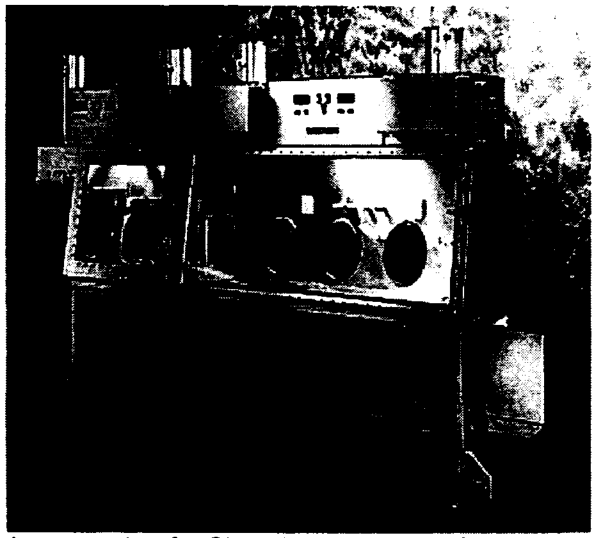
Posted on: 03/31/2003

Biosafety Ventilation Systems

Carl C. Schultz, P.E.

The events of September 11, 2001 have ushered in an ominous era where the study of dangerous biological agents is at the forefront. Consequently, many institutions and organizations are planning and building biosafety laboratories in order to secure research dollars. One differentiating factor of a biosafety laboratory is the unique demands placed on its ventilation systems. At the heart of biosafety is the containment of hazardous agents through multiple levels of barriers.



An example of a Class III biological safety cabinet The cabinet is maintained under negative air pressure, with supply air drawn into the cabinet through HEPA filters. Exhaust air is double HEPA filtered. (Courtesy of Baker Co.)

Primary barriers pertain to equipment such as gloves, gowns, masks, biosafety cabinets, respiratory protection, and positive-pressure ventilation suits as well as the use of good laboratory techniques.

Secondary barriers are addressed through facility design with airtight rooms, air handling and filtration, air locks, showers, laundry, sewerage treatment, waste disposal, sterilizers, redundant services, and equipment and material finishes.

Tertiary barriers deal with the physical operation with items such as walls, fences, security, and animal exclusion zones. Due to the varying risk of biological agents, the facilities that handle these agents need to be designed and classified accordingly.[1]

Biosafety Laboratories

Biosafety laboratories in the United States are categorized as one of four types, designated as Levels 1, 2, 3, and 4. A Biosafety Level (BSL) 1 or 2 facility would not necessarily have any special ventilation requirements. BSL 1 laboratories wor with strains of microorganisms not known to consistently cause disease in healthy adult humans, while BSL 2 laboratories deal with moderate-risk agents that are present in the community and are associated with human disease.

BSL 1 facilities rely on containment based upon standard microbiological practice without special primary or secondary barriers, other than perhaps a sink for hand washing. Agents at BSL 2 facilities can be used safely in activities on an open bench, granted that the potential for producing splashes and aerosols is low. Hepatitis B virus, HIV, and salmonellae are representative of the organisms assigned to these containment areas.

BSL 3 facilities require placing more emphasis on primary and secondary barriers in order to protect the community and the environment, as well as the laboratory personnel. Ventilation systems consequently play a major role in these facilities. This is because work is done with indigenous or exotic agents with a potential for respiratory transmission, which may cause serious and potentially lethal infection. Tuberculosis and the St. Louis encephalitis virus are representative of the microorganisms assigned to this containment level. Laboratory manipulations are performed in a biological safety cabinet or other closed equipment, which constitu primary barriers. Secondary barriers include controlled access to the space and ventilation systems that minimize the release of infectious aerosols from the laboratory.

BSL 4 laboratories work with dangerous and exotic agents that pose a high individual risk of life-threatening disease, which may be transmitted by aerosol an for which there is no available vaccine or therapy. Viruses such as Congo-Crimea hemorrhagic fever are manipulated at this biosafety level. The primary hazard to personnel working with BSL 4 agents are respiratory exposure to infectious aerosols, mucous membrane, or broken skin exposure to infectious droplets, and autoinoculation. Work with these agents poses a high risk of exposure and infecti to laboratory personnel, the community, and the environment.

Worker isolation from aerosols is accomplished by working in Class III biological safety cabinets or in a full-body, air-supplied, positive-pressure personnel suit. Th BSL 4 facility is generally a separate building or completely isolated zone designe with specialized ventilation and waste management systems to prevent release o viable agents to the environment.[2]

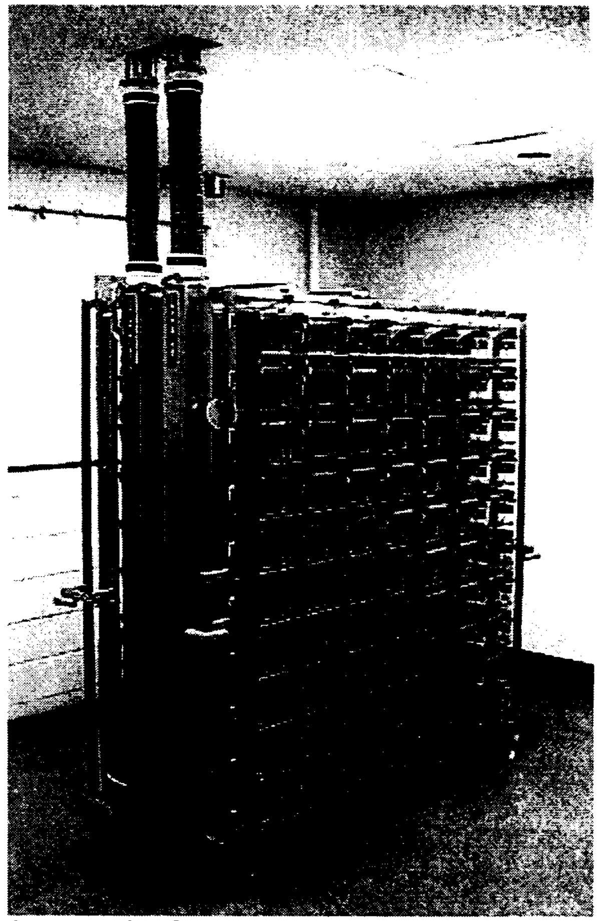
Class II Type A cabinets can be exhausted into the lab or outsi by way of a canopy connection, whereas Type B cabinets mus have a dedicated, sealed exhaust system with remote blower and appropriate alarm system.

Containment Laboratory Ventilation

BSL 3 and 4 facilities are often referred to as containment laboratories. They contain airtight rooms and duct systems to ensure that the agents being studied remain in the laboratory. Consequently, all mechanical and electrical service penetrations through the containment barrier are equipped with containment seals.

Airflow must be directional,

moving inward toward the containment zone and must be nonrecirculated. Air device placement should work to minimize dead air spaces where contaminated air can accumulate. Supply of 100% outdoor air is required, as recirculation of even HEPA-filtered air is not permitted.



An example of a ventilated cage rack, used to house small animals, such as rodents. (Courtesy of Allentown Caging Equipment Co.)

However, air from a Class II or III biological safety cabinet (BSC) which is HEPA-filtered, can be recirculated in a Level 3 facility if the cabinet is tested and inspected at least every 12 months. The supply air system must be interlocked with the exhaust ventilation system to prevent positive pressurization. Room air supply and exhaust ductwork should be equipped with bubble-tight dampers to permit sealing for decontamination of individual containment areas.

For instance, the decontamination procedure for a BSC may include sealing off the cabinet and boiling a formalin solution to generate formaldehyde gas. The cabinet fan would recirculate this gas for an hou and then the cabinet would sit idle for another 15 hours before purging. This illustrates how important it is for the containment zone and ductwork to be sealed not only at the perimeter but also between individual areas within the containment zone.

Exposed ductwork should stand clear of walls to allow access for maintenance of equipment filters and lighting, and to permit leak testing. HEPA filters should be installed as close as possible to the source of the hazard to minimize the length o contaminated ductwork, and they should be monitored by magnehelic gauges or other appropriate devices.

Biosafety Level 4: Maximum Containment

True BSL 4 facilities, or maximum containment laboratories, are few and far between, with the federal government operating such labs in Fort Detrick, MD; Bethesda, MD; and Atlanta. A non-profit organization, the Southwest Foundation Biomedical Research, operates one in San Antonio, and there are several either planned or under construction in locations such as Montana and Galveston, TX.

There are two models for BSL 4 laboratories. One is the cabinet laboratory where all handling of the agent is performed in a Class III BSC, which is discussed later. The other model is the suit laboratory where personnel wear a protective suit. Use of Class I and II cabinets are permitted in the suit laboratory. The BSL 4 laborator in San Antonio recently replaced its cabinet laboratory with a suit laboratory. You may recall that a suit laboratory was depicted in the movie Outbreak, starring Dustin Hoffman who portrayed an Army medical expert sent to combat a deadly virus that destroyed a small California town and threatened the world.

The BSL 4 containment zone should be located in a separate building or sealed room with independent air supply and exhaust systems. These air systems and components need to be sealed airtight and be accessible from outside the containment area. A ventilated air lock is required for the separation of higher anc lower containment areas. The air lock is to have interlocking pneumatic or compressible sealed doors with manual overrides.

The cabinet laboratory is arranged to ensure passage through a minimum of two doors prior to entering any room containing the Class III BSC. The personnel working in the suit laboratory wear a one-piece, positive-pressure suit that is ventilated by a life-support system protected by HEPA filtration. The life-support system includes redundant breathing air compressors, alarms, and emergency backup air tanks. A chemical shower is provided to decontaminate the surface of the suit before the worker leaves the area.

An emergency power source is provided for the exhaust system, life-support systems, alarms, lighting, entry and exit controls, and BSCs. The air pressure witl the personnel suit is positive to the surrounding laboratory. The air pressure withi the suit area is lower than that of the adjacent area. The entry to the containment area is equipped with magnehelic gauges or pressure-monitoring devices to prov directional flow. The containment area is equipped with audible alarms to detect depressurization.

Supply air to the cabinet room or suit area and associated decontamination show and air lock is protected by passage through a HEPA filter. The exhaust of the laboratory's suit area, decontamination shower, and decontamination air lock is treated by passage through two HEPA filters in series prior to discharge to the outside. Redundant supply fans are recommended, and redundant exhaust fans are required.[2]

HEPA Filtration

The development of the HEPA filter during World War II was critical in providing tl necessary containment in the modern biosafety laboratory. These filters are constructed of fiberglass "paper" that is pleated to maximize the surface area of tl filter and have a minimum particulate removal of 99.97% for particles of 0.3 microns. The randomly oriented microfibers cause the particles in the airstream tc move in a circuitous path, forcing even the smallest particles to collide with and adhere to the filter.

The filter housings on contaminated exhaust streams should be constructed to facilitate decontamination or should be of the bag in/bag out design. This design should also be of the fluid-seal type that incorporates a knife edge that mates into fluid-filled perimeter channel on the face of the filter. There should be a safety feature where the filter locking arm and the access door interface in such a mann that minimizes the possibility of the door being closed until the filters are correctly seated in the housing.

Prior to leaving the factory, each knife edge should be checked with an alignment gauge to ensure proper alignment with the filter. The filter-sealing mechanism should be replaceable and should be operated through the changeout bag by a locking handle. The mechanism should exert equal force at the top and bottom edge of the filter when engaging and disengaging the filter from the knife edge.

Three glove sleeves are provided in each bag to facilitate handling of the filter during changeout. For visibility during this procedure, the bag includes clear PVC the mouth with an elastic shock cord hemmed into it, so that it fits securely when stretched around the bagging ring. To prevent the bag from sliding off the bagging ring during the changeout process, a nylon security strap is provided at each filter access port. A nylon-cinching strap is also provided at each port to tie off the slac in the bag while the system is in operation.

Biological Safety Cabinets

German scientist and 1905 Nobel Prize Winner Robert Koch discovered that gern could float in air and constructed the first BSC. Dr. Koch worked with anthrax, tuberculosis, and cholera and miraculously never succumbed to these diseases. His cabinet was a glazed tabletop box with two openings fitted with oilcloth sleeve for the scientist's arms. The problems associated with this cabinet were that the sleeves and seams leaked and that a hinged door at the top acted to induce air in and out when opened and closed.[3] BSC design has come a long way, with three main classifications: Class I, II, and III.

Class I cabinets are defined as ventilated cabinets for personnel and environment protection, with unrecirculated airflow away from the operator. Class I cabinets have a similar airflow pattern to a fume hood, except that the Class I cabinet has a HEPA filter at the exhaust outlet, and it may or may not be connected to an exhau duct system. Class I cabinets are suitable for work with agents that require BSL 1 2, or 3 containment.

Class II cabinets are ventilated cabinets having an open front with inward airflow f personnel protection, downward HEPA-filtered laminar flow for product protection and HEPA-filtered exhaust airflow for environmental protection. Class II cabinets are suitable for work with agents that require BSL 1, 2, or 3 containment. Class II cabinets are differentiated into various types based on their construction, air velocities, and patterns, and by their exhaust system.

For instance, Class II Type A cabinets may have contaminated plenums under positive pressure that are exposed to the room while Type B cabinets must surround all contaminated positive pressure plenums with negative pressure ductwork. Type A cabinets can be exhausted into the lab or outside by way of a canopy connection, whereas Type B cabinets must have a dedicated, sealed exhaust system with remote blower and appropriate alarm system.

Class III cabinets are totally enclosed and ventilated of gas-tight construction. Operations are conducted through attached rubber gloves. The cabinet is maintained under negative air pressure of at least 0.5-in. w.g. Supply air is drawn into the cabinet through HEPA filters. The exhaust air is treated by double HEPA filtration. The cabinet also has a transfer chamber capable of sterilizing work materials before exiting the glove box containment system. Class III cabinets are suitable for work with agents that require BSL 1, 2, 3, or 4 containment.[4]

Generally, exposure of unadapted animals to temperatures above 85 degrees F or below 40 degrees, without access to shelter or other protective mechanisms, might produce clinica effects which could be life threatening. It is often appropriate t have reheat valves fail closed, as animals can adapt to 55 degrees air but not 90 degrees temperatures.

Animal Facilities

Many biosafety facilities require the use of laboratory animals, consequently incorporating features and concepts associated with vivariums. The animals are kept in holding rooms, and they require between 12 to 18 ach. The purposes of th high ventilation rate include: supplying adequate oxygen; removal of thermal load caused by animal metabolism and respiration, lights, and equipment; diluting gaseous and particulate contaminants; adjusting the moisture content of room air and creating static-pressure differentials between adjoining spaces.

Small animals, such as rodents, are usually housed in ventilated cage racks. The racks do not necessarily act as a containment barrier, but they limit odors and exposure of personnel to allergens. These cage systems vary in manufacturer design, with certain models requiring both central supply and exhaust system connections. Other models require only connection to a central exhaust system a derive the supply air from the holding room itself. Supply and exhaust to these racks are HEPA filtered.

Regulation of body temperature within normal variation is necessary for the well being of mammals. Generally, exposure of unadapted animals to temperatures above 85 degrees F or below 40 degrees, without access to shelter or other protective mechanisms, might produce clinical effects which could be life threatening. It is often appropriate to have reheat valves fail closed, as animals ca adapt to 55 degrees air but not 90 degrees temperatures. Recommended drybulb temperature for several common species are indicated in Table 1. The range of daily temperature fluctuations should be kept to a minimum. Relative humidity should also be controlled, but not nearly as narrowly as temperature. The acceptable range is between 30% and 70% rh. The temperature ranges in Table may not apply to captive wild animals.[5]

Practical Considerations

Animal	Drybulb Temperature F
Mouse, rat, hamster, gerbil, guinea pig	64 to 69
Rabbit	61 to 69
Cat, dog, non-human primate	64 to 84
Farm animals and poultry	61 to 81

Table 1. Recommended drybulb temperatures for common laboratory animals.

More than a few contai labora are curren being planned, and it is important for the designer of the ventilation systems to pay close attention to important details and concepts. For instance, a client once had a BSL 3 facility th was nearing completion and was ready to come online when the supply air syster failed and caused the ceiling to collapse. The combination of a tight building and a exhaust system rated at 9 in. of static pressure was too great for the ceiling suppo system to handle.

Luckily, injury was avoided. Instituting sequences of operation to limit the magnitude of the building negative pressure is important not only to protect the structure and equipment, but also to allow occupants to open doors in order to ex the containment area.

The pressures involved in containment laboratories are typically very high becaus there are often two sets of HEPA filters in series. One inch of water pressure differential will produce 5.2 pounds of pressure per square foot on surfaces such a doors and ceilings. Large doors are common in these laboratories in order to accommodate the passage of carts and racks and for getting biological safety cabinets in and out. A large animal facility, of course, could have very large doors compounding the problem of pressure differentials during abnormal system operation.

During testing of the HVAC systems on a recent BSL 3 project, the supply air system was shut down, and as a result, water sprung out of the water closets and onto the floor. The vent piping for the water closets was the only passageway between the outdoors and the containment space. All other sanitary waste vents were tied into the HEPA-filtered exhaust system. Vents connected to this system require admittance valves or other similar devices to limit the magnitude of the negative pressure. Otherwise, water will not stay in the traps but will immediately pulled back into the sanitary line.

Another factor to consider is the accessibility of ventilation system components, which are preferably located in an interstitial space above the containment area. This space will contain supply and exhaust valves, humidifiers, reheat coils, HEP/ filters, piping, ductwork, and isolation dampers. It is important to provide wide access pathways for maneuvering of carts that may be required to change the HEPA filters and also to locate equipment at optimum elevations for servicing. **ES**

URS is a global leader in engineering and architectural services with over 300 offices worldwide. Professional staff includes planners, engineers, architects, scientists, and construction managers. URS provides technical solutions in numerous sectors such as facilities, air and surface transportation, water, wastewater, industrial, and environmental. The diverse facilities practice encompasses health care, aviation, education, and government. For more information, visit the company website at www.urscorp.com.

References

1 Carl C. Schultz, "Biosafety Wastewater Sterilization," *PM Engineer* 8, no. 11 (November 2002): 40-47.

2 U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Institutes of Health, "Biosafety in Microbiological and Biomedical Laboratories," Fourth Edition (May 1999).

3 Norman T. Berlinger, "Why There Hasn't Been an Anthrax Outbreak," *Invention & Technology* 18, no. 3 (wi 2003).

4 Labconco, "Personnel & Product Protection: A Guide to Biosafety Enclosures," (1998).

5 National Research Council, "Guide for the Care and Use of Laboratory Animals," (1996): 28-32.

Schultz is an engineering project manager with URS Corporation in its Columbus, OH office. He is a graduate of the Ohio State University with a BSME and has 15 years of experience designing mechanical systems for hospitals, laboratories, prisons, data centers, and large office complexes. In addition, he has extensive design experience with central steam, high-temperature hot water, and chilled water plants. He has earned two Technic‹ Excellence Awards during his tenure at URS Corporation. He is a registered professional engineer in over a dozen states and is the author of many technical articles related to HVAC and plumbing system design. Contact hir at carl_schultz@urscorp.com.