculty		W 978-934-2894 H C
Thomas Shea	Biology Dept Faculty		W 978-934-2881 H C
Thomas Wilson	Ctr for Health & Disease Res Faculty		W 978-934-4509 H C
Karen Thompson	Biology Dept. Technician		W 978-934-2865 H C
Bruce Young	Physical Therapy Dept Faculty	Solomont Way, Suite 5 Weed Hall	W H C

Communication and Risk Reduction

All personnel that report routinely for work at the ORS Facility will be trained in emergency response procedures. An action plan based on the level of emergency will be communicated to all personnel during training events. A communication mechanism will be set up for all staff during training sessions in the event that phone or internet services are not available during an emergency.

Facility Security

Access to the facility is by secure card access. In the event of a power failure, the University Police can be contacted to get access to the facility. Only authorized persons will be allowed access. (Ensure animal care personnel are listed as among the emergency responders so the UML Police will allow them access to respond.)

Backup of Records

All records will be backed up once per month and saved electronically on the UML secured server, which is backed up at an off-site facility.

Emergency Response Training for Personnel

All personnel that have research animals and responsibilities in the animal facility will be briefed on the types of emergencies and the actions that may be required for each. The emergency contact list will be updated each semester. Disaster plan drills will be conducted annually.

Other Links

http://www.cdc.gov/od/ohs/
http://www.nih.gov/grants/olaw/guidebook_excerpt.doc

(Post in ORS Facility)
Appendix G. Level 3 Emergency Disaster Plan

Precautions

Minimum of one extra week of food supply in facility at all times.
Minimum of more than one extra week of bedding in facility at all times.
Adequate supply of bottles, sipper tubes, and stoppers for one week of water.

Any special food must be provided in sufficient amounts for one week by the PI. (If not on hand at the beginning of the alert, animals are fed regular food and water when the special supplies are exhausted.

Step 1 – Alert

Facility Preparation by Staff

When advance notice is provided, staff must prepare facility to go unmanned for up to one week.

Contact all ORS staff to assist with preparations
Ensure adequate supplies of CO2 and isoflurane on hand
PIs must euthanize non-essential animals within 24 hours (if long-term closure)
Store extra water in carboys or other appropriate containers
Change out cages
Secure doors
Backup computer files
Brief all staff about appropriate next steps

Animal Species Preparation

The goal is to reduce census levels where possible to reduce the need for cage changes during the emergency. Below are recommended numbers per cage.

- Mice – reduce to three per cage
- Rats – reduce to two per cage
- Hamsters – reduce to 4-5 per cage
- Gerbils – reduce to 5 per cage (If young are present with a male and female adult and are close to becoming independent, decrease cage density by removing the male)
- Guinea Pigs – no more than three adults per unit with water bottle in reserve

General Husbandry Emergency Procedures

If guidelines are followed, food, bedding, and water procedures will hold for 3 to 4 days with only health checks and minor spot changes and watering. If power is out, it will be difficult to conduct normal husbandry. Even if bedding was changed yesterday, it must be re-done to prepare for several days away and must be at least 1.5 times the normal amount of bedding for additional absorbency. Bedding should NOT be added to an already soiled cage. Start with a clean cage and fresh bedding. All soiled bedding must be appropriately disposed of.

Water containers must be filled at the last minute to keep them as fresh as possible. Close the container tightly. For rats, hamsters, and guinea pigs, all bottles must contain 16oz. All extra water bottles should be filled and stored for replacements. Coordinate who will be responsible to conduct health check in 2 to 3 days.

Step 2 – Recovery

Personnel arrive and conduct inventory and status of animal facility condition and condition of animals (if not long-term closure). Requests for supplies are generated and begin clean up and normal husbandry procedures. Normal work schedule is resumed as quickly as possible. Evaluate emergency plan procedures and revise based on recent experiences.

Appendix H. Controlled Substance Usage Log

CONTROLLED SUBSTANCE USE AND DISPOSAL RECORD

UML DEA License # RT0325820
UML MA/DPH Registration # MT0591607K

Disposal Route Codes:
T–Triumvirate Environmental, weekly pickup
E– Requires Special Advance Notice to EHS for proper disposal
U– Used for approved IACUC procedure(s)
O– Other, Specify _____

Controlled Substance_____
Manufacturer_____
Date Received_____
Expiration Date_____
Units/Container _____ Concentration_____ Volume_____ Lot #_____
Expired Drug Disposal Method_____ Witness Initial

Date	Initial Volume	Amount Withdrawn	Balance Remaining	PI/User	IACUC Protocol #	Species	Unused Drug Mixture Disposal	Witness Initial	Comments