2014 WORLD LABORATORY ANIMAL LIBERATION WEEK  
(April 18-28)

The week surrounding April 24, the birthday of Hugh Dowding, who founded Britain’s National Anti-vivisection Society (NAVS), again has been named World Laboratory Liberation Week (WLALW) by the group Stop Animal Exploitation Now (SAEN). SAEN says, “It’s a national week of protests, media events, etc. at laboratories to stop testing and research on animals.”

Duke University animal care and use facilities have processes in place for this higher profile week. An advisement from Dr. John Norton, Director, DLAR notes:

⇒ Entrance into an animal facility by Duke faculty, resident, post-doc, student or other personnel requires the visible wearing of a Duke photo identification badge. Visitors to the animal facilities must sign the guest book, obtain a visitor’s badge, and be escorted by Duke personnel.

⇒ All animal facilities require entrance by card reader access. Do not open doors into these areas for individuals not wearing proper Duke identification and without a reason for being in these areas.

⇒ Report to Duke Police (684-2444 or 911) or DLAR administration (681-6792) any observations of suspicious individuals or events in proximity to any vivarium or animal use area.

⇒ Photography and Videography in all animal research areas, whether performed by outside companies, vendors, etc. or Duke personnel, must be approved by the DLAR Director or Deputy Director in advance. Outside photographers must be accompanied on all visits.

⇒ All contact with the news media must be referred to and coordinated with the Medical Center News Office (MCNO; office: 684-4148 or the 24 hour on-call public information officer 919-257-7163). Media covering any animal research issue on campus must always have a MCNO escort and without a reason for being in these areas.

⇒ A special pass is required for parking in areas adjacent to the animal care areas during the dates of the World Laboratory Animal Liberation Week. Vehicles without the parking pass may be subject to towing. Please contact Peg Hogan (684-3885) for further information if parking is required in these areas.

TEENS IN THE LAB THIS SUMMER?  TAKE NOTE….

Summer is a great time for potential young scientists to gain some valuable experience working in a “real world” research laboratory. However, if you plan on hosting minors (anyone under the age of 18) this summer, please note there are special policies in place for minors working in labs. In addition to policies to protect Duke employees in the lab, there are also measures in place to ensure the safety of any minors in the work area. Research labs, in particular, can have a number of physical, chemical, radiological and biological hazards that may be unfamiliar to minors, and these policies help keep them protected during their time in the lab.

The Occupational and Environmental Safety Office (OESO) has a safety policy that covers minors and non-employees in the work area (http://www.safety.duke.edu/SafetyManuals/University/1_6MinorsNon-Employees.pdf). This policy states that no one under the age of 14 can work or volunteer at Duke Medicine, and children under 14 must have written OESO approval to enter a lab. Those between the ages of 14-17 may not perform any work that is determined to be hazardous or potentially harmful, including:

⇒ work that may expose them to infectious diseases transmitted via aerosols.
⇒ tasks that may expose them to blood or body fluids, infectious diseases or hazardous chemicals as listed on OESO’s Particularly Hazardous Substance List (http://www.safety.duke.edu/LabSafety/Docs/PHS_by_CAS.pdf).
⇒ areas where there is potential exposure to radiation in excess of 0.1 rem (0.001 Sievert) total effective dose equivalent or in excess of 10% of the limits for general employees. No minor is allowed to handle radioactive materials directly. If an AU (Authorized User) is planning on hosting minors in the lab this summer, notify the Radiation Safety Officer (684-2194) prior to arrival.
⇒ areas that are under construction.
⇒ areas where ABSL2 studies are being performed.

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PROTOCOLS NOT GETTING TO IACUC@DUKE.EDU?

I am sure that by now you are aware the Duke email systems are in a transition to Microsoft Office 365, a cloud-based service. While the transition has been on-going for quite a while now (see the original I.T., announcement here), more departments are coming on-line every month. The mail box size for the new system is 25GB for University Exchange users. The old document limit was 2GB, so for most folks, this move means a larger attachment size can be transmitted now. But even so, we had several calls regarding an inability to transmit files to IACUC@Duke.edu.

The best work-around is simply send the documents in two or more messages. There is no requirement that every document must come in to the IACUC on the same email message, just that all documents must come into the email account IACUC@Duke.edu. We can resemble your various documents when they arrive, but it may be a good idea to give us a heads-up that some documents will be coming in a follow-up message.

Progress is good, and from our perspective we welcome the modifications to the email system. Sometimes with enhancements are accompanied with issues — let us know, we'll work with you.

Wishing you a successful research month,
These procedures should only be followed when the fire alarm is activated during an anesthetized animal research procedure. Research procedures on deceased animals or other animal components are not covered by this policy. Individuals working on other than anesthetized animals are REQUIRED TO LEAVE THE AREA IMMEDIATELY UPON FIRE ALARM ACTIVATION.

**SCHEDULED FIRE DRILLS**

The OESO Fire Safety Office will post notices of a scheduled fire drill at least 48 hours in advance stating the date and window of time the drill will occur. If an unavoidable conflict arises, the research personnel must notify the OESO Fire Safety office immediately. Our main office phone number will be posted on the notice. If no prior notification is given, the drill will be held, and ALL OCCUPANTS ARE REQUIRED TO EXIT THE BUILDING IMMEDIATELY!

**FIRE ALARM ACTIVATIONS**

In every surgical lab, there will be a poster permanently displayed in a visible location which lists a building contact person, an alternate contact person, and their mobile phone numbers. The designated contact persons for fire alarm evacuations will be determined by the department(s) upon the receipt of this policy. Alternates will also be determined. A list of contact persons and their cell phone numbers will be distributed to all animal procedural areas.

- If the fire alarm is activated, the research personnel shall first check the areas for signs for smoke, fire, toxins or other dangers. ONLY if they do not see any immediate signs of smoke, fire, or other hazards, they will immediately contact the department designated contact person in the building and state that they are remaining in the laboratory because they are performing an animal procedure on an anesthetized animal. If they decide to evacuate, they shall still notify the building contact of this as well. This ensures proper accountability.

- If the research personnel and designee are remaining in the lab, the laboratory designee (if applicable) will continue to serve as a lookout person for signs for smoke, fire, or other hazards, and in charge of communications with the building contact person. If no others persons are in the lab to serve as a laboratory designee, the research personnel must watch for signs of changing conditions to the best of his/her ability.

- The building contact person will notify responding units of the person(s) remaining in the laboratory and their exact location.

- The building contact person will notify the research personnel or his/her designee immediately if conditions deteriorate and evacuation is necessary.

- If evacuation is necessary, the research personnel and his/her designee will then take steps to safely and quickly euthanize the animal (e.g. perform a bilateral thoracotomy while anesthetized), if conditions allow, and evacuate the building immediately.

- If the research personnel are alone when conducting the procedure, the research personnel shall notify the building contact person that the procedure is complete. Any alarms after this point will require prompt evacuation from the building for all occupants.

This policy & procedures were granted by safety as a means of recognizing the potential pain and suffering, and or loss of animal life due to a fire alarm that was the result of a minor event (e.g., popcorn burning, a bad lab reaction down the hallway creating a minor amount of smoke. This policy does not authorize or allow placing human life at risk! Whenever engaging this policy, always assure that people come first, there are individuals who are aware, assisting and alerting when necessary. We do not want to waste an animal's life because of burned popcorn; we even more do not want to injure or lose a human because of a serious fire event.
PHARMACEUTICAL GRADE COMPOUNDS
(Frequently Asked Questions)

Editorial Note: Questions and answers are based on a webinar given by representatives of the Office of Laboratory Animal Welfare at NIH (OLAW), the United States Dept. of Agriculture (USDA), and the Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC), held on March 1, 2012. The full text of the webinar is available at {http://grants.nih.gov/grants/olaw/e-seminars.htm}.

Question: Are investigators required to use a compounding pharmacy when it is necessary to use a specific mixture of experimental drugs, chemicals or other formulations?
Answer: NIH, USDA and AAALAC consider the compounding of investigational agents or the customized manipulation by dilution or addition of vehicles to pharmaceutical-grade substances for administration to animals as necessary and acceptable scientific activities carried out by researchers. However, these activities should be described in the animal study and reviewed and approved by the IACUC.

Question: May investigators use a commercial compounding pharmacy to prepare specific mixtures of experimental drugs?
Answer: Yes. There may be circumstances where the customized manipulation of an FDA approved drug by a licensed pharmacist is needed to meet the needs of a research study. Examples include mixing two injectable drugs into a specialized formulation, preparing a paste from crushed tablets or adding flavoring to a drug. FDA states that for compounding by a pharmacy or veterinarian to be legal, it cannot be from bulk or raw active ingredients, although FDA does under specific circumstances allow this practice.

Question: May investigators prepare the specific mixture themselves in the laboratory?
Answer: Yes. However, these activities should be described in the animal study and reviewed and approved by the IACUC.

Question: When it is necessary to add a vehicle or diluent to a chemical or substance that will be administered to an animal, is it required to use a pharmaceutical grade material?
Answer: It depends on the route of administration and the need to maintain sterility. Our concern is that it doesn't injure the animals and is appropriate for the science. Professional judgment should be used in making this determination. For oral administration, the vehicle or diluent should be food grade. For injections such as intramuscular, intraperitoneal, or subcutaneous, the diluent or vehicle should be sterile and physiologic.

Question: Is the dilution of a drug such as Ketamine with saline for use in the mouse considered compounding?
Answer: No, it is considered an adulteration of the original product, but one that is necessary to ensure that the appropriate dosage is administered. As long as proper sterile technique and a sterile diluent are used, there should be no issues of concern for the IACUC.

Question: Does the requirement distinguish between the use of non-pharmaceutical-grade substances for medical / veterinary and research use?
Answer: The general philosophy concerning the selection and use of compounds for clinical or therapeutic applications and for research applications in laboratory animals is the same. The Guide recognizes that pharmaceutical-grade compounds afford the subjects protection against toxic or unwanted side effects potentially minimizing important variables in scientific studies. Compounds used in veterinary and human clinical applications are routinely available in a pharmaceutical-grade and should be used whenever possible. However, scientific studies may require the use of compounds that are not available in pharmaceutical-grade, or that may only be available in a pharmaceutical-grade that is legitimately deemed unacceptable for particular scientific reasons. In these cases, with appropriate IACUC oversight, non-pharmaceutical-grade compounds may be acceptable when prepared and maintained using sound pharmaceutical practices.

Question: Does the requirement force us to use a more expensive substance that does not confer any additional benefits over a less expensive substance?
Answer: The question as stated does not reference any quality factors of the substance other than expense and AAALAC supports the prudent use of scientific resources. If both have acceptable efficacy, there is no need to spend any more money than is necessary.

Question: Can the IACUC approve the use of tribromoethanol (also known as Avertin)?
Answer: Avertin is the trade name for the injectable anesthetic agent 2,2,2-tribromoethanol. Avertin was once manufactured as a pharmaceutical-grade drug. It is no longer available commercially. The preparation and use of tribromoethanol for anesthesia needs to be scientifically necessary, appropriately justified and approved by the IACUC, taking into consideration the side effects, stability, storage requirements and other considerations associated with the preparation of this agent. There are multiple reports in the literature of physiologic harm to animals including ileus, adhesions and mortality from the use of tribromoethanol. AAALAC has no objections to the use of Avertin in IACUC-approved protocols. However, OLAW would advise IACUCs to critically evaluate the proposed use of tribromoethanol and the consideration of alternative methods that avoid or minimize discomfort, distress and pain. Furthermore, OLAW has recently learned of journals turning down studies for publication that described use of tribromoethanol.

Question: Can non-pharmaceutical-grade pentobarbital be used for euthanasia?
Answer: It can be used if scientifically justified and satisfies the paragraphs from the Act and the Regulations previously cited.
PHARMACEUTICAL GRADE COMPOUNDS
(Frequently Asked Questions—continued)

Question: Is it necessary to use USP or Grade A (Medical) CO2 to euthanize rodents?
Answer: Either USP Grade A (medical) or Grade B (industrial) carbon dioxide may be considered acceptable as they each provide a minimum purity for carbon dioxide of 99.0%. Carbon dioxide should be supplied in compressed gas in cylinders. The use of dry ice is unacceptable according to AVMA Euthanasia Guidelines (PDF).

Question: Can euthanasia solution be diluted and used as an anesthetic for survival surgery? Can euthanasia solution be used as an anesthetic for non-survival surgery?
Answer: No. Typically these solutions are not sterile and contain drugs other than anesthetic agents that could harm or kill the animals even if diluted. A euthanasia solution may not be used as an anesthetic for survival or non-survival procedures. OLAW in concert with USDA agree that a procedure may be performed as a part of euthanasia. And this would be limited to terminal perfusion or exsanguination. In both cases, death is an immediate outcome of the procedure.

Question: Is it OK to use non-sterile euthanasia solution for euthanasia?
Answer: Yes. This is consistent with the adequate veterinary care under the Animal Welfare Act, Paragraph 2143, Subparagraph (a)(3)(A) and the Animal Welfare Regulations 9 CFR Chapter 1, Paragraph 2.33, Subparagraph (a), (b)(2) and (4) in which a humane death is achieved.

Question: Does the NIH non-pharmaceutical-grade substance policy apply to aquatic species?
Answer: Yes. The guidance is applicable to aquatic species because the composition of the drug either -- both the purity, solubility and toxicity -- are just as relevant in the case of aquatic species as well as other animals. And special attention needs to be given to drug concentrations in the volume of water in which the animal is placed.

Duke Animal Care and Use Program Training Opportunities

The Office of Animal Welfare Assurance (OAWA) and the Division of Laboratory Animal Resources (DLAR), support of the Duke Animal Care and Use Program (ACUP), by providing training for principle investigators and research staff who conduct work with animal models.

Some of the training opportunities available are as follows:

⇒ Monthly Brown Bag Seminars – provides continuing education for the Duke research community through topical and timely seminars. AALAS CE credit approved and also meets the requirement for the Duke IACUC annual CE policy.

⇒ OESO on-line training – Animal Handlers Parts I, II & III are required for all new research staff listed on an animal model protocol.

⇒ AALAS Learning Library – The Duke ACUP/OAWA maintains 2,000 accounts with this on-line training resource available through the American Association for Laboratory Animal Science. There are 144 courses currently available. Open to all research and animal care staff.

⇒ Animal Tracks – A monthly publication from the OAWA that contains new and pertinent information on animal care and use, research methodologies and regulatory updates.

⇒ Individual and lab training – OAWA and DLAR staff are available to provide individual and lab staff training on a variety of subjects and procedures. To include handling and restraint, euthanasia, injection and withdrawal techniques, aseptic surgery procedures, consultation on anesthesia equipment, etc.

Contact Bill Wade @ 668.6722 w.wade@duke.edu or Michelle Calkins @ 681.1831 michelle.calkins@duke.edu for training assistance.
RESEARCH ANIMAL COORDINATORS ARE AVAILABLE TO ASSIST DEPARTMENTS WITH COMPLIANCE

The Duke Research Animal Coordinator Certification (RACC) program lists the following individuals as available to assist researchers with training, protocol, and compliance issues. These are the front line ‘answer people’ for the animal research laboratory. If they don’t know the answer, they certainly know exactly whom to call to get the answer. Email your RAC today!

**Neurobiology/Neurology:**
Katherine Harley: harley@neuro.duke.edu  
Monica Carlson: monica.carlson@duke.edu  
Brian Mace: brian.mace@duke.edu  
Laura Oliveira: oliveira@neuro.duke.edu  
Wei-Hua Qian: wqian@neuro.duke.edu  
Stefanie Tokiyama: tokiyama@neuro.duke.edu  

**Steadman Nutrition Center:**
Rajamani Arumugam: arum001@mc.duke.edu  
Paul Anderson: ander116@mc.duke.edu  

**Chemistry:**
Simone Degan: simone.degan@duke.edu  

**Ophthalmology:**
Penny Ferr-Leeper: penelope.ferryleeper@duke.edu  
Marybeth Groelle: groel003@duke.edu  
Jianming Qiu: jianming.qiu@duke.edu  
Iris Navarro: iris.navarro@duke.edu  
Angela Dixon: angela.horman@duke.edu  
Kristine Porter: kris.porter@duke.edu  

**Immunology:**
Dongmei Liao: dongmei.liao@duke.edu  

**Pharmacology/Cancer Biology:**
Iris Navarro: iris.navarro@duke.edu  
Tomasa Barrientos de Renshaw: tomasa.barrientosderenshaw@duke.edu  
Emily Riggs: emily.riggs@duke.edu  

**Cell Receptor/Biology:**
Chris Ingersoll: cingersoll@receptor-bio.duke.edu  

**Surgical Sciences/Neuro Oncology:**
David Snyder: david.j.snyder@duke.edu  
George Pitoc: george.pitoc@duke.edu  
Martin Roskoski: martin.roskoski@duke.edu  

**Pathology:**
Jui-Chih Chang: jui-chih.chang@duke.edu  

**Duke Human Vaccine Institute:**
Brice Barefoot: brice.barefoot@duke.edu  
Kris Riebe: riebe002@mc.duke.edu  
Hilary Bouton-Verville: hilary.bouton-verville@duke.edu  
Ching-Ju Chen: ching-ju.chen@duke.edu  
Hongjie Pan: hongjie.pan@duke.edu  

**Molecular Genetics/Microbiology:**
Dana Sisk: dana.sisk@duke.edu  

**Biomedical Engineering:**
Jessi Cruger: jessi.cruger@duke.edu
Welfare vs. Rights

Animal Welfare is the desire to implement humane care and use standards for animals in research, testing, teaching, and exhibition. Animal welfare is based on the belief that animals can contribute to human welfare by providing food, fiber, work, companionship, entertainment, or by serving biomedical research or education, and humans have moral obligations to provide for the well-being of animals. Ensuring proper animal welfare requires adhering to responsible practices in all aspects of animal well-being, including proper housing, management, disease prevention and treatment, responsible care, humane handling, and, when necessary, humane euthanasia. In so doing, animal welfare supports the use of animals by humans, and seeks to improve their treatment and well-being.

Animal Rights on the other hand, is based on the philosophical view that animals have similar, or the same rights as humans. As a result, animal rights advocates do not distinguish between human beings and animals. Animal rights proponents believe that humans do not have the right to use animals at all, including the use of dogs and cats as companion animals or pets. No matter how humane, animal rights proponents reject all animal use as exploitation, and therefore wish to ban all use of animals by humans. As expressed by a prominent animal rights activist, "I don't believe human beings have the 'right to life.' That's a supremacist perversion. A rat is a pig is a dog is a boy."

NABR, like the members we represent, is committed to Animal Welfare. We support the judicious, humane use of animals in biomedical research, higher education, and when necessary in product safety testing. In support of this commitment NABR advocates for the development and implementation of public policy based upon sound scientific information and current standards of practice as defined by experts in veterinary and biomedical science. To this end, NABR relies upon the input of our members in the biomedical community when developing policy positions and public statements.

Additional Information:

The Animal Welfare Act

The USDA Animal Welfare Information Center (AWIC)

The NIH Office of Laboratory Animal Welfare (OLAW)
**Introduction**

Approximately 95 percent of all laboratory animals are mice and rats. Easily housed and bred, short lived (2-3 years), small, and relatively inexpensive, these rodents have become the animal model of choice for modern medical and scientific researchers. Because their physiology and genetic make-up closely resemble that of humans, rodents play an invaluable role in biomedical research. In the last decade, scientists discovered how to breed mice with genetic alterations that mimic human diseases. This capability has revolutionized medical research and dramatically increased the number of mice needed in medical science. The mouse genome contains essentially the same complement of genes found in the human genome, so studying how the genes work in mice is an effective way of discovering the role of a gene in human health and disease.

**Man-made, genetically altered rodents**

Transgenic and knockout rodents have been created with revolutionary new technology. While transgenic mice have had a foreign gene (a piece of DNA) artificially added to their genomes, knockout mice have had a specific gene “turned off” or made useless. A great deal of promising research relies on these genetically altered mice. Transgenic rats also have been used in medical studies and found to be better models than mice for studying certain human diseases. Genetically altered rodents have allowed scientists to observe what happens during the progression of Parkinson’s disease, cancer, cystic fibrosis, heart disease, memory loss, muscular dystrophy, and spinal cord injuries. Recently, the mouse and rat genomes were sequenced. This achievement promises to significantly advance biomedicine.

**Naturally occurring immunodeficient mice**

SCID (severe combined immune deficiency) mice and nude (or hairless) mice are born without thymus glands and lack functioning immune systems. These mice are very important models for studying both normal and malignant human tissue. They also are needed to develop and evaluate new drugs without risking human lives.

**Alzheimer’s Disease**

Scientists have evidence that a buildup of plaques containing amyloid protein deposits in the brain is a characteristic feature of Alzheimer’s disease (AD), a disorder that affects patients’ memories and personalities. Rats and transgenic mice bred to carry a gene that over expresses human amyloid protein have become indispensable for understanding and evaluating new drugs to prevent or delay the onset of AD. And recently, researchers have shown that vaccinating these mice with modified amyloid protein slowed the progression of the disorder. Patients are now being tested to see if the vaccine is well tolerated and can help overcome AD.

**Aging**

Measuring physiologic changes over an entire life span would take many decades to complete in humans. However, such studies can be accomplished on “fast forward” in normal mice and rats. Research has shown that a reduced intake of calories in rodents markedly increases longevity, retards physiological deterioration, delays, and in some cases, prevents the incidence of age-associated diseases.

**Carcinogen Testing**

Scientists are evaluating several lines of knockout mice to study the mechanisms of carcinogenesis. They propose that such animals might be needed for routine testing of chemicals for carcinogenic potential. The results can be obtained more rapidly with fewer animals, and the outcome can be used effectively in chemical and drug safety assessments.

**Cancer**

During the past decade much of our knowledge of how environmental agents damage DNA and cause mutations that enhance cancer risk has come from studies with rats and mice. Scientists have produced cancer resistant mice that lack the ability to produce cyclin D1, a protein found in abnormally high amounts in human breast cancers.
They propose that cyclin D1 therapy might be highly selective in inhibiting the growth of human breast cancer cells.⁶

**Cystic Fibrosis**
Cystic fibrosis (CF) is a childhood disease characterized by chronic lung congestion and digestive problems. CF is incurable and patients rarely live to see the age of 30. Scientists now know that CF is caused by a small defect in the gene that manufactures CTRF, a protein that regulates the passage of salts and water in and out of cells. Studies with CTRF-deficient mice have shown that the disease results from a failure to clear certain bacteria from the lung, which leads to mucus retention and subsequent lung disease. These mice have become models for developing new approaches to correct the CF defect and cure the disease.⁷

**Drug Addiction**
Rats trained to self administer cocaine have high predictive value for human addiction because they share common triggers of relapse. In mapping the brains of adult rats that kicked the cocaine habit, researchers found that in relapse, the “high” from cocaine occurs in an area separate from where the brain retains cocaine-seeking behavior. This finding opens the possibility for developing new targets for anti-craving medication.⁸

**Spinal Cord Injury**
Scientists are using rats to study the mechanisms underlying long-term recovery of motor skills after spinal cord injury. They found that motor function is related to the number of intact axons, the part of the nerve cell that transmits signals to motor neurons. Recent studies have demonstrated that axonal sprouting or regeneration at the injury site correlates with functional recovery and can be enhanced by the application of certain growth factors to the spinal tract. Development of these approaches to neural repair may ultimately generate new strategies for treating human spinal cord injury.⁹

**Heart Attack**
New research has revealed that the heart muscle regenerates to some extent after a heart attack. A new strategy for treating this condition is being studied in transgenic mice. Researchers are experimenting with injecting stem cells (primitive bone marrow cells) into the periphery of the injured area to stimulate self-repair. The studies showed that the cells promoted structural and functional repair of the damaged tissue.¹⁰

**References**