Tony Della-Porta knows there is no such thing as a perfect biocontainment facility. He also knows the importance of improving standards, increasing safety, and enhancing staff training at BSL-3 and BSL-4 laboratories throughout the world. The bird flu virus and the SARS virus, both potentially fatal infectious agents handled by high-containment microbiology labs, present a compelling case about the need for more stringent standards.

“We have looked at facilities in numerous countries, including the United States, Australia, New Zealand, Russia and China,” says Della-Porta, managing director of Biosecurity & Biocontainment International Consultants Pty Ltd (Bio2ic) in Geelong, Australia. “The only common thread between the countries is that every facility has issues to address.”

Della-Porta led the World Health Organization (WHO)/Centers for Disease Control (CDC) team that investigated the SARS laboratory infection in Singapore three years ago, and he advised the WHO regarding the 2004 SARS case in Taiwan.

During the investigation of the Singapore SARS incident, numerous lab deficiencies were deemed to be contributing factors to the infection. The problems included laboratory contamination, insufficient record keeping procedures, a lack of security, inadequate staff training, and a host of structural shortcomings such as improper equipment to monitor air pressure differentials. These are precisely the type of problems that Della-Porta believes must be corrected in order to avoid future infections and the release of agents into the community.

Citing the Issues

The lack of a uniform standard for the design, construction, and operation of biocontainment facilities is noticeable throughout the world. In order to properly design and operate a facility, it is critical to understand the type of viruses that will be handled, the specific characteristics of each virus, and the routes of infection that may occur.

Della-Porta believes all countries should create guidelines for certifying labs and monitoring the structural integrity and operating procedures within BSL-3 and BSL-4 labs. The varying designs and biocontainment standards make it very difficult to monitor issues.

Concerns regarding the following issues are noted at numerous facilities around the world:

- Penetrations and finishes
- Adoption of cleanroom principles instead of containment principles
- Lack of definition of containment requirements, such as air pressure, air flow, and changes in air rates
- Safety signage
- Dangerous situations with inert gasses and chemicals
- HEPA filter housings
- Construction materials
- Training and documentation
- Security
- Emergency exits
- Hand wash sinks and gowns

“There should be an openness in discussing safety concerns, reporting incidents, and viewing safety as a culture rather than an imposed obligation,” says Della-Porta.

Confronting the Issues

Penetrations and Finishes

“It does not matter how well a facility is designed if the penetrations are not done properly,” explains Della-Porta. “All services need to be brought in through airtight, sealed penetrations.”

Power, communication, and gas services can be surface-mounted in moduline ducts. Ordinary power points and electrical fittings should not be mounted in walls because they will leak. Instead, special airtight plugs are necessary, unless a moduline fitting is used. Rubber gaskets for doors and pass boxes must be mounted correctly and be airtight when the door is sealed.

“One of the facilities we looked at in China appeared to be perfect on the outside. However, we discovered gaps in the pass box rubber seals where you could feel the air coming through,” says Della-Porta. “What we saw at a facility in Taiwan demonstrates why special care must be taken when retrofitting. We saw electrical fittings where holes were drilled to make penetrations when a retrofit was done and this is totally unsuitable.”
The 2003 SARS laboratory infection in Taiwan stemmed from a lack of management controls on the operation of the laboratory and training of staff. In this case, a principal investigator in a BSL-4 lab used 70 percent ethanol to decontaminate a spill in an isolator chamber. He opened the Class III biological safety cabinet without wearing a respirator and contracted the SARS virus.

Lack of Definition of Containment Requirements

Problems occur when an approach based on cleanroom design is applied to biocontainment. Cleanroom design has a very small pressure differential and mounting the HEPA filters in the walls as terminal filters makes it difficult to decontaminate and test them.

Pressure differentials are extremely important for maintaining containment of infectious diseases. Air pressure reversals were noted in high-security facilities where air was flowing in the wrong direction. There are also concerns about insufficient changes of air, especially since one particular facility had three changes per hour. The inability to control pressure differentials has caused walls to crack and ceilings to collapse. Pressure differentials must be adequate enough to ensure that a reversal of pressures cannot occur and that a sufficient differential is maintained even when the air lock is opened.

“We have also seen instances where the building monitoring systems are unable to respond quickly enough when a supply or exhaust fan fails,” says Della-Porta. “There must be a way to actually stop the fans instantly rather than waiting for the process to go through a computer system. Biocontainment facilities should also use building materials that can withstand at least double negative air pressure.”

The areas of highest risk, such as animal laboratories, should be at the lowest possible pressure to prevent pathogens from escaping into surrounding areas of lower risk. Della-Porta is currently providing consulting services to a BSL-3 lab in Thailand that is handling the avian flu. Pressure in the animal laboratory is at -120 pascals, while the pressure in the labs is at -90 pascals, the decontamination chamber is at -75, the showers are at -30, and the surrounding service corridor is at 0 pascals. Della-Porta explains that 100 pascals is equal to 0.4 inches of water.

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Safety Signage

“I was appalled that even in the most advanced laboratories in the world safety signage was either absent or incorrect,” says Della-Porta. “A lot of these labs have hazardous chemicals and inert gases, yet the proper safety signage is missing.”

There are two types of general signs, including the red, black, and white ones which display the word “Danger” to alert individuals about potentially fatal situations, and specialized signs to warn of microbiological hazards. The specialized signs feature the biohazard symbol inside a triangle and are typically yellow throughout the world, except in the United States where they are orange.

Blue signs signal the need to wear certain personal protective equipment, such as safety glasses, a gown, solid shoes, or hearing protection. Red signs indicate the presence of flammable materials and the location of fire extinguishers. A white circle outlined in red with a diagonal red line denotes that items, such as food or sharp tools, are not permitted in certain areas. Emergency exits, eye wash stations and first aid availability should be visible with the proper signage. Informative signs should also be displayed to provide an emergency telephone number and the name of the laboratory manager.

Inert Gasses and Chemicals

Oxygen levels need to be maintained above 19.5 percent in order to provide a safe environment. Inert gases, such as liquid nitrogen, should only be used in well ventilated areas, which can be difficult to achieve in high-containment facilities.

“Some people only think about liquid nitrogen as a substance that is freezing in properties, but if the oxygen in a room has been replaced with nitrogen, that creates a deadly situation,” says Della-Porta.

One major lab examined by Della-Porta contained a large supply of liquid nitrogen and the two oxygen meters were reading 0.2 percent and zero percent. The meters were inside the lab, instead of on the outside where they could serve as a warning of low oxygen levels. If the meters had been accurate, members of the inspection team would have been overcome by deadly gasses. The meters had actually failed and were never repaired. Oxygen levels must be continually monitored and audible and visible alarms must activate when there is an insufficient supply.

HEPA Filter Housing

Most standards require HEPA filtration of exhaust air from a BSL-3 lab. In the United States, however, this requirement only applies to ABSL-3 and BSL-4; BSL-3 is subject to risk assessment.

“Following a risk assessment, non-aerosol transmitted diseases can be used in U.S. labs that don’t have HEPA filtration, but that is not permitted anywhere else in the world,” says Della-Porta. “I encourage people to build laboratories to the highest level of standard rather than the lowest because if you want to work with avian flu, the facility will not meet the new containment requirements.”

Problems are also common with HEPA filter canisters, which are difficult to decontaminate, and it is difficult to scan test the filters. The location of the canisters is important, as well. They should not be located at floor level and they should not be close to an animal area where they can become contaminated.

HEPA filter canisters must be designed for biological...
work and not the radiochemical industry. They should include ports that can be opened along with a pre-filter. There is an ability to have damper valves for fumigation and ports for injection of substances used for scanning the filters and the ability to scan the surface of the filter rather than doing a complete test. Pinpoint holes in filters are not detected by doing a total test because of the dilution factor. Filters should be scanned after they are put into place to ensure there is no damage.

**Construction Materials**

Sandwich panel walls and ceilings are airtight and can resist pressures up to 400 pascals. They can contain fire-retardant polystyrene or rock wall fillings and the surfaces can be steel, aluminium, enamel, or other suitable coating. They can be pre-coated to suit a facility’s needs. The system for installing and sealing is similar to construction used for cold rooms, and it is easy to retrofit the panels in any building. Glass panels and windows can be mounted in the structure.

“I encourage having as much natural light as possible because it has a positive impact on staff,” says Della-Porta.

**Documentation and Training**

“This seems to be a forgotten thing. Training the staff that will work in facilities and the engineering team that will maintain them is not usually taken into consideration until after facilities are completed,” notes Della-Porta. “The problem is, especially with the engineering staff, that they will have trouble learning how to operate a facility if they have not been part of the entire development process.”

The lack of staff training is cited by Della-Porta as a leading cause of safety-related accidents within labs. Therefore, every lab should create the appropriate, competency-based training standards.

Laboratories must also have suitable record keeping to document specifics about who is working in the facility, the type of research taking place, and the kind of agents being handled.

**Security**

“With the number of facilities coming online, there is a major safety and security risk that we are about to face,” warns Della-Porta.

The lack of proper security is a safety issue in many BSL-3 and BSL-4 labs, prompting the need for a thorough evaluation of security concerns. Biometric devices, such as finger, iris, or palm scanners, should be used for entry into high-risk labs, as well as using access cards. Access to these labs should be properly documented and monitored. In addition, inventory records should be computerized and regularly monitored, long work hours in the labs should be discouraged, and an emergency response plan should be developed to address laboratory incidents.

**Emergency Exits**

Depending on the size of a facility, fire regulations may require alternate emergency exits. Break glass panels may provide such an exit as they are cheaper than airtight doors and they work well. The panels are easy to seal, can be replaced quickly, and break into small pieces (safety glass). The staff can safely exit, and is protected by a fire door.

**Hand Wash Sinks and Gowns**

Hand wash sinks are often placed in the wrong position by being located in the airlock just outside the door going into the lab, rather than being inside the lab. Staff members have to touch the door handle and, therefore, everyone who enters the lab is contaminated. The sink should be located just before the door going out as staff leaves the lab. Light-activated, hands-free sinks are reliable and prevent contamination.

Laboratory coats also present concerns because of the problems of contamination of staff, if there is a biological spill. Back-fastening, solid fronted gowns are strongly recommended because they can readily be removed when contaminated and are not a status symbol to be worn outside the laboratories.

“All of these are issues that need to be addressed and if we don’t address them, we are going to have significant problems in the future,” says Della-Porta.

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**Biography**

Tony Della-Porta, managing director of Biosecurity & Biocontainment International Consultants in Geelong, Australia, is an internationally renowned expert in biosecurity, biocontainment, and biological safety. He led the World Health Organization/Centers for Disease Control team that investigated the SARS laboratory infection in Singapore in 2003, and assisted the WHO with its investigation of the SARS infection case in Taiwan in 2004. Della-Porta has served as a consultant to the health departments in New Zealand and Australia regarding biosecurity needs and laboratory capacity to respond to disease emergencies. He is providing advice to Hong Kong University about the construction and operation of a biocontainment facility to handle high-virulence influenza. He served as a member of the WHO Smallpox Team that recently inspected the CDC in Atlanta and VECTOR in Novosibirsk. Prior to becoming managing director of the consulting firm, he worked at the Australian Animal Health Laboratory from 1972 until 2003.
This report is based on a presentation given by Tony Della-Porta at Tradeline’s International Conference on Biocontainment Facilities in March 2006.

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**Figure 1**
Pressure differentials should ensure that a reversal of pressures cannot occur. The areas of highest risk, such as animal laboratories, should be at the lowest possible pressure to prevent pathogens from escaping into surrounding areas of lower risk. Pressure in the animal laboratory is at -120 pascals. One hundred pascals is equal to 0.4 inches of water. (Image courtesy of Tony Della-Porta.)

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**Figure 2**
HEPA filters in biocontainment facilities are often incorrectly mounted beneath biological safety cabinets. In this instance, air cannot reach the filter in a proper manner. (Photo courtesy of Tony Della-Porta.)

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**Figure 3**
The SARS laboratory infection in Taiwan occurred because the person did not use a vaporized hydrogen peroxide generator like this one to clean up a spill. Instead, he used 70 percent alcohol and put his head in a BSL-3 biological safety cabinet without using a respirator. This room is not airtight because ordinary power points are mounted on the wall. (Photo courtesy of Tony Della-Porta.)