Occasionally the IACUC receives questions about the protocol review process. A common question such as length of time to approval depends on a number of factors such as the assigned pain category or number of revisions needed. Understanding the approval process is important to the animal user and can help in planning ahead for future projects. In reading, if additional questions arise, please feel free to email any questions to utiacuc@utk.edu.

Administrative Review. Upon submission to the IACUC office, the protocol is reviewed administratively. This step ensures all questions are answered. The administrative review also makes sure the Flow Chart and Appendices are appropriate. If clarification or further information is required at this stage, a timely response from the PI is critical. Following administrative review, the protocol is forwarded to the Office of Laboratory Animal Care (OLAC) for veterinary review.

Veterinary Review. OLAC veterinarians review the protocol assessing veterinary care touch points, which include procedures, anesthesia, analgesia, euthanasia and post-procedural monitoring. Veterinary reviews are done every Wednesday. For inclusion in the weekly veterinary review, protocols must be submitted to the IACUC office no later than 4 pm Monday.

IACUC Coordinator. Following veterinary review, OLAC releases the protocol with the pain and distress (p/d) category to the IACUC coordinator. If more animal use information is needed based on the veterinary review, questions are forwarded to the PI for resolution. Once all questions are resolved, the protocol is then sent to the IACUC chair for reviewer selection.

IACUC Chair. The reviewer selection process by the Chair is challenging. The committee is composed of individuals with varying expertise. In addition to their varying knowledge base, the IACUC member chosen to review a protocol must be in a different department from the PI to minimize conflict of interest. Compounded with those two issues, is availability. For all committee members, their IACUC role is not their primary responsibility. They may be in clinics, the classroom, the field, or out of the office on business or annual leave. Trying to effectively
share the workload is a difficult balancing act for the Chair.

**Committee Review.** There are two methods of committee review.

a. **Full Committee Review (FCR).** FCR requires discussion at an IACUC meeting; meetings are held monthly on the first Tuesday of each month. FCR requires the protocol to be distributed to all members at least two weeks before the scheduled meeting. Protocols that automatically require FCR are p/d Category D that include a survival surgery and Category E.

b. **Designated Member Review (DMR).** Protocols not designated for FCR following OLAC veterinary review are slated for DMR. The coordinator sends the protocol via email to all IACUC members. The comment period is seven days during which time the protocol may be called to full review by any IACUC member or comments/questions submitted to the coordinator for the reviewer to consider as required modifications. Simultaneously, the chair receives the protocol to determine the reviewer. Following the seven day review period by the IACUC, if the protocol is not called to FCR, the IACUC member who is selected to review the protocol is sent an email notification of their DMR assignment along with a standardized review form to document protocol review. The DMR may result in required modifications to secure approval, a direct approval recommendation, or a call by the reviewer for FCR. Any required modifications are sent to the PI for resolution. Once the protocol is returned to the IACUC office, it is sent back to the designated reviewer to see if all items are appropriately addressed. When the reviewer is satisfied with the revised document, the protocol will undergo final edits by the IACUC office and then forwarded to the Chair for signature of approval.

In the best case scenario where no revisions are needed at any step of the process, protocols are reviewed and approved in approximately two weeks. If protocols require revisions in any of the steps, it lengthens the review process, which is greatly dependent on the response time from the PI and the promptness and availability of the reviewer to complete the review.

The Institutional Animal Care and Use Committee is one of the most important and time consuming committees at our University. Our members are dedicated to evaluating animal welfare issues and making sure all necessary regulatory components are being met within the written protocol.

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**Meet the New IACUC Chair**

The Institutional Animal Care and Use Committee at UTK utilizes a rotating system of faculty members being appointed to the Chair position after serving a period of time on the committee. After serving 2 years on the committee, Dr. Melinda Hauser was appointed IACUC Chair this past summer. Dr. Hauser completed her undergraduate and graduate training at the University of California, Irvine in Comparative Physiology, before moving to East Tennessee for Post-Doctoral work at ORNL. Currently Dr. Hauser is a Research Assistant Professor in the Department of Microbiology. She has experience with mouse model systems, specifically investigating virulence of fungal pathogens, including Candida albicans, Aspergillus fumigatus, and Wangiella dermatitidis. Her current research focus is on the regulation of G-protein coupled receptor (GPCR) function using the yeast Saccharomyces cerevisiae as a model system. Her goal as chair of the IACUC is to insure that the protocol approval process is as seamless as possible for investigators, while at the same time maintaining the highest possible standards for animal care.
Having a research facility that is free from insect and rodent infestations is crucial to the integrity of the research projects conducted within the facility. This is why they implement pest control programs. According to the Guide, each facility should implement a regularly scheduled and documented program of pest control and monitoring (Guide, p74). Facility managers have the dutiful job of overseeing pest control program within their own facility. Part of their responsibility includes effective measures that deny pest entry into the research facility. Should pests enter the facility; prompt action must be taken to eliminate them.

Traditionally, we think of pest control as the general application of one or more pesticides. In a research facility it is more complicated than that. We do treat the common areas and hallways with pesticides. However, some research projects can be affected by chemicals, this is why pesticides are not used in animal rooms. Instead, glue boards, fly traps, live traps and electric bug zappers are used in the dedicated animal rooms as well as in hallways and common areas.

Sanitation, good housekeeping and a sound structure are also important to pest prevention. All facilities must ensure that windows, doors and exterior walls are sealed to prevent entrance of pest and predators. Other ways of ensuring a pest free facility is by keeping cardboard boxes, feed bags, and other supplies off the floor, maintaining clutter free animal rooms and work areas, and by complying with a routine cleaning schedule.

A good pest control program involves everyone at the facility. Each person at the facility has to be vigilant, compliant with sanitation rules and report any pests immediately to the facility manager.
Spotlight on Models in Animal Research

Ralph Lydic, PhD and Helen A. Baghdoyan, PhD

Ralph Lydic is the Robert H. Cole Professor of Neuroscience and he holds joint appointments in the UT Department of Psychology, in Anesthesiology at the UT medical center, and at Oak Ridge National Laboratory. His NIH funded research program is focused on efforts to understand the neurochemical mechanisms regulating anesthesia, sleep, and pain.

Helen A. Baghdoyan received her Ph.D. in Neuropharmacology from the University of Connecticut and completed post-doctoral training at the Harvard Medical School. Her research is focused on understanding the neurochemical mechanisms important for generating states of consciousness such as sleep and general anesthesia. She is currently Professor of Psychology and Beaman Professor at UTK, Co-Director of Anesthesiology Research at the UT Medical Center, and Joint Faculty at Oak Ridge National Laboratory.

Our NIH funded research programs are using congenic lines of mice to achieve a better understanding of clinically relevant problems such as opiate-induced depression of breathing, pain, and changes in brain chemistry that occur when consciousness is lost during sleep and general anesthesia. The goal of this article is to emphasize the extraordinary value of animal research for understanding how the brain functions to regulate conscious and unconscious states.

Across phyla all animals exhibit behavioral cycles of rest and activity. Complex multicellular organisms appearing 600 million years ago and mammals appearing about 60 million years ago all experienced periodic cycles of light and darkness. These solar cycles regulate energy capture by all organisms and underlie cycles of behavioral activity and rest. Among mammals, the rest-activity cycles have developed into states of consciousness expressed as sleep and wakefulness. In all placental, terrestrial mammals sleep states are further elaborated into episodes of rapid eye movement (REM) sleep and non-rapid eye movement (NREM) sleep. Mammalian sleep cycles vary by species, habitat, age, and whether an animal is nocturnal or diurnal. Although sleep is a ubiquitous feature of mammalian biology, the neuronal and molecular mechanisms that generate states of sleep and wakefulness remain incompletely understood.

Sleep is as important as exercise and nutrition in contributing to the divide between health and disease. The U.S. Centers for Disease Control and Prevention (CDC) frequently summarizes evidence that, although sleep is essential for health, humans in the U.S. are chronically sleep-deprived. About one-third of adults do not get enough sleep. The importance of sleep for health is further emphasized by the fact that the CDC maintains a web page devoted entirely to sleep and sleep disorders.

The National Institutes of Health one of the 27 disease-focused institutes is the National Center for Sleep Disorders Research. At the National Institutes of Health one of the 27 disease-focused institutes is the National Center for Sleep Disorders Research.

Sleep is widely studied from the perspectives of both clinical and basic neuroscience. The discovery that sleep is characterized by impaired regulation of autonomic physiology also emphasizes the relevance of sleep research. For example, all homeotherms lose their normal ability to regulate core body temperature during REM sleep. When mammals enter REM sleep, blood pressure is wildly irregular and heart rates can sporadically increase to match rates achieved during maximal exercise. Mammals are effectively
paralyzed during REM sleep during which the brain inhibits skeletal muscle tone. Muscles in the upper airway that are key for normal breathing have very low tone during REM sleep. The normal compensatory breathing responses to high levels of carbon dioxide or low levels of oxygen are depressed during REM sleep. Although sleep and anesthesia are different states of consciousness, anesthetic drugs also cause impaired breathing, in part because anesthetics act on some of the same brain networks that generate sleep. Animal research plays an essential role in elucidating the brain mechanisms that cause anesthetic-induced and sleep-dependent autonomic dysregulation.

The ability of animal research to identify mechanisms regulating sleep and wakefulness is essential for developing rational, as opposed to empiric, therapies. We enthusiastically support the One Health perspective www.onehealthinitiative.com/about.php that research promoting the health of human and non-human animals is a value-added achievement.

The heating, ventilation, and air conditioning (HVAC) system in an animal facility plays an important role in the overall function of animal facilities. The Guide for the Care and Use of Laboratory Animals (Guide) provides laboratory animal facilities with engineering standards such as 10-15 air changes per hour (ACH) to maintain acceptable air quality in the lab animal room. Additionally, these environmental conditions are intended to provide comfort to laboratory animals, safety to the animal caregivers, and metabolic stability in animals for experimental consistency.

HVAC design will vary based on the type of animal room involved. Consideration should be based on species of animal housed, function of the animal (breeding vs experimentation), animal biological safety level (ABSL), and type of caging used. Differential pressures can be used to create an air barrier between two areas or zones in a facility. Differential pressures should be set so that air flows from the cleaner areas of the animal facilities to the dirtier or potentially contaminated areas. Breeding rooms are often maintained at a positive directional pressure to ensure a clean environment for the animals. On the other hand, ABSL 2 and quarantine rooms will be at negative directional pressures to ensure that possible contaminants are contained within the room. The Guide recommends the use 100% fresh air to ventilate animal rooms. Use of recycled air entails risk of cross contamination because many animal pathogens can be airborne or travel on fomites.

In some situations, the use of a broad ventilation guideline might overventilate a room with only few animals whereas it might underventilate a room with a large number of animals. Modern HVAC systems such as variable air volume systems allow ventilation rates to be set in accordance with heat load and other variables while still maintaining a minimum of 10-15 ACH. Fresh air at the appropriate temperatures must be available 24 hours per day, year round. HVAC systems should be designed to provide adequate air exchange and maintain critical air differential pressures even during mechanical breakdowns and power outages. Having an emergency electrical supply is essential to maintaining at least some of services of the HVAC system during power outages.

The successful operation of any HVAC system requires regular maintenance and evaluation, including measurement of its function. Such measurements include supply and exhaust air volumes, fluctuation in temperature and humidity, and air pressure differentials between spaces.