Reducing incidents in BSL-3 and BSL-4 laboratories.

Best practices for improving biosafety during transfers.

Abstract. This paper details how biosafety officers, laboratory owners, architects, laboratory planning teams and purchasing managers can strengthen the safety of BSL-3 and BSL-4 facilities. Historical data from previously reported incidents at research laboratories reveals the need for better solutions to transfers. The paper provides important procedural recommendations to educate BSL-3 and BSL-4 facility managers and occupants about methods to enhance overall biosafety.

When decontamination doesn’t work.

Routine transfer of materials into, out of and within contained areas represents a key challenge for BSL-3 and BSL-4 facilities due to risks attributed to compromised containment. Infectious disease research conducted at BSL-3 and BSL-4 facilities requires the highest degree of containment to prevent occupational hazards. These can impact the facility and adjacent community. The threat associated with incidents of broken containment are particularly dangerous in BSL-4 facilities.

BSL-4 facilities contain ‘headline viruses,’ such as Ebola, Zika, and others, that pose pandemic risks and currently lack treatments and vaccinations. Though various biosafety protocols have been deployed to prevent the number of incidents in research institutes, problems with decontamination continue to pose a risk. Between June and July 2014, the U.S. Centers for Disease Control and Prevention (CDC) reported three biosafety incidents, the first of which was partially due to “a mechanical malfunction in an autoclave.”

After a self-imposed moratorium on the external transfer of infectious agents, intended to provide time for tightened biosafety procedures, the CDC reported another incident which involved the potential transfer of live Ebola virus to a BSL-2 facility in December of the same year. The National Institutes of Health reported the discovery of previously forgotten vials containing smallpox virus that were “in an unauthorized cold storage area.”

Another facility that sets the bar for biological safety is the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) which, in 2015, reported 18 incidents with BSL-3 laboratories and 51 incidents with BSL-4 facilities, one of which involved Potential Biological Exposure (PBE). High-profile biosafety breaches such as these underscore the reality that incidents can happen anywhere.

Accidents at any infectious disease facility awaken concerns about biosafety procedures because pathogen contamination or exposure impacts more than just research. The impact of procedural failings reaches far beyond the laboratory to potentially affect humans, animals and agriculture. The situation with these breach occurrences is, however, not always sufficiently acknowledged in news mass media or brought to the public awareness in its full extent. The importance of biosafety procedures and optimized specification of autoclaves is not sufficiently stressed. Problems are much more widespread than currently perceived.
Eliminating performance malfunction.

Both aging and new equipment can cause problems with containment and decontamination. Older technology often uses manual processes which increase issues with flow control and throughput. The latest technology brings new safety innovations often developed specifically to address previous issues. Aging technology lacks safety features that can protect research and the environment. Manual door sequencing on older models, for example, can compromise operator safety, especially where the lack of door interlocks allows operators to open doors before cycle completion. Such human error releases pathogens that have not been deactivated. Aging technology also requires more frequent maintenance to ensure performance and prevent shutdowns and downtime.

While shutdowns are a huge problem for all research facilities, they can be particularly detrimental to vivariums. Creation of animal waste and the need for decontaminated water and food are continuing processes. The impact of downtime for maintenance can be minimized by a proactive performance process. This proactive method anticipates component wear and tear, leverages statistical information from other globally positioned field installations and benefits from the specification proficiency of authorized technicians. Additionally, predictive performance processes position parts and service assets at a place and time where facility management can orchestrate required services with the lowest impact on throughput, overtime and process interruption.

Regardless of age, autoclaves that are not properly specified at the time of installation compromise personnel and research integrity in cases where animals or specimens are introduced to other pathogens that interfere with the testing of vaccinations and treatments. If technicians lack the necessary training to ensure proper specification, facilities risk purchasing equipment that does not meet the performance requirements of biosafety levels 3 and 4. Autoclaves must be specified within a specific range for the intended application in order to meet compliance. Additionally, when technicians lack the necessary training for proper autoclave specification, research and overall biosafety are compromised.

Importance of community support.

Though new facilities typically have the benefit of the latest technology they still face challenges. Community support and public understanding are essential for the successful construction of BSL-3 and BSL-4 facilities. Without public support, many BSL-3 and BSL-4 facilities do not receive the necessary approval to perform the full range of research they were constructed to manage.

In 1985, the Australian Animal Health Laboratory (AAHL), part of the Commonwealth Scientific and Industrial Research Organisation (CSIRO), opened in Geelong, Victoria Australia. Though the BSL-4 facility was originally intended for diagnosis and vaccine production research on foot and mouth disease (FMD), opposition from local farmers has prevented any research on FMD in the facility. This is analogous to opening a research facility in Africa that is dedicated to fighting the spread of the Ebola virus but never getting the chance to conduct research in the field.

A similar example of the impact community support has on the operation of research facilities is seen with Boston University’s National Emerging Infectious Diseases Laboratory (NEIDL). The university’s medical campus completed construction of the NEIDL facility in fall of 2008. Though the facility received the necessary federal regulatory approval for the BSL-4 laboratory, public controversy has led to litigation that, according to the BU university newspaper has “kept much of the…laboratory space closed.” Opposition has been so strong that it brought about a proposed city ordinance in March 2014 to ban all BSL-4 research in the City of Boston. Though this was rejected by city council two months later, as of 2016 the lab remains closed to BSL-4 operation.

To persuade the public in favor of BSL-3 and BSL-4 facilities, particularly in areas with a higher risk of specific pathogenic outbreaks, it is therefore important for the facility’s senior leadership to openly communicate with and educate the community before the construction of a new facility. At the same time, leadership must do everything possible to reduce or eliminate the chance of incidents. Biosafety can be improved through choosing an autoclave properly designed for the sterilization of materials into, out of and within the containment area.
What to look for in an autoclave.

BSL-3 and BSL-4 facilities are required to use autoclaves, or another method of deactivation, in standard operating procedures to ensure complete decontamination of materials and equipment. According to the CDC “a method for decontaminating all laboratory wastes should be available in the facility, preferably within the laboratory.” Facilities that operate at the BSL-4 level must additionally use double door or “pass-through” autoclaves for transfer of materials into the laboratory when not brought in through the change room.

The CDC further mandates that these doors must be “interlocked in a manner that prevents opening of the outer door unless the autoclave or fumigation chamber has been operated through a decontamination cycle.” The use of door interlocks for flow control is an essential method for ensuring the complete decontamination of materials and preventing laboratory incidents.

Both new and existing facilities should be equipped with a double door autoclave system designed to anticipate all eventualities and account for procedures that will further reduce the chance of incidents. Many factors must be considered in the earliest planning stages of new facilities in order to ensure long term biosafety. An experienced architectural and laboratory planning team must weigh costs and benefits of designing a pass-through transfer system from the ground up. Solutions might include reducing some necessary design considerations through purchasing pass-through autoclaves that have been specifically designed and field-tested for years to comply with all containment objectives.

Key autoclave features. The most effective sterilizer models in both BSL-3 and BSL-4 facilities are those with a pass-through configuration that provides flow control for material transfers between containment areas. In BSL-3 and BSL-4 zones, sterilizers must have a containment barrier or biological seal integrated into the design of the installation to create a built-in transfer port between areas of containment. This seal must be tested, verified and monitored to ensure operator and environmental safety and eliminate cross contamination within the facility.

Sterilizers with integrated contamination control barriers or biological seals must meet defined criteria within the requirements for BSL-3 and BSL-4 facilities. Pass-through sterilizer designs provide a gas tight seal for material sterilization and transfer. Gas tight seals eliminate cross contamination and protect processes and operators. For most applications, moist heat is the most effective deactivation method available. When materials sensitive to moist heat need to be transferred within the lab, pass-through sterilizers are particularly useful because they can be adapted under the necessary procedures and processes to allow pass-through without a sterilization cycle. This facilitates the transportation of live animals into other containment areas. Autoclaves can also be adapted for use with hydrogen peroxide gas generators for the transfer of electronics or the bio-decontamination of samples or other items using H₂O₂ vapor.

The value of a brand. When purchased on the open market, a trusted brand with a documented performance history will expedite the acquisition process and offer the benefits of consultative solutions for containment and transfer developed throughout the global biological safety community.

For facilities that specialize in pathogens or contaminated materials that cannot be resolved by existing autoclave models, working with an experienced, global company offers significant advantages. An experienced consultative supplier can facilitate the innovation of new autoclave designs that address application specific needs or new processes not available on the market. Such consultative partnerships are mutually beneficial in bringing forth technological innovations while encouraging valuable support from the general public as the history of performance can be leveraged to demonstrate biosafety.

The reputation of the selected autoclave manufacturer is critical in the efforts to assure a community-wide understanding of processes and safety measures to protect personnel and the environment. Sterilizer companies must have a documented portfolio of successful installations related to new construction, retrofit, standard product installation and custom modified products engineered for highly specific applications.

Equipment manufacturers must offer the benefit of wide-ranging research and development experience. Professionals should conduct extensive testing and provide continued support services after installation and commissioning. To ensure timely maintenance, it is important to select a manufacturing company with a global reach and trained technicians who are in place for quick response. A good autoclave supplier should also provide calibration assistance as part of their continuing services after the initial sale as this is a critical factor in compliance requirements. Selecting the right autoclave for a specific application is the first step to ensuring proper performance but it is not the only consideration.
Fixing process inefficiencies in performance testing.

It is equally important to include frequent performance testing as a part of regular laboratory procedures to guarantee continued optimum performance. While nearly all facilities conduct daily leak tests, many do not regularly assess the overall autoclave performance. Frequent performance testing is the only way to measure the level of organism inactivation or monitor chemical indicators to verify time and temperature. Such tests are vital methods of ensuring desired decontamination or sterilization outcomes. While tests may add additional costs, they provide a measurable return on investment and are far less costly than incidents caused by inadequate deactivation.

The performance of laboratory personnel is also a critical component of the efficacy of sterilization procedures. When the autoclave is performing correctly, incomplete decontamination can still occur as a result of improper loading through human error. While Bowie-Dick tests ensure the effective removal of air from products and the autoclave chamber itself, improperly packed loads can create air pockets that impede the complete removal of air. Because laboratory waste is usually packaged in autoclave bags, issues with insufficient deactivation can compound when time and temperature requirements are not met.

The takeaway.

Pass-through autoclaves integrated in the facility with a biocontainment barrier ensure safe transfer of materials into and out of containment zones, proper flow control and optimum throughput within the facility. Properly designed transfer control ensures a one-way process flow and guarantees that both doors on a pass-through sterilizer are never opened at once. This limits the possibility of material and environmental contamination from the release of pathogens still present in an incomplete sterilization cycle.

A pass-through autoclave greatly reduces the risk associated with transfers of laboratory materials in BSL-3 and BSL-4 facilities, but only when it is of proper design and quality. It is important to understand, however, that an effective autoclave is only part of the solution. It is equally important to establish a plan of predictive performance testing, manage all sources of contamination and follow a proper maintenance schedule.

Ultimately, facility owners are responsible for overall risk assessments. Important factors associated with the use of autoclaves as contamination barriers must be considered when developing a laboratory management plan to ensure the most effective and efficient transfers. Risk assessment and risk management planning can help BSL-3 and BSL-4 facilities more effectively control the safe flow of materials within containment areas.

When making purchasing decisions the history of product and manufacturer performance must be considered. The manufacturer must also offer a track record of success, support training, best practices and continuing education. Getinge GEB Biocontainment sterilizers were specifically developed for U.S. government use as a result of anthrax cases in 2001. Getinge has over 100 years of experience designing high-performance life science equipment for standard and custom applications. For information on Getinge’s GEB Biocontainment Sterilizers visit http://www.getinge.com/life-science/products-within/sterilization-equipment/geb-steam-sterilizers/.

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