PROCEDURE FOR HANDLING FIRE ALARM ACTIVATION DURING ANESTHETIZED ANIMAL PROCEDURES

The IACUC and OESO partnered some months ago to develop a clear set of expectations for situations when animals are under anesthesia and the fire alarm rings. The purpose of the partnership and resulting policy was to assure we protect human life while also satisfying ethical precepts of animal use and respect to animal life—preventing suffering as well as prematurely euthanizing animals.

The procedures described in this article (see the policy on the animal program website) 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 included in this discussion and persons participating in these activities 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. The OESO main office phone number is posted on the notice they publish. 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, the PI must permanently display in a visible location: a building contact person, an alternate contact person, and their mobile phone numbers. The designated contact persons (and Alternates) for fire alarm evacuations are determined by the department(s). A list of contact persons and their cell phone numbers must be posted in affected animal procedural areas.

CAGE SPACE REQUIREMENTS FOR MICE

The most recent version of the policy on caging density reflects the updates contained in the 8th edition of The Guide for the Care and Use of Laboratory Animals. Listed below are some of the more important details to aware of. Please share this information with your staff to ensure compliance.

The Duke animal program has rodent caging ranging from 67 - 75 square inches. This policy is based on a standard cage of 75 square inches. If cages are larger or smaller than 75 square inches, then The Guide recommendations shall be used, unless IACUC approval is received for the altered housing density.

OVERCROWDING: An incident is defined when the following two (2) conditions are met.

- a. A cage exhibiting excessive density has not been corrected by the PI within two business days of DLAR notification. Excessive density events resolved by the PI within two business days of notification by DLAR are not be counted as an incident; and
- b. Any number of cages that occur within a 3 business day period of the first identified incident are considered a single incident. Subsequent unresolved overcrowding events are considered separate incidents if they occur >3 business days from the first identified and unresolved overcrowding incident.

For example:

⇒ Overcrowded cages are identified on a Monday (calendar day 1), and Tuesday (calendar day 2) of the same week. Neither are resolved within 2 business of DLAR notification. These are considered the same incident.
⇒ Overcrowded cages are identified on Monday (calendar day 1) and Thursday (calendar day 4) of the same week. Neither are resolved within 2 business of DLAR notification. These are considered two separate incidents.
If the fire alarm is activated, the research personnel 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.

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.

While the OESO has recognized the ethical concerns with euthanizing animals whenever a fire alarm is heard; there is no excuse for placing the life of a human at risk. This institutional policy allows for laboratory flexibility as long as there is an action plan, appointed roles, and proper planning. This decision is the ‘right’ response to the challenges of protecting human life while also assuring ethical animal care & use.

Based upon The Guide, the caging densities are: Based on the above space requirements, for Duke caging systems, no more than two adults may be in a cage when a litter is born. A litter includes any number of pups born to a single dam at the same parturition. In cases of extremely large litters, it may be helpful to divide the litters between two cages and foster half of the litter on to a nursing dam. It is not acceptable to add a nursing dam to a cage where there is a large litter.

More than one litter and two adults per cage will require IACUC-approval as an exemption (Section U: Exemption from Animal Welfare Standards). Any exemption must be marked on the designated cage card.

Pups must be weaned by 21 days of age unless delayed weaning has been approved by the IACUC or by DLAR veterinary staff for health concerns. Cages should be marked with date of weaning. Requests for delayed weaning based upon animal welfare concerns will be processed as minor with veterinary review according to the Policy on IACUC Review and Approval Practices for Protocol Amendments. Breeding cages containing pups 22 days of age or older without IACUC approval for extended weaning (generally identified in the protocol) or DLAR exception due to a failure to thrive syndrome, are considered overcrowded.

No more than one litter may be present in the cage. An exception to this policy is appropriate in certain ‘failure to thrive’ or ‘poor breeder’ situations. More than one litter can be present in the cage regardless of the mother to which they belong if there is an IACUC exemption or DLAR exception in place. When litters need to be separated, the mothers and litters must be observed sufficiently to determine the appropriate mother for each litter before mice are moved from one cage to another.
ZOONOSES: POTENTIAL BIOHAZARD ISSUES

Zoonoses—diseases that can be transmitted from animals to humans. May be found in nearly all animal species.

Potential biohazard issues: Although the risk of transmitting zoonotic disease in an animal facility is small, it should be understood that nearly all animal species are known to be a host of at least one zoonotic agent. Quality veterinary care programs, proper quarantine of new arrivals and the purchase of animals from reputable suppliers significantly reduces the risk of such agents from entering animal facilities.

EXPOSURE TO ALLERGENS are perhaps the most common health concern in research animal facilities. The true ‘damage’ from allergen exposure depends on parameters such as animal species, ventilation system, work practices and the employees “Health screen”. Allergic reactions to animals are among the most common conditions that adversely affect the health of workers involved in the care and use of animals in research. All animal handlers (Duke employees, students or other personnel) must complete the Employee Occupational Health and Wellness (EOHW) Placement “Health Review for Animal Handlers” prior to the start of work with animals and a Periodic Health Review for Animal Handlers form at least annually thereafter. A significant component of these tools is used to assess your risk of animal related allergies.

CONTROLLING EXPOSURE TO ALLERGENS:
There are several environmental measures in place to control exposure to allergens, including:

- Ventilated cage rack systems
- Ventilated Bedding Dump Stations
- Biological Safety Cabinets
- HEPA-filtered Change Stations

There are also several Personal Protective Equipment (PPE) measures that will limit or prevent allergen exposure:

- Gloves
- Gowns
- Shoe Covers
- Hair Bonnets (Bouffant Caps)
- Masks - Respirators**
- Face Shields
- PAPR**

**Note - Specific training from OESO is required for the wearing of a respirator (N-95) or PAPR device.

NEW RESTRICTIONS ON TRANSPORTING OF LIVE ANIMALS

China Eastern and United Airlines have announced they will no longer ship non-human primates used for biomedical research. This decision represents an abrupt about-face from the pro-research stance advocated by a United official in 2011. China Eastern was the only regularly schedule carrier remaining that was shipping primate from China to the rest of the world.

While not a prohibition of shipping, all future shipments will require a charter flight, thereby making the purchase of primates much more expensive.

MEDICAL SCHOOLS, TEACHING HOSPITALS INFUSE BILLIONS INTO ECONOMY

The nation’s medical schools and teaching hospitals had a combined economic impact of $587 billion and supported nearly 3.5 million jobs directly or indirectly in 2011, according to a new economic impact analysis recently released by the American Association of Medical Colleges.

POSTERS AVAILABLE FREE
From Americans for Medical Progress

Of course he looks tired. For two years he’s been working on a cure for cancer.

Sure he’s fat–but he’s a lifesaver.

*Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.

Sure he’s fat–but he’s a lifesaver.
REPORTING MISSING or ESCAPED ANIMALS

Even under the most controlled circumstances, adverse events may occur. When an animal escapes the holding cage, it is important that measures to capture the animal are engaged. It is not acceptable to consider it ‘returned to the wild’ or ‘free to roam the building.’ The goals of recapture are to: a) prevent an injury to an animal unaccustomed to the out-of-doors; b) to prevent a transgenic animal from passing their modified genes to other animals; and c) to prevent the spread of potential pathogens (if the animal is infectious).

According to Duke animal care program polices, all personnel who work with animals must be trained in handling, restraint, and capture of animals. The responsibility for ensuring appropriate training of the research staff lies with the PI (for PI managed spaces) and with DLAR (for DLAR managed spaces).

Select considerations for recapturing animals include:

- A rodent which has escaped should not be handled by hand. Use a hard container (e.g., a cup or empty cage) when capturing animals.
- Animals found in a trap or on the floor must be placed in a clean cage with food and water.
- A label using the word “compromised” must be affixed to the cage. This denotes that the animals may not be healthy and should be handled as if infected.
- A DLAR veterinarian must be notified immediately after the animal is captured.
- If the responsible PI can be determined, they will be notified immediately.
- If you suspect an animal is missing, check the room mortality log to see if an animal has died and the carcass removed for refrigerated storage.
- If you cannot determine that an animal is missing, or you know it is missing and cannot find the remains, then contact the DLAR supervisor.

It is especially important to notify DLAR management if the missing animal is a transgenic animal, KO/KI, or an animal with recombinant DNA. According to NIH policy, loss of these animals may require notification of the NIH Office of Laboratory Animal Welfare.

STANDARD OPERATING PROCEDURE REQUIREMENTS FOR ABSL2 CONTAINMENT AT DUKE

The Principal Investigator (PI) has the responsibility to inform the laboratory personnel of the appropriate research procedures. When using hazardous or regulated biological agents the PI must prepare a written Standard Operating Procedure (SOP) outlining the necessary precautions to safely conduct research. An SOP is a set of specific guidelines designed to address the methods that will be used and the safe handling of biological agents. The SOP must be available in the laboratory.

The SOP is a valuable tool and worth the preparation time. A well-written SOP can be used to satisfy several compliance requirements. SOP should be written for all procedures that pose an identified potential risk to the health and safety of the laboratory personnel, although a separate SOP does not need to be written for each individual experiment, procedures with the same hazards can be combined into one SOP.

The process of writing SOPs requires an individual to think through all steps of a procedure and perform a risk assessment before work has begun. The best approach to writing an SOP is to do it, write it and test it. Be brief and succinct; the shorter the better. A SOP template is available on OESO Biosafety Web Site:

http://www.safety.duke.edu/BioSafety/Animals.htm

OESO HAS SEVERAL GUIDELINES FOR SOP DEVELOPMENT OF HAZARDOUS AGENT USE IN ANIMAL PROTOCOLS

OESO Biosafety Division has a great web site which assists researchers with specific SOP development! For example:

- Guide for Developing an SOP for the use of Biohazards in Animals
- Guide for Developing SOP for the use of Hazardous Drugs
- SOP for the use of Toxic Chemicals in Animals
- Guidelines for the Safe Handling of Animals Exposed to LPS in Research
- Radiation Safety Animal Care and Use Protocol Wizard

You can reach this site and use this links be going to the OESO Biosafety site at:

http://www.safety.duke.edu/BioSafety/Animals.htm
Research leading to almost every Nobel Prize in Medicine awarded since 1901 was dependent on data from animal models. This fact dramatically demonstrates the important contribution animal models in biomedical research make to both international and American medical progress. In fact, since 1979, every Nobel Prize in Medicine awarded was dependent on data from animal models with the exception of the 1983 Prize awarded to Dr. Barbara McClintock for her work in plant genetics. This list is only the last few years, but for the complete list of all animal research related prizes, visit the Foundation for Biomedical Research.

<table>
<thead>
<tr>
<th>Year</th>
<th>Nobel Laureate</th>
<th>Animal Model</th>
<th>Contribution to Modern Medicine</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>Bruce A. Beutler</td>
<td>Mice</td>
<td>Discoveries concerning the activation of innate immunity</td>
</tr>
<tr>
<td>2011</td>
<td>Jules A. Hoffmann</td>
<td>Flies</td>
<td>Discoveries concerning the activation of innate immunity</td>
</tr>
<tr>
<td>2011</td>
<td>Ralph M. Steinman</td>
<td>Mice</td>
<td>For his discovery of the dendritic cell and its role in adaptive immunity</td>
</tr>
<tr>
<td>2010</td>
<td>Robert G. Edwards</td>
<td>Rabbits</td>
<td>The development of in vitro fertilization</td>
</tr>
<tr>
<td>2009</td>
<td>Carol W. Greider</td>
<td>Protozoan, mouse</td>
<td>Discovery of how chromosomes are protected by telomeres and the enzyme telomerase</td>
</tr>
<tr>
<td>2009</td>
<td>Elizabeth H. Blackburn</td>
<td>Protozoan, mouse</td>
<td>Discovery of how chromosomes are protected by telomeres and the enzyme telomerase</td>
</tr>
<tr>
<td>2009</td>
<td>Jack W. Szostak</td>
<td>Protozoan</td>
<td>Discovery of how chromosomes are protected by telomeres and the enzyme telomerase</td>
</tr>
<tr>
<td>2008</td>
<td>Harald zur Hausen</td>
<td>Hamster, mouse, cow</td>
<td>Discovery of human papilloma viruses causing cervical cancer</td>
</tr>
<tr>
<td>2008</td>
<td>Françoise Barré-Sinoussi</td>
<td>Monkey, chimpanzee, mouse</td>
<td>Discovery of human immunodeficiency virus</td>
</tr>
<tr>
<td>2008</td>
<td>Luc Montagnier</td>
<td>Monkey, chimpanzee, mouse</td>
<td>Discovery of human immunodeficiency virus</td>
</tr>
<tr>
<td>2007</td>
<td>Mario R. Capecchi</td>
<td>Mouse</td>
<td>Discoveries of principles for introducing specific gene modifications in mice by the use of embryonic stem cells</td>
</tr>
<tr>
<td>2007</td>
<td>Sir Martin J. Evans</td>
<td>Mouse, Chick</td>
<td>Discoveries of principles for introducing specific gene modifications in mice by the use of embryonic stem cells</td>
</tr>
<tr>
<td>2007</td>
<td>Oliver Smithies</td>
<td>Mouse</td>
<td>Discoveries of principles for introducing specific gene modifications in mice by the use of embryonic stem cells</td>
</tr>
<tr>
<td>2006</td>
<td>Andrew Z. Fire</td>
<td>Nematode roundworm</td>
<td>Discovery of RNA interference - gene silencing by double-stranded RNA</td>
</tr>
<tr>
<td>2006</td>
<td>Craig C. Mello</td>
<td>Nematode roundworm</td>
<td>Discovery of RNA interference - gene silencing by double-stranded RNA</td>
</tr>
<tr>
<td>2005</td>
<td>Barry J. Marshall</td>
<td>Piglet</td>
<td>Discovery of the bacterium Helicobacter pylori and its role in gastritis and peptic ulcer disease</td>
</tr>
<tr>
<td>2004</td>
<td>Richard Axel</td>
<td>Mouse, Drosophila (fruit flies)</td>
<td>Discoveries of odorant receptors and the organization of the olfactory system</td>
</tr>
<tr>
<td>2004</td>
<td>Linda B. Buck</td>
<td>Mouse</td>
<td>Discoveries of odorant receptors and the organization of the olfactory system</td>
</tr>
<tr>
<td>2003</td>
<td>Paul C. Lauterbur</td>
<td>Clam, mouse, dog, rat, chimpanzee, pig, rabbit, frog</td>
<td>Discoveries concerning magnetic resonance imaging (MRI)</td>
</tr>
<tr>
<td>2003</td>
<td>Sir Peter Mansfield</td>
<td>Clam, mouse, dog, rat, chimpanzee, pig, rabbit, frog</td>
<td>Discoveries concerning magnetic resonance imaging (MRI)</td>
</tr>
<tr>
<td>2002</td>
<td>H. Robert Horvitz</td>
<td>Nematode</td>
<td>Genetic regulation of organ development and programmed cell death</td>
</tr>
<tr>
<td>2002</td>
<td>Sydney Brenner</td>
<td>Nematode</td>
<td>Genetic regulation of organ development and programmed cell death</td>
</tr>
<tr>
<td>2002</td>
<td>John E. Sulston</td>
<td>Nematode</td>
<td>Genetic regulation of organ development and programmed cell death</td>
</tr>
</tbody>
</table>