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for answers to your
animal use questions*

Working Safely in a Biosafety Cabinet

Class II biosafety cabinets (BSC) are recommended for work with animals, tissue and cell culture systems that are potentially biohazardous or must be protected from contamination. Class II BSC's are classified as type A (air recirculated within the work area) and type B (air exhausted to the outside of the building) cabinets. Whichever type of cabinet is used it will provide effective protection only if correct work techniques are followed.

A Class II BSC protects the user by creating a flowing curtain of air across the face opening of the cabinet that acts as a barrier to contain airborne particles within the cabinet. Disruption of this air barrier may occur when a worker's arms move in and out of the cabinet, room doors are opened or closed or people walk by the front of the cabinet. To reduce the possibility of disruptions in the barrier, materials needed within the cabinet should be placed inside before starting work and arms should be moved in and out of the cabinet slowly, perpendicular to the face opening.

Material within the BSC is protected from contamination by a stream of HEPA filtered air flowing from the top to the bottom of the cabinet. The cabinet blowers should be operated for 3-5 minutes prior to beginning work to remove particulates within the cabinet. In addition, the interior work

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Norovirus in Laboratory Mice

Noroviruses (previously called "Norwalk-like viruses") are responsible for up to 50% of all food borne gastroenteritis outbreaks in the United States and are the most common cause of infectious gastroenteritis among persons of all ages (Widdowson, Monroe et al. 2005). Noroviruses belong to the *Caliciviridae* family and exist as numerous strains with a currently known host range that includes humans, mice, cows and pigs.

The murine norovirus strain (MNV) was first described in 2003 after researchers at Washington University in St. Louis observed deaths in RAG/STAT1^{-/-} mice (deficient in signal transducer and activator of transcription factor 1 and recombination-activating gene 2) due to an unknown infectious agent. Karst (Karst, Wobus et al. 2003) identified the infectious agent as a norovirus and inoculated various mouse strains with the virus as part of their investigation. They found that infection of

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Pet Rodents as a Potential Source of Salmonellosis

Salmonellosis is estimated to cause disease in 1.4 million people annually in the United States. *Salmonella* bacteria are found in the intestinal tract of many species of animals and transmission occurs by ingestion of feces. In 2004, the U.S. Center for Disease Control (CDC) documented the first salmonellosis outbreak associated with pet rodents. From December 2003 to September 2004 15 human cases of salmonellosis associated with rodent exposure were identified from ten states. The majority of patients were young (median age 16 years), and although no deaths occurred, six patients required hospitalization. Mice, rats and hamsters purchased from multiple retail pet store chains and pet distributors were identified as the source of exposure in these cases. *Salmonella enterica* serotype Typhimurium isolates obtained from both humans and rodents involved in this outbreak were resistant to multiple antibiotic drugs. *S. Typhimurium* was also recovered from transport containers, cages and bedding contaminated with rodent droppings.

Many pet animals, including reptiles, mice, rats, hamsters, chicks, ducklings and hedgehogs, have been shown to be potential sources of human exposure to *Salmonella*. *Salmonella* bacteria can persist in the environment and exposure may occur without direct animal contact. Mice and rats obtained from commercial laboratory animal vendors and housed in PSU animal facilities are routinely tested for the presence of pathogenic microorganisms, including *Salmonella*, and are not considered to be a likely source of exposure. However, students and staff who come in contact with infected pets at home or in retail pet stores could potentially transmit pathogenic microorganisms to research animals in our facilities. To help prevent such exposure, employees should not handle research animals without wearing protective clothing (i.e., dedicated lab coat), exam gloves and shoe covers. It is also recommended that investigators strongly discourage their employees and students from keeping rodents and reptiles as pets.

Reference:

Outbreak of Multidrug-Resistant *Salmonella* Typhimurium Associated with Rodents Purchased at Retail Pet Stores – United States, December 2003 – October 2004. MMWR May 6, 2005/ 54(17): 429-433.



Tips for Working in Animal Rooms

1. Wear appropriate attire i.e., shoe covers and lab coat or gown (to be used in that room only) and exam gloves. Certain animal rooms may have more stringent requirements for entry.
2. Open rodent cages within a biosafety cabinet (if one is in the room). Do not place or open cages on the floor.
3. Animals must not be left unattended outside of the animal rooms. Mice/rats scheduled for euthanasia by ARP personnel should be left in their animal room with appropriate instructions on their cages.
4. Do not consolidate cages of animals unless euthanasia is to occur immediately. Overcrowding will lead to stress and possible fighting injuries if strange animals are left together for more than a few minutes.
5. Make sure water bottles are correctly replaced onto the cage lid after opening the cage. Mice/rats will become dehydrated and may die if unable to reach water overnight.

Norovirus in Mice, continued from page 1.

RAG/STAT1^{-/-} mice with MNV was associated with death due to encephalitis, meningitis, cerebral vasculitis, pneumonia and hepatitis.

The same study showed that STAT1 receptors were required for survival after MNV infection. RAG1^{-/-} and RAG2^{-/-} mice inoculated with MNV did not die but became persistently infected, indicating that B and T cell dependent adaptive immunity is not required for protection from lethal MNV infection.

IFN $\alpha\beta$ γ R^{-/-} mice (deficient in both interferon $\alpha\beta$ and interferon γ receptors) were 10,000 times more susceptible to lethal infection with MNV than wild-type controls after intracerebral and intranasal inoculation. However, mice lacking just one of the two interferon receptors (IFN $\alpha\beta$ or IFN γ) were no more susceptible to death than immunocompetent mice (Karst, Wobus et al. 2003).

Immunocompetent mice orally inoculated with MNV were transiently infected and may mimic asymptotically infected carriers in human populations (Karst, Wobus et al. 2003).

The significance of MNV other than as a sporadic fatal disease of certain immunocompromised mouse strains is unknown. Recent survey testing of mouse serum samples by a commercial diagnostic laboratory revealed that 29.9% of samples were positive for MNV (Research Animal Diagnostic Laboratory 2005). This suggests that infection of mice in laboratory animal facilities is common. Further research is needed to determine the importance of MNV as both an animal model of human norovirus and a naturally occurring pathogen of mice.

References:

Karst, S. M., C. E. Wobus, et al. (2003). "STAT1-Dependent Innate Immunity to a Norwalk-Like Virus." *Science* **299**: 1575-1578.

Research Animal Diagnostic Laboratory, University of Missouri (2005). Murine Norovirus. <http://www.radil.missouri.edu/info/MNVinfo.asp>.

Widdowson, M.-A., S. S. Monroe, et al. (2005). "Are Noroviruses Emerging?" *Emerging Infectious Diseases* **11**(5): 735-737.

Training Posters in Animal Facilities

ARP is developing a series of training posters that will be displayed in the PSU laboratory animal facilities. Poster topics are chosen for their relevance and importance to work with laboratory animals and are intended as a quick educational resource for staff, students and faculty using the animal facilities. The posters will be hung in conspicuous spots in the animal facilities and changed on a regular basis.



ARP is also creating a poster outlining the steps involved in using the gas anesthesia equipment available in facility procedure rooms. These posters will be hung near the anesthesia equipment and provide step-by-step instructions for using gas anesthesia in rodents.

Watch for these posters in your facility!

Animal Resource Program

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🔑 In addition to other security changes, locks in the CBL have been recently changed and new keys distributed. Animal facility keys are assigned to individuals. Do not give your key to other people to use or store keys in common areas.

The Animal Resource Program (ARP) is committed to providing PSU faculty, staff and students with high quality, cost-effective research animal resources. In addition to suitable housing facilities and animal husbandry services for animals used in biomedical research, ARP provides veterinary and diagnostic services, personnel training and expertise in laboratory, agricultural and wildlife animal technology and medicine. ARP veterinarians are also available to participate in collaborative research projects with PSU investigators. Areas of interest include animal behavior and welfare, infectious disease, and pathology.



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surface including the walls (not the supply filter diffuser) and interior surface of the window should be wiped with an appropriate disinfectant.

The user's arms should not rest flat across the front grille as this will allow room air to flow directly into the work area rather than through the front grille. The front grille must not be blocked with notebooks, pipetting devices, plastic wrappers or other material for the same reason. For effective protection, arms should be held slightly above the front grille and work should be performed at least four inches behind the front grille.

If using a BSC to work with rodents in microisolator housing the cages should only be opened within the cabinet. Cage filter tops, water bottles and wire lids must remain within the cabinet to avoid contamination. Mice may be handled with disinfected gloves or forceps although care must be taken to avoid wetting mice with potentially irritating disinfectant solution.

Additional information on working in a biosafety cabinet is available at <http://www.cdc.gov/od/ohs/biosfty/bsc/section5.htm>.