Environmental Enrichment

Joleen Adams, DVM

It has long been our position to ensure appropriate care and use of our laboratory animals, a position that supports both animal welfare and research integrity. It is well accepted in the research community that animals which are well adapted to their environment make more ideal research subjects. A very effective method of ensuring the well-being of our research animals is to provide an enhanced environment in which the animals can interact. This is the stance that both the Animal Welfare Act and Regulations (AWARs) and the Guide for the Care and Use of Laboratory Animals (the Guide) take regarding the care and use of research and teaching animals. We rely heavily upon current federal regulations and policies regarding the care and use of research animals. The recently updated Guide now stresses the importance of providing research animals with species appropriate environmental enrichment. We are in the process of incorporating these new recommendations into the environmental enrichment program for the research animals at the University of Tennessee.

The Animal Welfare Information Center (AWIC) has extensive information regarding environmental enrichment strategies for both USDA and non-USDA covered animals used in research. The website stresses the importance of providing animals with an enhanced environment, and we have heavily relied upon this information source for guidance in revising our enrichment plan.

The Guide now contains sections devoted to environmental enrichment for both terrestrial and aquatic species typically used in the research setting. The University of Tennessee takes these recommendations very seriously, and the Office of Laboratory Animal Care has been working extensively with the animal care staff, the IACUC, and PIs to incorporate these suggestions into our enrichment SOPs.

There are several types of enrichment that can be provided to our research and teaching animals. Various housing methods, manipulanda such as Kong toys for our canines, and nutritional items such as foraging crumbles for our rodents can be provided. Social housing is a very effective means of providing an enhanced environment to our animals and, per the Guide, should be the default method for housing social species. Our felines and several of our rodent species are group housed as long as this housing method is consistent with research objectives. Recent additions to our canine teaching pool are now being pair housed with great success. Social housing allows animals to engage in species specific behavior and reduces anxiety and stereotypies often elicited by single housing.
Manipulanda are also provided to many of the research and teaching animals. Kong toys are a great way for our canines to engage in species specific behavior of chewing and gnawing. Providing enrichment that stimulates mental and physical activity works well for our felines and rabbits which have both interactive toys as well as manipulative toys provided to them. For our rodents, we think it is important that they be allowed to build nests and forage. So far, we have been very pleased with the success that has occurred by providing them with huts and nest building material (ex. nestlets and enriched bedding) that they can utilize.

Of course, there exists a balance between research needs and welfare needs of the animals. If social housing is inappropriate due to the research objectives, other enrichment strategies congruent with the research can be employed. Other research objectives might also affect the type of enrichment utilized. Nutritional studies might preclude environmental enrichment strategies that utilize food treats. However, animals on nutritional studies may need another form of enrichment, and this can easily be accomplished as long as this research need is conveyed. Other animals that are prone to becoming overweight may have their daily kibble ration placed in a treat dispensing ball instead of being provided with additional treats. There are numerous methods that can be utilized to make the enrichment program work in harmony with research objectives as well as with animal well-being.

Providing an enriched environment is critical for ensuring the welfare of our research and teaching animals. The environmental enrichment plan currently being updated incorporates the recommendations made both by USDA and the recently updated Guide for the Care and Use of Laboratory Animals. We are confident that having everyone who has a stake in the care and use of our research and teaching animals involved in the development of the enrichment SOPs will create an animal care and use program that exceeds expectations benefiting not only the animals but our research as well.

New Procedures for Hazard Use

William Hill, DVM, MPH, DACLAM, CPIA

Do your animal experiments involve hazard use? If so, the recently developed standard operating procedure (SOP), Hazard Identification and Risk Mitigation for Laboratory Animal Personnel, will be pertinent to your work. The SOP was approved by our institutional official, Dr. Jim Thompson, on November 9, 2011, and is effective immediately. For your information, the entire SOP is included in this newsletter.

Cage side training, led by a campus safety expert, is now required for all at-risk personnel prior to initial procurement or transfer of animals to protocols involving hazardous agents. At-risk personnel include the principal investigator, laboratory staff, husbandry staff, facility manager, and facility veterinarian. Individuals requesting IACUC approval to be added to existing protocols using hazards must complete the required training prior to being added to the protocol. Also, look for orange cage cards in your facility. All cages housing animals used on protocols with hazards will now be identified with an orange cage card. As a principal investigator, you must now notify your facility manager at least 24 hours before hazard use. Principal investigators will also be responsible for labeling each primary closure with a safety sticker appropriately identifying the hazard in use.

Workplace safety is a shared responsibility. The Office of Laboratory Animal Care and our campus safety experts look forward to working with you to ensure the safety of all animal caretakers and users.
The University of Tennessee, Knoxville Area (UTK-A)
Animal Care and Use Program

Standard Operating Procedure
Hazard Identification and Risk Mitigation for Laboratory Animal Personnel

1.0 Scope and Application

In accordance with the Guide for the Care and Use of Laboratory Animals, the institutional Occupational Health and Safety Program should identify potential hazards in the work environment and determine appropriate strategies to minimize risks. Moreover, personnel at risk should be provided with clearly defined procedures and equipment to safely conduct their duties, understand the hazards involved, and be proficient in implementing the required safeguards. To ensure conformance with Guide recommendations, effective hazard control and prevention strategies are required.

2.0 Summary of Method

- Each protocol for use of live vertebrate animals received by the UTK-A Institutional Animal Care and Use Committee (IACUC) will be reviewed by the UTK-A biosafety officer prior to IACUC review. The biosafety officer will identify if radiological, biological or chemical hazards are associated with the proposed work. When hazards are identified, the biosafety officer will forward the protocol to the appropriate campus safety expert for risk assessment and to determine appropriate risk mitigation practices.

- Each protocol for use of live vertebrate animals received by the UTK-A IACUC will be reviewed by the occupational health nurse prior to IACUC review. The nurse will ensure enrollment or waiver of Occupational Health Program participation for all protocol personnel.

- Protocols with identified hazards, as determined by the appropriate campus safety expert, will require generation of an Animal Hazard Control Form (AHCF). The AHCF will identify the hazard and outline specific risk mitigation practices for personnel. The AHCF will be developed by the appropriate campus safety expert in consultation with the principal investigator, the facility veterinarian, the facility manager, and the occupational health nurse. The facility manager will prominently display the AHCF at the entrance of the secondary enclosure housing animals with identified hazards.

- Training specific to the hazardous agent involved, including discussion of potential exposure routes and risk mitigation strategies, will be required for all personnel at risk prior to initial procurement or transfer of animals to protocols involving hazardous agents. The facility manager will be responsible for notifying, in writing, the appropriate campus safety expert that a request to procure or transfer animals to protocols involving hazardous agents has been initiated. The appropriate campus safety expert will be responsible for scheduling the required training. Training will occur cage-side and include the campus safety expert, facility veterinarian, facility manager, husbandry staff, principal investigator, and laboratory personnel. The campus safety expert will notify the IACUC, in writing, of protocol personnel who complete the required hazardous agent specific training.

  - IACUC staff will notify the biosafety officer of all requests to add personnel to active protocols with identified hazards. Addition of personnel to approved protocols involving hazards will require hazardous agent specific training, as described above, prior to IACUC approval.

- All primary enclosures housing animals used on protocols with identified hazards will be prominently identified with an orange cage card. Responsibility for identification of secondary enclosures housing animals with hazards will be shared between the facility manager and protocol personnel. At least 24 hours before hazard use, the principal investigator will notify the facility manager of hazard material introduction. At the time of hazard introduction, the principal investigator will be ultimately held responsible for ensuring each primary enclosure is labeled with a safety sticker appropriately identifying the hazard in use (i.e. radiological, biological or chemical).

3.0 Reference


Author: Dr. William A. Hill

Approved by: [Signature]

Approval date: [Date]
In the context of biological safety, risk assessment is the process where agent-related factors and lab activities are evaluated to determine the appropriate biosafety level for the proposed work. The biosafety level (BSL) is a combination of work practices, engineering controls (i.e., containment devices) and personal protective equipment that will minimize the potential for environmental release of lab materials and infectious disease risk for laboratory personnel. An animal biosafety level is a combination of facilities, equipment and procedures that are used when conducting studies involving live animals and infectious agents (including recombinant organisms). The combination of these elements is intended to protect research and animal care personnel from acquiring infections as well as to "contain" the infectious disease hazard so that other animals in the facility are not affected. Animal biosafety levels are typically categorized as follows:

**Animal Biosafety Level 1** - suitable for work in animals involving well-characterized agents that are not known to cause disease in immunocompetent adult humans, and present minimal potential hazard to personnel and the environment;

**Animal Biosafety Level 2** - suitable for work involving laboratory animals infected with agents associated with human disease and pose moderate hazards to personnel and the environment;

**Animal Biosafety Level 3** - suitable for work with laboratory animals infected with indigenous or exotic agents, agents that present a potential for aerosol transmission, and agents causing serious or potentially lethal disease;

**Animal Biosafety Level 4** - required for work with animals infected with dangerous and exotic agents that pose a high individual risk of aerosol-transmitted laboratory infections and life-threatening disease that is frequently fatal, for which there are no vaccines or treatments; or a related agent with unknown risk of transmission.

Based on the CDC/NIH *Biosafety in Microbiological and Biomedical Laboratories, 5th ed.* (BMBL), the UT-Knoxville-based Biosafety Office and Institutional Biosafety Committee (IBC) consider the following when conducting a risk assessment and assigning a (animal) biosafety level:

**The pathogenicity (ability to cause disease) of the infectious or potentially infectious agent.** Infectious dose, severity of the disease, history of laboratory-acquired infections and incidence in the community must be evaluated. In terms of risk, a lower infectious dose, greater disease severity, past history of lab-acquired infections, etc. are all associated with a higher risk level.

**The availability of effective prophylaxis and/or treatment.** It is important to identify and outline available pre-exposure prophylaxis (i.e., effective vaccines) and post-exposure prophylaxis, including passive immunizations and treatment options. Although greater disease severity often correlates with a higher biosafety level, the assignment of the biosafety level must also be determined within the context of therapeutic intervention, available vaccines, susceptibility to antibiotics or antiviral agents, etc.

**The immune status of the employee.** The outcome of infection is ultimately determined by interaction with the host, with immune status directly connected to susceptibility. Opportunistic pathogens and agents that are a part of normal microbial flora which are of no or low concern to healthy adults can cause disease in immunocompromised individuals. Therefore, underlying conditions and the risk to pregnant women (and their unborn baby) should be identified.

**The route of transmission of the infectious or suspected infectious agent.** Unless noted otherwise, it should be assumed that agents have multiple routes of transmission. Parenteral (injection), oral (ingestion), mucosal, and airborne (inhalation) routes must be considered, and for every agent, the potential for aerosol transmission must be evaluated. Aerosols are considered the most dangerous route of transmission because of the large number of personnel that can be infected and because most laboratory-acquired infections are known (or suspected) to be contracted via aerosol exposure. The route of transmission in the community should also be noted.
The agent’s viability in the environment. Factors (desiccation, exposure to sun or UV light, susceptibility to heat or chemical disinfectants, etc.) that affect the infectious agent’s stability in the environment must be evaluated. There is a greater risk associated with organisms that can persist in the environment. Agent stability is also related to aerosol infectivity; inactivation of viable aerosols limits transmission via this route.

The origin of the potentially infectious agent. Evaluation of the origin should include host (e.g., symptomatic or asymptomatic animal), geographical location (e.g., domestic or foreign), association with zoonotic infection or disease outbreak and ability to endanger other animals (intraspecies or interspecies). The host range of the agent should also be determined.

The concentration of infectious organisms. The risk is higher for manipulations of (highly) concentrated samples. In addition to concentration, the evaluation of the sample should include the volume or amount of material being handled.

The planned activities. The activities should be evaluated for, among other things, their propensity to generate aerosols and how much handling of the sample materials is required. Examples of activities include sonication, centrifugation, those requiring or resulting in agent amplification and those involving sharps.

The experience/skill level of at-risk personnel. At-risk personnel directly handling the infectious or potentially infectious materials should be identified and their experience and skill level evaluated. Depending on the operation, at-risk personnel might also include maintenance workers, custodial staff, etc. If additional training is necessary to ensure safety, it should be considered.

Genetic manipulations. When working with genetically altered infectious agents, factors such as transgene source and nature/function, enhancement or attenuation of virulence, and environmental impact must be assessed. The NIH Guidelines for Research Involving Recombinant DNA Molecules specifies that animal challenges with recombinant microorganisms/viruses are to be conducted at ABSL-2 (or higher, depending on risk assessment).

Animal-specific factors. In addition to the above, consideration must be given to how the infectious agent is likely to behave in the challenge animal(s). Factors include: challenge dose, method of challenge dose administration, immune status of the host animal (e.g. nude or SCID mice may allow for rapid replication and dissemination of the agent), route of excretion, and duration of agent shedding if excreted.

Questions about biological safety risk assessments or assigned animal biosafety level? Contact the UTK/UTIA/GSM Biosafety Office at (865) 974-1938 or branger@utk.edu.

An Overview of Guidelines and Regulations
Chris Carter, LVT, RLATg

As many of us are well aware, laboratory animals are a tightly regulated group with a myriad of regulations and policies. The three big names when it comes to oversight of animal research activities are: USDA-APHIS, OLAW, and AAALAC. Each agency has their own set of rules or guidelines, and each share similarities in their oversight and implementation of regulatory policy and guidelines. The Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) has the distinction of being the only non-governmental agency and carries no regulatory authority. AAALAC uses the Guide for Care and Use of Laboratory Animals (The Guide), the Guide for Care and Use of Agriculture Animals in Agriculture Research and Teaching (the Ag Guide), and a peer review process as their standard for accreditation. The Guide and the Ag Guide as the names imply provide guidance for all aspects of the animal care and use program from species specific housing to veterinary care to physical plant specifications. To maintain an AAALAC accredited research and teaching program, institutions agree to a site visit every three years where AAALAC will conduct a comprehensive review of the animal care and use program. Having an AAALAC accredited program demonstrates the institution’s commitment to responsible use and care of animals and is a symbol of quality assurance recognized around the world.

The Office of Laboratory Animal Welfare (OLAW) is the branch of the National Institutes of Health (NIH) with the responsibility for laboratory animals that are supported by a Public Health Service (PHS) agency. A few of the most notable PHS agencies are the Food and Drug Administration, Centers for Disease Control and Prevention, and the NIH. OLAW is responsible for implementing the PHS policy as is mandated by the Health and Research Extension Act of 1985. Before an institution can receive a grant or contract from a PHS funding agency, the institution must have an approved Animal Welfare Assurance with OLAW. This Assurance is an agreement between the institution and OLAW stating that the institution will comply with the PHS Policy, the Guide, and the Animal Welfare Act and Regulations.
Lastly, the Animal Care division of the United States Department of Agriculture – Animal and Plant Health Inspection Service (USDA-APHIS) is responsible for enforcing the Animal Welfare Act (AWA) and Regulations. The AWA limits the oversight of the USDA to any warm-blooded animal which is being used for research, teaching, testing or experimentation. The exception to this rule are birds, rats of the genus Rattus and mice of the genus Mus bred for use in research and other farm animals used for the improvement of animal nutrition, breeding, management, or production efficiency. Any institution using an animal as defined by the AWA must be registered or licensed with the USDA and file a yearly report detailing animal usage. Also, a USDA inspector will make an unannounced visit and inspect the facilities housing USDA covered animals ensuring that the institution abides by the minimum standards defined in the AWA and regulations. Any deviation from the AWA is cited in their report and repeat offences can result in fines, litigation, or suspension. All USDA reports are made publicly available on their website.

It is important to understand that the information distributed to the animal users in the form of IACUC protocols, standard operating procedures, and training have a foundation in these regulatory documents and guidelines. Compliance is a group effort and is essential to maintaining a top-notch animal care and use program.

Spotlight on Animal Models in Research
John Malone, PhD

My students and I have studied various aspects of “perception in pigeons,” or discrimination learning and stimulus generalization, during the past several decades. The same work could be done with human subjects, but pigeons are harder, more convenient, cheaper, and less influenced by human society. That is, a pigeon never calls a visual display of 600nm “red” or a light flickering at 60Hz “steady.” Their lack of molding by human education, particularly in language use, along with their excellent vision, makes them excellent subjects. The full rationale for the importance of understanding discrimination learning begins with Aristotle’s belief that the act of discrimination, or the sorting out of objects of perception, was the most basic psychological process (see my Psychology: Pythagoras to Present, MIT Press, 2009, 2010).

Over the years, my students and I have used operant methods, featuring occasional mixed-grain food deliveries paired with the birds’ pecking of specific “target” stimuli on a back-lit transparent response key. We’ve used various stimulus continua, including line tilt and “color,” but now use only flicker frequency of white light, a clean continuum that is independent of angle of view, wavelength, or intensity of light. Our efforts show that sequential effects influence judgments of individual stimuli. These effects depend on immediately-preceding stimulus values, and sometimes on stimuli further removed. For example, a stimulus 5 in the middle of a continuum of stimuli arranged according to intensity (or frequency, or other continua) will be judged greater if preceded by the sequence 1,2,3,4 and lesser when preceded by the sequence 9,8,7,6. We have some evidence that such local effects may become permanent or at least predict later durable effects. These “Adaptation-Level Effects” have been shown in judgments of human subjects, though there is no evidence of a contribution to eventual stable effects. Those effects are not as clear as those we have shown in our less-educated subjects.

The object of our research over the past two years has been very different and led to a complex series of experiments concerning the “Overjustification Effect” with pigeon subjects. The data analyses (and interpretation) are in process, but the effect itself is easy to understand. Amazingly, there are countless studies reported over the past thirty years purporting to show that material rewards (as well as praise) for superior performance have an unwanted and detrimental effect on future performance. This applies to both animal and human subjects. We were led to this topic by Chris Skinner, Director of School Psychology in the College of Education, Health, & Human Science, who proposed a cooperative project. One may imagine the appeal that a “no rewards or punishments” view might have for a certain kind of educator and work promoting this opinion has been richly supported by grants and led to scores of workshops, lectures, and meetings. Our work won’t cancel the OJE movement, but we hope that it will point out its reasonable and narrow bounds.
announcements

Office of Laboratory Animal Care

All About A-L-L Training
Jane Czarra, RLATg

If you work with animals in teaching, research, and husbandry or by sitting on the Institutional Care and Use Committee, you are familiar with the AALAS Learning Library (ALL). Most likely the “Working with the IACUC” training comes to mind. We would like to bring to your attention the many courses available to you as institutional members of the ALL.

The course catalog includes topics such as analgesia, anesthesia and surgery, bioethics, biosecurity, environmental enrichment, biomethodology for common lab animal species, and additional information for US mandates and guidelines. Each time you complete a course, a transcript is generated in the ALL database. You may print certificates for your records or ask the group coordinator, Jane Czarra, to print your transcripts.

For the animal care staff, there are courses geared toward preparation for all three levels of AALAS technician certification. For all certified technicians, completion of additional courses not related to certification, can be counted as CEU credits toward maintaining your registered technician status.

AALAS is dedicated to the advancement of responsible laboratory animal care and use. Please take advantage of this on-line resource. To log in as an institutional member please follow the directions found on the IACUC website under “Accessing the Online Training Modules”: http://iacuc.tennessee.edu/training/

Dr. Dana Glass-Mattie, Director of Animal Compliance Support
Patricia N. Coan, DVM, PhD, DACLAM

Please join us in welcoming Dr. Dana Glass-Mattie as our new Director of Animal Compliance Support (DACS). Dr. Glass-Mattie is responsible for ensuring that our animal-based research and teaching is conducted in the most humane manner possible and in full compliance with all relevant regulations and policies.

Dr. Glass-Mattie received her DVM from Auburn University and was in small animal practice for 10 years where she really honed her veterinary skills. In 1999, she began working at Lovelace Respiratory Research Institute, Albuquerque, New Mexico as a research associate and laboratory animal veterinarian for the next three years. Dr. Glass-Mattie moved to Oak Ridge, TN in 2002 and worked at Y12 for the next few years in chemical safety and hazardous waste removal in a compliance support position. Dr. Glass-Mattie began working at ORNL in 2004 where she has been a toxicologist and laboratory animal veterinarian. Dr. Glass-Mattie’s vast experience as a practitioner, researcher, and compliance manager make her a perfect fit for our DACS. She has a good understanding of research design and implementation and will be a great asset for our animal users.

Dr. Glass-Mattie will plan, implement, and direct compliance policies, protocols, and develop a robust post-approval monitoring program. Dr. Glass-Mattie will coordinate audits of all active IACUC protocols and also direct and manage a training program for animal use issues, including but not limited to compliance and protocol development, for investigators. She will also provide administrative oversight of the IACUC and will be available to provide any guidance and/or questions in regard to protocols.

Dr. Glass-Mattie may be reached at 974-9074 or dglassma@utk.edu.