Update on the Eighth Edition of the *Guide for the Care and Use of Laboratory Animals*

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The *Guide for the Care and Use of Laboratory Animals* (the *Guide*) is an internationally accepted reference on animal care and use. In the United States, institutions receiving NIH support, such as the University of Tennessee, are required to base their animal care and use programs on the *Guide*. Since its first publication in 1963, the Guide has been updated seven times—most recently in 2011.

The 2011 *Guide* revision has generated much discussion in the lab animal and research communities. Although still based on performance standards, the new *Guide* contains 29 new “musts”. The Guide defines a “must” as a mandatory requirement or duty for providing humane care and use. Here at the University of Tennessee, the new requirements will likely have the greatest impact on the function and responsibilities of the IACUC and OLAC.

NIH has yet to officially adopt the 2011 *Guide*. The period of public comment on adoption and implementation ended on May 24, 2011. If NIH makes a decision to adopt the revision, an updated implementation plan will be disseminated. Previous plans were to require implementation by March 31, 2012. The Association for Assessment and Accreditation of Laboratory Animal Care International (AAALACi), the voluntary accreditation body of animal care and use programs, has indicated plans to use the 2011 Guide as the basis for program evaluation beginning in fall 2011. We can all breathe a sigh of relief; our next AAALACi site visit is not until summer 2013!

A digital version of the new Guide is available for download at [http://grants.nih.gov/grants/olaw](http://grants.nih.gov/grants/olaw)
The following measures were put into place to correct our “Culture of Noncompliance” that caused our institution to be placed on Probationary Accreditation. Dr. Joseph DiPietro, President of the University of Tennessee, appointed Dr. James Thompson, Dean of the College of Veterinary Medicine, as our Institutional Official (IO). The IACUC reporting structure changed from reporting to the IO through the Associate Vice Chancellor, Office of Research to reporting directly to the IO. Dr. Thompson sent letters to all PI’s explaining AAALACi’s findings and stipulated that animal users must comply with Federal and institutional guidelines related to animal care and use. The letter further clarified that failure to comply would result in action by the IACUC and may include suspension of animal activity.

Dr. Ron Banks, Director, Office of Animal Welfare Assurance at Duke University, presented a half day seminar on Compliance for Animal Care and Use Programs in December 2010. The program included sessions on IACUC functions; why the IACUC is important to the PI and the institution; qualifications and training of personnel; and protocol compliance: what is and what isn’t compliance.

The January 26, 2011 Quest Newsletter included a paragraph about compliance in animal care and use protocols. Information of IACUC functions will continue to be available on the Quest Newsletter, and the UTK IACUC and UTK Office of Research websites. The Quest Newsletter is published every other week by the Office of Research and distributed in paper and email format to the faculty of the University.

All animal users were notified of a mandatory training module on February 22, 2011. The training module focused on compliance and included a test. The online training module explained applicable Federal legislation and guidelines related to animal care and use, provided data on recent UTK noncompliance events, and detailed the investigator’s role in achieving compliance. Those that did not take the online mandatory training lost their access to the dedicated animal facilities at the April 5th IACUC meeting.

A new position, Director of Animal Compliance Support was created. This position will report to the IO and will be responsible for assisting PI’s in meeting their compliance responsibilities. Post approval monitoring and investigator training are the focus for this position. Dr. Mark Campbell was appointed Acting Director of Animal Compliance Support on February 21, 2011. Providing support has been the key approach when visiting with PIs. PIs have agreed to additional training, self reporting and submitting amendments to update personnel or change procedures to maintain compliance. Interviews are underway with three qualified candidates. We hope to have this position filled very soon.

In response to the changes made, AAALACi has lifted our probationary status and reinstated the UTK to full AAALACi accreditation.

**Identification of a Suspect Case of MHV and Implications on Animal Research**

**Joleen Adams, DVM**

During our routine health surveillance in June, one of our sentinel mice came up positive for the coronavirus, *Murine Hepatitis* virus (MHV). Confirmatory tests were immediately submitted to a second diagnostic lab. Follow up serology on the positive animal’s cage mate was negative. The sample that initially tested positive was retested and also came back negative. As all subsequent test results were negative for MHV, we viewed the initial test result as being a false positive.

There are multiple strains of MHV, and one strain does not confer immunity against other strains. The polytropic biotypes are considered to result in a more severe clinical disease. However, enterotropic biotypes are considered more contagious and more prevalent. Clinical disease caused by MHV is dependent both upon the strain as well as host factors. Certain strains (ex. BALB/c), weanling and immunodeficient mice are more susceptible to disease caused by MHV.
Typically MHV does not result in clinical disease in immunocompetent mice and these animals will clear the virus within 30 days. This virus can cause clinical disease in immunodeficient and suckling mice less than 2 weeks old. These susceptible mice may exhibit a variety of signs including diarrhea, weight loss, neurologic signs, and/or acute death. It was in mice with neurologic signs that the virus was initially recognized in 1949.

The virus can have many effects on research. Studies involving breeding animals can be affected by early embryonic death, as fetal infection with MHV is usually fatal. Once the virus becomes enzootic within the population, infant mice acquire passive immunity from the dams. These mice will harbor a subclinical infection and will continue to shed the virus, acting as a source of infection for naïve mice. As such, to effectively eradicate the infection, most advocate complete cessation of all breeding until the virus has been eradicated, which could take months.

Infected immunodeficient mice cannot clear the virus and consequently become an important source for virus transmission. Depopulation of these animals is usually necessary for MHV eradication.

MHV can have multiple effects on the biological responses of mice. Infection with the virus can stimulate or alter the immune system, infect transplantable tumors, and alter tissue enzyme levels. A variety of research work can be impacted profoundly by MHV infection, including studies on infection, nutritional studies, tumor studies, and pharmacokinetic studies.

Since the virus can contaminate murine tumors and cell lines, a key to preventing introduction of the virus is through rigorous and vigilant testing of all biological materials that are murine derived or have been passaged through mice. RADIL offers a PCR test as an alternative to the traditional murine antibody production (MAP) test. The IMPACT is considerably cheaper than the MAP test offered by other diagnostic laboratories. Also, because IMPACT is a PCR test, the turn around time is much shorter.

The possibility of having MHV in one of our facilities was very concerning, and stringent control measures were immediately instituted to help mitigate the spread of the virus. OLAC would like to thank everyone involved for their help in implementing the quarantine control measures. Maintenance of the health of our research colony is not only necessary from an animal welfare point of view, but is vital for the continuation of high quality animal research at UTK.

**The Murine Tail Biopsy Procedure**

Chris Carter, LVT, RLATg

The harvest of tissue from the tail tip is a common procedure utilized to provide tissue for genetic analysis. When performed correctly, the tail biopsy procedure is a safe and humane method for collecting tissue from rodents. The UTK institutional animal care and use committee (IACUC) has adopted a policy for the tail biopsy procedure.

Since the tail is important in the regulation of body temperature, tail tips can be performed a maximum of two times on a single animal. The length of the tail biopsy should be no greater than 5 mm. Researchers should familiarize themselves with genotype assays and select techniques providing the needed information with the least amount of tissue collected.

In rodents less than 21 days, tail tip biopsy may be performed without the use of analgesia or anesthesia. The recommended age for performing tail biopsy is between 8 to 21 days of age. During this period, the caudal tails are soft and the bones have not completely mineralized. Therefore, amputation performed on animals less than 21 days old likely results in momentary pain. On the other hand, amputations performed on rodents older than 21 days of age are likely to involve more than momentary pain and distress, as well as the potential for significant hemorrhage.

More information on the tail biopsy procedure can be found on the UTK IACUC website:

http://iacuc.tennessee.edu/policies/murine_tail_tip.shtml
I joined the Department of Public Health at the University of Tennessee, Knoxville in 2010. Before my appointment at UTK, I received my PhD in Comparative Pathology from the University of California Davis in 2003 and was a senior project scientist at the Center for Health and the Environment, University of California.

Our group concentrates on area of research which encompasses environmental impacts on reproduction and physiological development. Specifically, we study the adverse effects of exposure to pollutants and chemicals not normally found in the body (xenobiotics) and their influence on the endocrine system. In our laboratory, we use rodents as a research model to explore whether early-life exposure to endocrine disruptors have a negative impact on the animal later in life, also known as Fetal Programming of Adult Diseases. In addition to our animal models, in vitro cell models help us to identify new endocrine disruptors commonly found in our daily environment and investigate the mode of action(s) underlying their endocrine disrupting properties. Since many current regulatory control measures have been formulated only after serious environmental damage and/or adverse human health outcomes have occurred, findings from our research will provide fundamental rationale and underscore the needs to investigate new potential risks early and thoroughly.

At UTK, I have been pleased to find a group of very talented and dedicated students (Rebekah Kennedy and Jiyoung Bae) to work with and enjoyed tremendous support from OLAC. Since we joined UTK, our group has established collaborations with Drs. Jay Whelan and Ling Zhao from the Department of Nutrition, and Drs. Hwa-Chain (Robert) Wang and Joseph Weigel from the College of Veterinary Medicine. These multidisciplinary collaborations have been valuable in widening the perspectives of our research.

**How To Choose A Disinfectant**

**Chris Carter, LVT, RLATg**

Choosing the most effective disinfectant can be a daunting task. Most would prefer that there be one clear choice for use in every application, but in reality there are many different types of disinfectants to choose from and usually only a few that are fit for each situation.

Disinfection is defined as the process that eliminates all pathogenic microorganisms on inanimate objects. According to the *Guidelines For Disinfection and Sterilization for Health Care Facilities*, disinfectants can be divided into three groups: high, intermediate, and low level disinfectants. High level disinfectants kill all microorganisms with the exception of spores. Intermediate level disinfectants kill mycobacteria, vegetative bacteria, most viruses and most fungi. Low level disinfectants kill most vegetative bacteria, some viruses, and some fungi.
When choosing a disinfectant, additional factors should be considered such as the presence of organic matter, type of microbial contamination, exposure time to germicide, physical nature of the object (e.g., crevices, porous surface), temperature, and pH, all of which can impair the effectiveness of a disinfectant (Rutala 2008).

Disinfectants come in many different formulations. The ideal disinfectant would have all of the following properties: quick kill, broad spectrum of activity, strong penetrability, nontoxic, be able to withstand organic load, compatible with the material being used, and cost effective. Unfortunately, a disinfectant having all of these properties does not exist. Some disinfectants have a wide spectrum of activity while others kill only a small range of pathogenic microorganisms but are preferred due to their non-corrosive and non-toxic properties. To provide guidance in choosing the appropriate disinfectant, the table below lists the most commonly used disinfectants and their properties.

<table>
<thead>
<tr>
<th>Disinfectant</th>
<th>Disinfectant level</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohols</td>
<td>Intermediate level disinfectant</td>
<td>Fast acting, No residue, Non-staining</td>
<td>Volatile, Evaporation may diminish concentration, May harden rubber or cause deterioration of glues, Intoxicating</td>
</tr>
<tr>
<td>Chlorine</td>
<td>Intermediate level disinfectant</td>
<td>Low cost, Fast acting</td>
<td>Corrosive to metals, Inactivated by organic material, Irritant to skin and mucous membranes, Shelf life varies</td>
</tr>
<tr>
<td>Hydrogen peroxide</td>
<td>Low level disinfectant (3%), High level disinfectant (5%)</td>
<td>Strong oxidant, Fast acting, Breaks down into water and oxygen</td>
<td>Corrosive to aluminum, copper, brass, or zinc, Surface active with limited ability to penetrate</td>
</tr>
<tr>
<td>Iodophors</td>
<td>Low level disinfectant for hard surfaces</td>
<td>Rapid action, Relatively free of toxicity and irritancy</td>
<td>Note: Antiseptic iodophors are not suitable for use as hard surface disinfectant, Corrosive to metal unless combined with inhibitors, Disinfectant may burn tissue, Inactivated by organic materials, May stain fabrics and synthetic materials</td>
</tr>
<tr>
<td>Peracetic acid</td>
<td>High level disinfectant</td>
<td>Rapid action at low temperature, Active in presence of organic materials</td>
<td>Can be corrosive, Unstable when diluted</td>
</tr>
<tr>
<td>Phenolics</td>
<td>Low/intermediate level disinfectant</td>
<td>Commercially available with detergents to provide one-step cleaning and disinfecting</td>
<td>Not recommended for use on food contact surface, Leaves residual film on surfaces, May be absorbed through skin or by rubber, Some synthetic flooring may become sticky with repetitive use</td>
</tr>
<tr>
<td>Quaternary ammonium compounds</td>
<td>Low level disinfectant</td>
<td>Non-irritating, Non-corrosive, Usually have detergent properties</td>
<td>Limited use as a disinfectant because of narrow microbicidal spectrum</td>
</tr>
</tbody>
</table>

Rutala, 2008
OLAC Training

Did you know that OLAC can provide training specifically tailored to meet the needs of your lab? Investigators that have taken advantage of this specialized training in the past have requested topics on lab animal anatomy, anesthesia, surgical prep, handling and restraint, blood sampling techniques, and tail biopsies. In addition, OLAC offers an open invitation to our rodent handling, restraint, and experimental techniques lab held at least three times per year. Feel free to contact OLAC with a training request and we will do our best to accommodate your needs.

Online Courses

Biomethodology of the Mouse and Biomethodology of the Rat are now available on the OLAC training page http://www.vet.utk.edu/olac/training.php

To sign up or schedule a training session please contact Jane Czarra either by phone: 974-5841 or email: jczarra@utk.edu

Meet the New JJARTU Research Coordinator

Roger Long has worked at UTK for over 20 years. Twelve of those years has been as maintenance supervisor of the Joe Johnson Animal Research and Teaching Unit (JARTU). Roger's experience and familiarity with the facility will make for a smooth transition into his new position as research coordinator.

The JARTU facility consists of three wings with over 35 laboratory rooms and currently houses livestock, aquatics, poultry, sheep, dogs, and cats. JARTU also provides suites for surgery, necropsy, and the mixing of feed rations. As research coordinator of JARTU, Roger will be responsible for the day to day activities such as animal care, facility upkeep, and coordinating personnel.