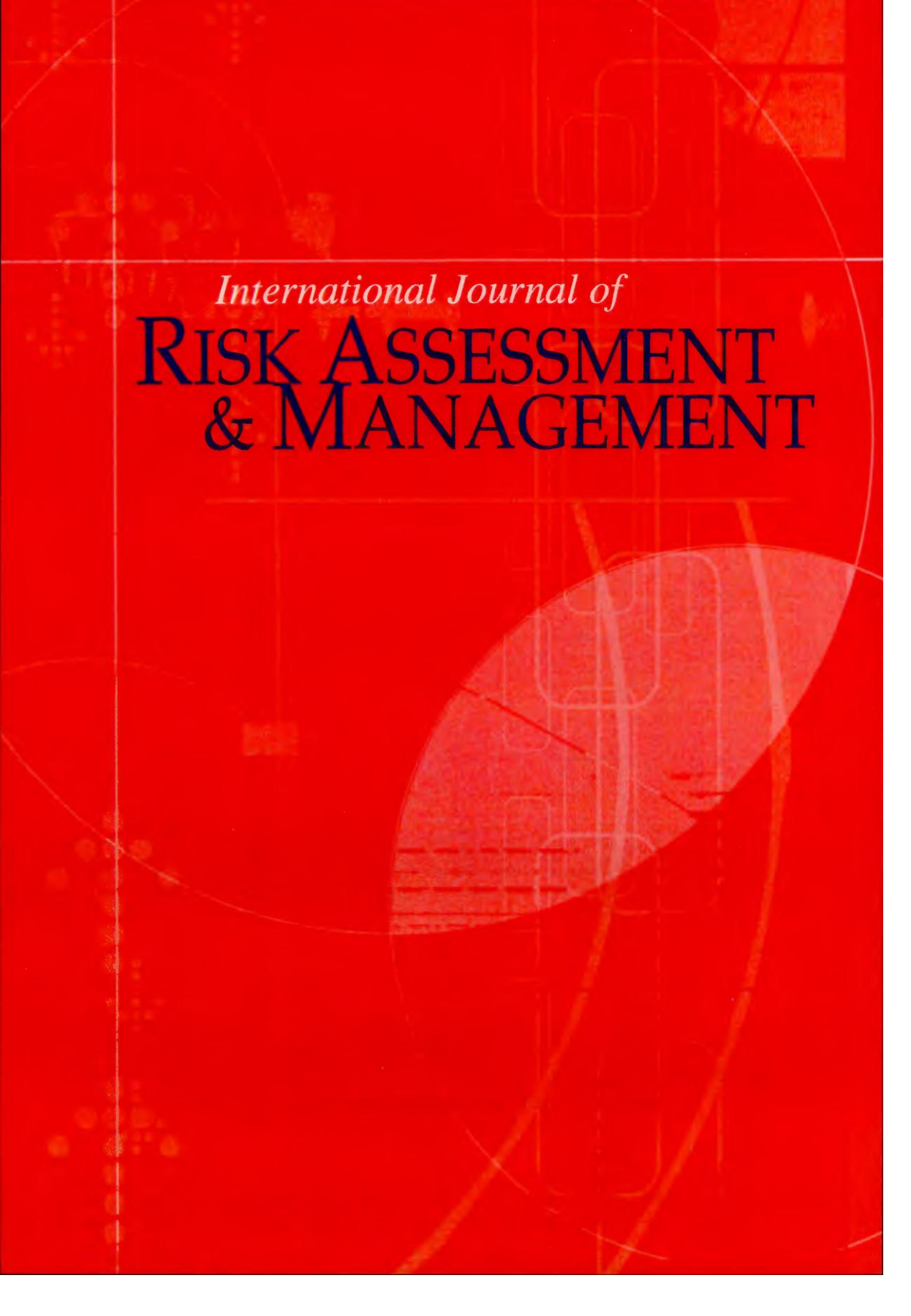
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Submitted Paper

Health and safety risk assessment methodology to calculate reverse airflow tolerance in a biosafety level 3 (BSL-3) or airborne infection isolation room (AII) environment

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Abstract: A novel methodology is proposed to calculate how much air displacement and contaminant leakage might occur during a power outage that may result in a momentary positive pressure reversal in a BSL-3 facility. Note that the ultimate goal in design and operation of a BSL-3 facility is to achieve sustained directional airflow such that under failure conditions the airflow will not be reversed. The proposed methodology should be applied *when and only when* all other measures to achieve zero tolerance have been ruled out. Only after determining that zero tolerance cannot be achieved for the BSL-3 facility in question should the model be employed to perform a health and safety risk assessment to determine the reverse airflow tolerance. The methodology is applicable to other room types, such as airborne infection isolation rooms, that use sustained differential air pressure as one means to prevent particle migration across a boundary.

Keywords: health and safety; risk assessment; reverse airflow; biosafety level; BSL-3; airborne infection isolation room; AII.

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Biographical notes: Farhad Memarzadeh is the Director of the Division of Technical Resources (DTR) at the National Institutes of Health (NIH). He has authored four books and written over 50 scientific research and technical papers in peer-reviewed journals. He is an International Consultant on biocontainment and medical research laboratories throughout the world. He has been a Guest and Keynote Speaker at over 50 international scientific and engineering conferences and symposia. He has been the Principal Investigator on numerous groundbreaking research studies. He pioneered NIHs Bio-Environmental Engineering Research Program that has set numerous national and international standards for better indoor air quality.

1 Introduction

In this paper, a novel methodology is proposed to calculate how much air displacement and contaminant leakage might occur during a power outage that may result in a momentary positive pressure reversal in a biosafety level 3 (BSL-3) facility. Note that the ultimate goal in design and operation of a BSL-3 facility is to achieve sustained directional airflow such that under failure conditions the airflow will not be reversed. The proposed methodology should be applied when and only when all other measures to achieve zero tolerance have been ruled out. Only after determining that zero tolerance cannot be achieved for the BSL-3 facility in question should the model be employed to perform a health and safety risk assessment to determine the reverse airflow tolerance. The methodology can be used to quantify contaminant migration across a boundary for other room types, such as airborne infection isolation rooms (AIIs) and patient protective environment rooms (PPEs), that use sustained differential air pressure as one means to prevent infectious particle transmission.

The NIH/CDC *BMBL 5th Edition* (2007) and *NIH Design Requirements Manual* (2008, NIH DRM) do not require that a BSL-3 lab have a separate air supply system. However, the BMBL 5th ed. states that the ventilation system in a BSL-3 lab or animal facility "must provide sustained directional airflow by drawing air into the laboratory from 'clean' areas toward 'potentially contaminated areas'. The laboratory shall be designed such that under failure conditions the airflow will not be reversed". This is referred to as 'zero tolerance reverse airflow' and is the gold standard for BSL-3 and ABSL-3 design. However, compliance with the BMBL is only required for institutions that are funded by the federal government. For all other academic and private institutions, the BMBL may serve merely as a guideline.

BSL-3 containment facilities are generally designed using concepts of primary and secondary barriers and principles of biosafety as defined in the BMBL 5th ed. and using design, commissioning and BSL-3 certification guidelines as defined in the 2008 NIH DRM. BSL-3 and ABSL-3 laboratories are the most difficult and complex biocontainment facilities to design and operate because of the wide range of pathogens that may be used in the lab and the range of design criteria that are recommended but not always required. Containment design is relatively straight forward for BSL-1, -2 and -4 facilities. It is not nearly as straight forward for BSL-3 facilities. Although, BSL-3 containment can be managed by engineering controls and operating and maintenance procedures, incorporating flexibility into a BSL-3 design at the front end of the process is more difficult. Not only does cost become a factor but future use must be considered as well. If one compares containment guidelines from various countries/agencies (e.g., Canada's *The Laboratory Biosafety Guidelines*, 2004; *Australian/New Zealand's Standard™ Safety in Laboratories Part 3*; *World Health Organization's Laboratory Biosafety Manual*, 2004; *NIH Design Requirements Manual*, 2008), one finds that there is a broad range of recommendations versus requirements for BSL-3. Della-Porta (2006), who led the World Health Organization (WHO)/Center for Disease Control (CDC) team that investigated the SARS laboratory infection in Singapore and has advised the WHO regarding the 2004 SARS case in Taiwan, notes that there are a lack of uniform standards for the design, construction and operation of biocontainment facilities worldwide. What might be a recommendation for one facility becomes a requirement for another depending on the interpretation of the facility usage and the projected needs. Some examples include inclusion of a pass through autoclave within the BSL-3 suite and a shower if shower-out

might be an eventuality. However, the importance and emphasis on operational and maintenance protocols to provide protection for the occupants and the environment cannot be underestimated.

Because of the scarcity of uniform standards and measurable tests for containment, many BSL-3 and ABSL-3 facilities have system and operational deficiencies that may be contributing factors to infection. These include air pressure reversals, insufficient air changes stack exhaust issues, lack of standard operating procedures for operations and maintenance, and a lack of training appropriate for the level of biocontainment used in the facility.

In order to control 'containment facility' costs and meet health and safety requirements, a rigorous risk based assessment should be performed by highly experienced and qualified experts (including occupational health and safety personnel, operations and maintenance personnel, engineers and users). The occupational health and safety officials then can use the risk assessment results to determine the extent of the safety features that need to be included in the lab design, keeping in mind that strict compliance to establish SOPs used by lab personnel provide an important level of control to pathogen exposure and potentially unsafe situations. Knowledgeable professionals performing the risk assessment must consider how the lab will be used and the performance specifications of the building control systems. Some factors to consider in the risk assessment include the pathogenicity of the organism, concentration of the agent and the infectious dose, the containment equipment, the animal models to be used; aerosol particle mechanics, and scrutiny of egress SOPs. On site observations strongly suggest that often the reason a biocontainment facility does not perform as it is intended is because the engineers/designers did not take into account the integration of the science, the agents, the user needs, possible future facility uses and operational and maintenance requirements in early and ongoing design. It is important to ensure system integration to the extent possible in both new and renovated facilities. Taking the design elements as an integrated whole and having ongoing dialogue with the users has the potential of reducing problems related to poor design.

Aerosolised airborne infectious pathogens and allergens created during laboratory procedures and animal handling are the primary health concern in a BSL-3/ABSL-3 laboratory or animal space. Typically, healthcare facilities are not designed with primary and secondary containment protections to the extent that they are used in a biocontainment lab. There is strong and sufficient evidence to demonstrate the association between ventilation, air movements in buildings and the transmission/spread of infectious diseases such as measles, tuberculosis, chickenpox, influenza, smallpox and SARS (Tang et al., 2005). Tang reported at least one secondary case of chickenpox arising from infectious air being transported out of an isolation room containing a patient with severe chickenpox via the opening of a hinged door. Airborne infectious particles may be generated by occupants who may be unaware that they are carrying an infectious agent that has the potential to spread throughout the facility. When the engineering systems that prevent contaminant leakage under normal operating conditions breakdown, it is conceivable that airborne infectious particles will leak into other building areas. Designers, owners and occupants need practical methodologies that can be applied to real life settings and can assist them in performing risk assessments to help design safer facilities.

While it may be permissible for a laboratory to be shut down in the event of a systems failure, the '*Guide for the Care and Use of Laboratory Animals*' (1996) requires that animal facilities remain operational at a reduced level in order to be accredited by AAALAC. Thus, it is highly recommended that a new facility have independent systems for BSL-3 areas as well as N+1 capacity for redundant supply and exhaust systems for containment laboratories and for animal welfare. Although typically, only the controls are on an uninterruptible power system (UPS) in a BSL-3 lab, it is highly recommended that supply and exhaust air fans also be connected to an emergency power network. Providing an UPS may be considered to bridge the gap from normal power to emergency power to mitigate the chance of pressure loss during a transfer from normal to emergency power and vice versa.

Contaminant leakage from differentially pressurised rooms is controlled by adjusting the HVAC system to provide the proper directional airflow under normal operating conditions. Proper directional airflow prevents aerosol contaminants from escaping into adjacent spaces through door gaps, door movement or normal entry and exit from the containment room, specifically from a BSL-3 or AII. However, if there is a mechanical or electrical system failure, the existing back-up systems may not be able to transition immediately from normal power to emergency generator power quickly enough to prevent reverse airflow. Click (2008), in a discussion on laboratory commissioning, notes that static pressure of the building shell can be affected when a laboratory loses power. If the air handling units are not backed up by a generator, the exhaust fans continue to remove air from the hoods and related lab space. In just a matter of minutes, the building is likely to become negatively pressurised, making it difficult for people to leave the building. Even when the air handling units are backed up by an emergency generator, there may be a 20 to 30 second lag as the building transitions from normal power to generator power. This lag may result in loss of control while the automated system restarts and assumes control. It is particularly important to consider the risk of an infectious agent being released from the containment zone during this critical lag time. Each BSL-3 laboratory is unique and has its own operational requirements. Therefore, the values needed to maintain the desired pressure differentials may vary by facility. Also, during commissioning of a facility it may take months to meet the BMBL requirement for zero tolerance.

Historically, contaminant leakage from differentially pressurised areas through door gaps or as the result of movement through an open door has been quantified using empirical methodologies such as tracer gas/smoke tests in specially designed test rooms. A NIOSH funded study used a tracer gas in a simulated differentially pressurised setting to examine the magnitude of air volume migration (AVM) when a swinging door was opened and closed, when a sliding door was opened and closed and when a mannequin was passed through either of the doorways (Hayden et al., 1998). Hayden noted that there are currently no documented data available that demonstrate the level of AVM from a negative-pressure isolation room but that by knowing the level of AVM during entry/exit through a doorway where there can be airborne contaminant migration across the boundary, an assessment of the risk of transmission of airborne infectious disease is made possible. The results of the Hayden study concluded that the measured flow differential was the only statistically significant factor in determining the level of AVM in the tested scenarios. It is worth pointing out that there is some evidence that a sliding door open and close cycle causes less AVM than a swinging door open and close cycle. Therefore, Hayden and others (Tang et al., 2005) have suggested that sliding doors may be a

reasonable design option in some circumstances based on a risk assessment. Although, sliding doors pose cleaning and operational problems in any biosafety level laboratory or animal facility, they should not be entirely ruled out as the technology improves. Also, their use may be more practical and applicable to some patient care facilities than to a laboratory.

2 Effect of people movement on AVM

The effect of movement of people on airflow produces a similar effect to door opening, but is more complex and difficult to calculate. The velocity of the layer of air closest to the body is comparable to a person's walking speed.

As a person moves at speed U, there is a volume flux, F, which is approximately equal to:

$$F = CAU / 2$$

where

C is the drag coefficient for a body (approximately equal to one)

A is the cross sectional area of the body (for a person about 1.7 m tall, 0.3 m wide and 0.15 m deep; $A = 1.7 \times 0.3 = 0.51$ m^2)

U is velocity.

In addition, there is a wake bubble of volume ξV, where V is the volume of the body. In this example, $V = 1.7 \times 0.3 \times 0.15 = 0.08$ m^3 (i.e., a person of 76.5 kg, since 1 m^3 = 100 × 100 × 100 cm^3 = 1,000 litre of water, assuming human body density has an average density equal to that of water)

Per Bush and Eames (1998), $\xi = 1$ to $3f$ or a person walking at speed

$U = 1$ m/s (2.2 MPH).

For a person walking at speed $U = 1$ m/s (2.2 MPH).

This corresponds to $F = 1 \times 0.51 \times 1/2 = 0.255$ m^3 = 255 L/s (540 CFM), with an attached wake of:

$$\xi V = 0.0765 - 0.2295 \text{ m}^3 = 76 \text{ to } 230 \text{ L/s (160 to 480 CFM)}$$

Thus, movement of people in a room plays a significant part in disturbing the flow and also in transporting infected air from one place to another (Hayden et al., 1998).

3 The causes of pressure reversal

Airflow and the associated particulate and aerosol contaminants carried along with the air current are dependent on differential pressure. Airflow moves from a high pressure region to a low pressure region. In BSL-3 labs, this is highly significant as the airflow from an animal holding room containing infected animals to a neighbouring room containing non-infected animals, e.g., can mean leakage of biohazardous agents. Schultz

(2007) notes that some designers develop unnecessary and elaborate control schemes. The approach may be to limit positive pressurisation by putting in redundant exhaust fans but failing to provide a feedback mechanism in the control system to shut the supply system off in the event of total loss of exhaust. Failure of both the primary and back up exhaust fan, the blockage of a biological safety cabinet either through clogged filters or by loose debris being pulled into the cabinet or onto the sash opening, or the closing of an exhaust valve or damper to the lab either through mechanical or control failure or through operator error can each cause total loss of exhaust flow.

Design philosophy and intent of any BSL-3 and ABSL-3 should be based on the specific scenarios of 'failure conditions' with respect to reverse pressurisation. The boundaries or limits of failure conditions are typically defined as part of the risk assessment based on multiple factors which include the biological agents to be used in the facility and the flexibility required for anticipated future use. Once again, the importance of conducting a risk assessment cannot be over emphasised. The value of an initial risk assessment, as well as ongoing iterations of the risk assessment as conditions or needs evolve, will pay off in terms of cost and safety benefits throughout the life of the facility.

BSL-3 HVAC systems are designed to have interlocking supply and exhaust fans. This does not address 'failure conditions' of local elements. Given even moderate interpretations of 'failure conditions', automated fast acting dampers on the BSL-3 supply, at the very least, would have to be installed with local hard wired differential pressure limit controls. If the system is not designed correctly, every time anteroom doors are opened it is conceivable to create a hyper-negative condition until the supply/exhausts can react synchronically. Scenarios such as this emphasise the need for a definition of 'failure conditions' specific to the facility and/or some exceptions or clarifications on the duration of the 'failure'. Assessing and maintaining envelope integrity is a key component of the successful operation of a building since the building envelope is a critical component of the building's HVAC systems. The integrity of the building envelope can have a major impact on the performance of HVAC systems and equipment. Conversely, the stresses caused by rapid pressure changes can adversely affect the building envelope. By failing to account for sudden shifts in pressurisation, the building structure may be damaged and indoor air quality may be compromised. Thus, the building must be designed to withstand the failure conditions as defined in the risk assessment.

Under normal operating conditions, offsets typically provided in a BSL-3 laboratory environment are not sufficient to prohibit bipolar flow caused by temperature differences when doors are opened. Offsets are unable to prevent the air exchange due to the turbulence and flow created by the motion of the door and the occupant. Empirical data show that air is exchanged across a typical anteroom or air lock even when doors are not opened simultaneously.

During a power failure where both supply and exhaust systems lose power at the same time, several system operations may occur that can result in a positive pressure reversal in the affected spaces. For example, when power is lost, fan wheel momentum cannot be controlled (free-wheeling). Depending on the relative momentum of the supply and exhaust fans in the system, the supply pressure may decay slower causing a propensity for driving the affected negative area to go positive. Although, quick closing supply fan isolation dampers with slow closing or fail open exhaust fan isolation dampers can help mitigate or reverse this event and keep the room or suite negative until fans have stopped, this can also cause excess pressure on the systems and zones. These excess

pressures can lead to duct and/or containment barrier structural failure which could lead to complete and extended breaches in the containment barrier. The same free-wheeling issue applies to adjacent spaces. If the adjacent spaces are significantly larger than the BSL-3 space, have a slower pressure decay and result in a pulse negative in the adjacent spaces, this can pull the BSL-3 suite positive with respect to the cleaner adjacent area. Providing dampers with controllable closing rates can help tune the pressure pulse of the adjoining spaces to help mitigate this event. However, costs can become excessive and projects can be delayed if zero tolerance criteria are applied to all BSL-3 containment facilities.

In the interval when the power is off and thus the fans are off, the minor pressure gradients that can be caused due to stack affect cannot be controlled. Also, wind currents can cause minor pressure gradients throughout the space. During component failure, if exhaust fans fail there will be a momentary reduction in exhaust static pressure. Experience shows that if at least one redundant fan is running when another fails, tracking control loops can be tuned to avert airflow reversal during this event depending on the magnitude of the drop. However, tuning loops too fast to account for infrequent occurrences is counter-productive, as it makes the airflow control system less stable during normally occurring disturbances in the airflow pressure balance such as duct static pressure control, doors opening, etc. Although distress or lockdown modes can be implemented to prohibit airflow reversals, setting them too tight to account for infrequent occurrences is counter-productive as it can become a nuisance to the investigators, and cause undue stresses on the facility and its components, and cause unsafe conditions for the occupants.

If the exhaust system fails, pressure will fall rapidly and continue to zero. Averting this dramatic pressure drop in time to avoid any flow reversal will typically require both tuning and distress mode set points that are counterproductive during normal operation. Additionally, adjacent space system/component failure can cause airflow reversals. For instance, a neighbouring vivarium supply system failure can cause a hyper-negative condition in the vivarium which can lead to a positive pressure in the BSL-3 lab. Even an adjacent BSL-3 zone, going into a lock down mode causing a hyper-negative condition can cause an adjacent zone to go positive.

Other scenarios that pose challenges in maintaining directional air flow include:

- switching from an operating lower priority system to back up a failed higher priority system (or similarly switching over a common backup fan from one system to another)
- local flow or pressure sensor failures
- controller failures
- damper failures.

These can cause significant dynamic upsets to the flow conditions. Even if they fail to maintain a negative in one area, it can result in a positive in another area depending on the configuration. Pressure reversal can occur during start up or return to normal after failure. Supply overshoot can occur when the exhaust, which always starts first, can causes some degree of excess negative in the space, at which point the supply is introduced into terminals that are ‘wound up’ trying to track the leading supply or maintain a more moderate space pressure. This is a common cause of a short pulse

positive in the BSL-3 space as the control loops react. The same is true as an adjacent zone starts (exhaust first) and potentially causes an excess negative until the supply starts. Again, the excess negative of an adjacent space can pull the BSL-3 positive.

The question is not necessarily whether it is possible to prohibit airflow reversal but whether and at what cost and project delay it is justified to get to a lower level of airflow reversal. Key considerations relative to this are:

- What is the air exchange due to egress that will occur anyway?
- What is the probability of the event?

It is imperative that the risk assessment evaluate the program needs and address these questions closely. The assessment must weigh the need for program flexibility and health and safety concerns against the efficacy of spending tens of thousands of dollars and/or delaying a project by making changes to go from an excursion that is commensurate with a person exiting. There is no doubt that to achieve zero tolerance in a BSL-3 facility when, under failure conditions, the airflow will not be reversed, as the BMBL 5th ed. states, has costs associated with it. These costs will affect both budget and project delivery due to design, construction, commissioning, and activation activities that must account for the complexity and interdependence of the systems.

4 Estimation of air leakage due to positive pressure

The incidence of airborne-transmitted infectious diseases in the indoor environment is dependent upon at least eight factors:

1 number of infection aerosol particles

2 number of susceptible hosts

3 length of exposure

4 ventilation rate

5 settling rate of contaminated aerosols

6 survival of pathogens attached to aerosol

7 temperature

8 humidity.

The proposed methodology assumes a worst case scenario combination of these factors in a BSL-3 area in order to demonstrate two facts. First, leakage will occur in the described pressure reversal scenarios because even when controls are backed up by an emergency generator there is a lag as the building transitions from normal power to generator power if there is no uninterruptible power source (Click, 2008). Second, as the proposed model demonstrates, there is greater contaminant leakage from the BSL-3 lab into the corridor when a door is opened and closed than there is through the door gap during the interval before power is restored. Thus, even if the contaminant concentration is considerably less than 100%, or under worst case scenario conditions as defined above, and there is not uniform mixing of particles in the air, there is still the potential for AVM and contaminant leakage across the door gap or when the door is opened and people pass

through. The presence of airborne contaminants is not limited to a catastrophic spill at the time of the power failure. Airborne contaminants may be generated and spread at the time of failure by many other factors that might seem less significant than a catastrophic spill but would be more likely in a real life situation. These include the processing of tissue culture or opening a lyophilised sample in the biosafety cabinet at the time of system failure; by animal transfers that are made at the time of the power outage, or by manipulation of chemicals in a fume hood as just a few examples.

If zero tolerance reverse airflow cannot be achieved in a BSL-3 facility, an acceptable window of tolerance that is specific to the design and use of the facility and determined by occupational health and safety experts, may be calculated using this methodology as part of the risk assessment for a BSL-3 lab or ABSL-3 animal facility. The methodology may also be used to quantify contaminant migration across a boundary for other room types, such as AIIs and PPEs, that use sustained differential air pressure as one means to prevent infectious particle transmission. Leakage from temporary pressure reversal should be carefully monitored and kept in perspective. Consideration has to be given to the existing conditions of the facility including its age; whether routine re-commissioning and recertification is performed and compliance met and whether ongoing risk assessments for new agents and/or conditions have been performed.

Technically, a positively pressurised room is analogous to an inflated balloon. Imagine deflating a balloon using your fingers as the valve at the balloon neck. When you release the neck of the balloon, the pressure is decreased and eventually reaches environmental pressure. The time it takes to 'deflate' a balloon depends on how tightly your fingers are holding the 'neck'. In the BSL-3 negatively pressurised room, we know that the room is not air tight. There may be leakage of air and contaminant through door gaps or other possible leakage points in the BSL-3 room. But how well is it sealed under normal operating conditions?

Let's start with how to define the tightness of a room. Under the normal operating condition, the room is negatively pressurised by a higher exhaust and lower supply of air. The relationship between the pressure differential and airflow differential is:

$$Q = f(\Delta P)^n \tag{1}$$

where

Q volume flow rate (cfm)

f flow coefficient (cfm/inH_2On)

ΔP pressure difference (inH_2O)

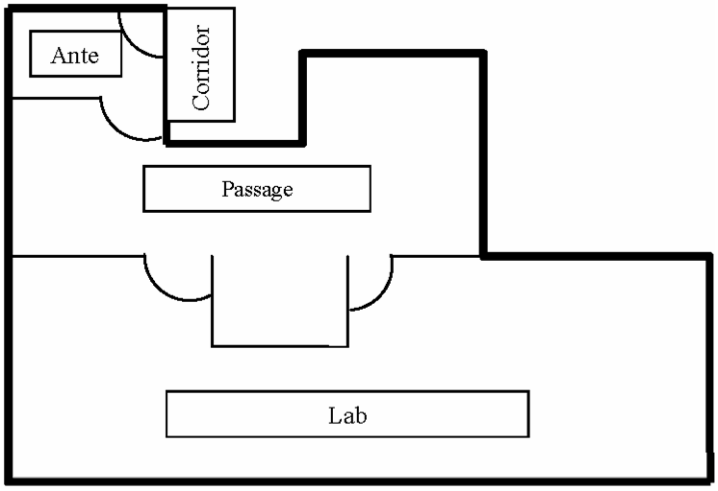
n flow exponent.

n is a number that also controls the speed of the pressure release. For extremely tight rooms, such as BSL-4 labs, $n = 1$ is common. However, for most other rooms, we will assume $n = 0.5$ for illustrative purposes.

For a given ΔP, the smaller the f value, the less air, therefore the 'tighter' the room (or balloon). So f is a characteristic value of the room and may be determined by plugging in operating room pressure and flow differential for the facility being evaluated. When the room pressure goes positive, the same equation applies, therefore, at any given moment, if we know ΔP, we can easily calculate Q.

For this example, ABSL-3 lab suite is conceptually divided into three 'sections': an animal holding room, i.e., the lab; an intermediate space such as a 'passage or equipment room' and an anteroom that leads to the corridor, as shown below.

Figure 1 A diagrammatic ABSL-3 lab



The pressure of each space is maintained negative to the neighbouring room under normal operating conditions, i.e., $P_{o,lab} < P_{o,pass} < P_{o,ante}$.

Using equation (1), *f* values for each room can be determined as:

$$f_{lab} = \frac{Q_{o,lab}}{\left(P_{o,pass} - P_{o,lab}\right)^n} \tag{2a}$$

$$f_{pass} = \frac{Q_{o,pass}}{\left(P_{o,ante} - P_{o,pass}\right)^n} \tag{2b}$$

$$f_{ante} = \frac{Q_{o,ante}}{\left(P_{o,corr} - P_{o,ante}\right)^n} \tag{2c}$$

Right after the pressure reversal, air starts to leak through the door gap and other leakage areas in the lab to the passage, from the passage to the anteroom and from anteroom to the corridor – as if three balloons were somehow put together in series. At any given time *t*:

$$Q_{lab} = c_{lab}\left(P_{lab} - P_{pass}\right)^n \tag{3a}$$

$$Q_{pass} = c_{pass}\left(P_{pass} - P_{ante}\right)^n \tag{3b}$$

$$Q_{ante} = c_{ante}\left(P_{ante} - P_{corr}\right)^n \tag{3c}$$

The amount of contaminant leaked to the next room is simply:

$$C_{leak,\,lab} = c_{lab} Q_{lab} \Delta t \tag{4a}$$

$$C_{leak,\,pass} = c_{pass} Q_{pass} \Delta t \tag{4b}$$

$$C_{leak,\,ante} = c_{ante} Q_{ante} \Delta t \tag{4c}$$

The concentration of each room also changed according to:

$$c_{lab,t+\Delta t} = c_{lab,t} - \frac{C_{leak,lab}}{V_{lab}} \tag{5a}$$

$$c_{pass,t+\Delta t} = c_{pass,t} - \frac{C_{leak,pass}}{V_{pass}} \tag{5b}$$

$$c_{ante,t+\Delta t} = c_{ante,t} - \frac{C_{leak,ante}}{V_{ante}} \tag{5c}$$

During this process, each room's pressure changed because as the mass of the air leaves the room, eventually, all the rooms are deflated and the pressure of all the rooms becomes the pressure of the outside corridor. In other words, pressure equilibrium is achieved between the rooms. Therefore, at any given moment, the mass of room air changes according to:

$$M_{lab,\,t+\Delta t} = M_{lab,t} - \Delta t \rho_{air} Q_{lab} \tag{6a}$$

$$M_{pass,t+\Delta t} = M_{pass,t} - \Delta t \rho_{air} Q_{pass} \tag{6b}$$

$$M_{ante,t+\Delta t} = M_{ante,t} - \Delta t \rho_{air} Q_{ante} \tag{6c}$$

The pressure of each room is directly linked to the mass by the ideal gas law:

$$P_{lab} = \frac{M_{lab}}{V_{lab}} R_{air} T_{lab} \tag{7a}$$

$$P_{pass} = \frac{M_{pass}}{V_{pass}} R_{air} T_{lab} \tag{7b}$$

$$P_{ante} = \frac{M_{ante}}{V_{ante}} R_{air} T_{lab} \tag{7c}$$

Putting all the pieces together, we can now calculate the air leakage due to a pressure reversal in a typical BSL-3 suite like this:

Given conditions: contaminant concentration of each room *c*, initial pressure of each room *P*, and small Δt:

1 determine f coefficient of each room using operating condition and equation (2)

2 use equation (7) to calculate initial mass of each room

3 use equation (3) to calculate flow rate leaked to each room

4 use equation (4) to calculate contaminant leaked to each room

5 use equation (5) to update concentration in each room

6 use equation (6) to update mass in each room

7 use equation (7) to update pressure in each room

8 repeat steps 2–8 until the pressure of all rooms reaches equilibrium to the corridor.

Take the above suite s an example, the room volumes are: lab: 6,840 ft^3; passage: 3,744 ft^3; anteroom: 1,080 ft^3.

Figure 2 A diagrammatic ABSL-3 Lab

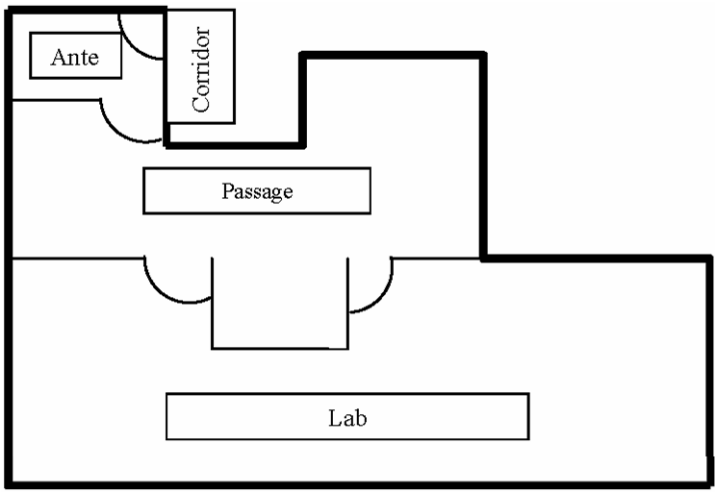


Table 1 Room operating conditions before and immediately following power outage

Input	*BSL-3 → equipment room*	*Equipment room-anteroom*	*Anteroom → corridor*
Room operating condition			
Room volume	6,840 ft^3	3,744 ft^3	1,080 ft^3
Pressure difference	–0.09 inH_2O	–0.05 inH_2O	–0.03 inH_2O
Flow rate through door gap	110 cfm	110 cfm	110 cfm
Room temperature	74 F	74 F	74 F
Room tightness			
Pressure exponent	0.5	0.5	0.5
Room condition right after AC shut down			
Initial volume fraction of contaminant	100%	0%	0%
Pressure differential to next room	0.1 inH_2O	0.2 inH_2O	0.1 inH_2O
Elapsed time after power outage *t*	60 s		

Assuming normal operating conditions are:

$$P_{o,lab} - P_{o,\,pass} : -0.09 \text{ inH}_2\text{O}$$

$$P_{o,\,pass} - P_{o,ante} : -0.05 \text{ inH}_2\text{O}$$

$$P_{o,ante} - P_{o,corr} : -0.03 \text{ inH}_2\text{O}$$

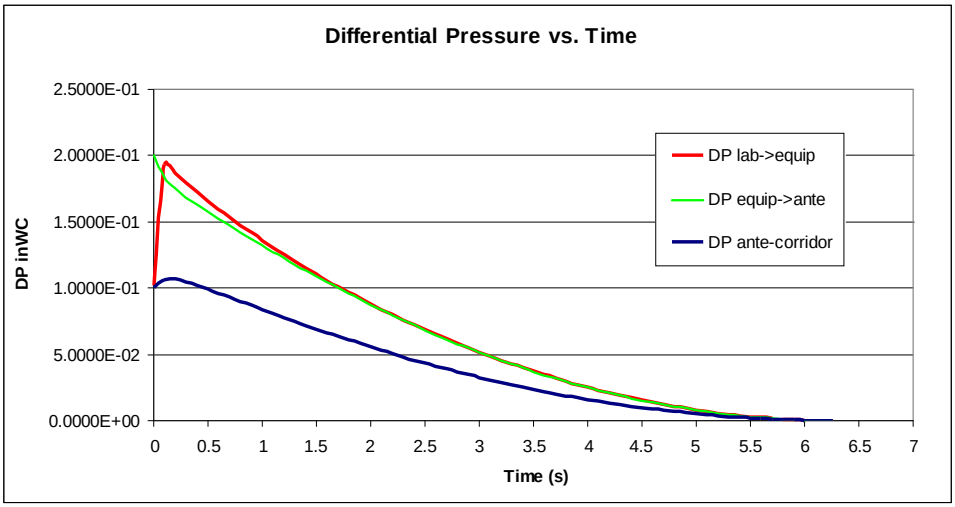
Assume the n = 0.5, the flow coefficient f for lab, passage and anteroom is 366, 491, and 635 respectively.

If it is assumed that the lab air exhibits the characteristics of a worst case scenario combination of factors as previously described, and upon loss of power, the initial 'reversed' pressures are 0.1, 0.2, 0.1 in H_2O for lab, passage and anteroom respectively, using the steps listed above, the results show that all three of the rooms will return to 'neutral condition' in about 6.2 seconds and 11.4 ft^3 of air and 0.00004 ft^3 of contaminant will be leaked from the BSL suite to the corridor.

Table 2 Results showing concentration of leaked contaminant before rooms return to 'neutral condition'

Output	*BSL-3 → equipment room*	*Equipment room-anteroom*	*Anteroom → corridor*
Total leaked air at time t	8.407 ft^3	11.168 ft^3	11.434 ft^3
Total leaked concentration at time t	*8.402 ft^3*	*0.0126 ft^3*	*0.0000446 ft^3*
Time required for pressure returns neutral T_N	6.256 s		
Total leaked air at time T_N	8.407 ft^3	11.168 ft^3	11.434 ft^3
Total concentration leaked at T_N	*8.402 ft^3*	*0.0126 ft^3*	*0.0000446 ft^3*

Figure 3 Differential pressure vs. time graph (see online version for colours)



5 Estimation of air leakage due to door movement

Opening a hinged door can lead to a sweeping action which can also move a considerable volume of infectious air across the open doorway. A typical hinged door (about 1 m wide) opening relatively slowly sweeps out one-eighth of a circle of circumference (C) $2\pi = 6.3$ m ($C = 2\pi r$). For our example, if the door edge travels about 6.3/8= about 0.8 m in about 2s, generating an airflow with speed of approximately 0.8/2 = 0.4 m/s (≈80 FPM). In practice, doors may be opened faster and wider than this. As the door opens, air inside the room is dragged (or 'entrained') into the region swept by the door, leading to a large exchange of air across the doorway. Tang et al. (2005) suggest that such problems with hinged doors may be reduced by the use of sliding doors in the future if the technology becomes compatible with the requirements for BSL-3 containment.

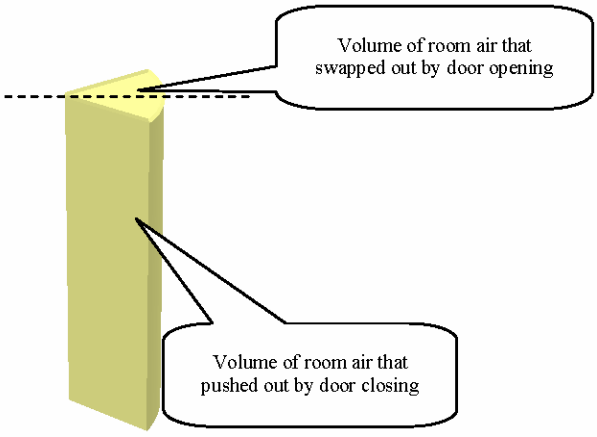
When people enter or leave the lab suites by opening or closing doors a vacuum space is created behind as the doors open and close. Using the following assumptions:

- the vacuum volume is being filled with both room and outside air
- half of the vacuum volume is filled with room air, half with outside air
- the door opens fast enough, so the filling effect happens right after the door opens
- the outside air that entered the vacuum 'swaps' out the equal amount of room air.

When a door is closing, the volume that door swept is assumed to be pushed out of room

The volume of contaminated room dirty air leaked out during door opening can be calculated by $V_{open} = H\frac{1}{4}W^2\theta$.

Figure 4 Door geometry (see online version for colours)



And the amount of air being 'pushed' out by the door when closing is $V_{close} = H\frac{1}{2}W^2\theta$.

Also, another part of the airflow that is caused by flow difference (which is to produce negative pressure) is $V = Q\Delta t$.

Total amount of air leaked is then $V_{leak} = \frac{3}{4} HW^2\theta$.

Take the doors in the suite as an example. The height is 84" and width 42", 2" thick; doors open to 45° and open and close in two seconds.

Table 3 Door geometry/motion and room condition before opening/closing the door

Input	*Lab → equipment room*	*Equipment-anteroom*	*Anteroom-corridor*
Door geometry			
Width *W*	42 in	42 in	42 in
Height *H*	84 in	84 in	84 in
Thickness	2 in	2 in	2 in
Door motion			
Opens to (deg) θ	45°	45°	45°
Time taken to open/close (s) *T*	2 s	2 s	2 s
Room condition			
Flow differential	110 cfm	110 cfm	110 cfm

Using the same operating differential pressure, the above calculation yields: total volumes leaking out of each room of approximately: 43 ft^3.

Assuming the door to the lab opens and closes first, followed by opening and closing of the passage room door and lastly opening and closing of the anteroom door, the total contaminant leaked from the anteroom to the corridor is 0.02 ft^3.

Table 4 Results showing concentration of leaked contaminant by opening/closing the door

Output	*Lab → equipment room*	*Equipment-anteroom*	*Anteroom-corridor*
Total leaked air	43.64 ft^3	43.64 ft^3	43.64 ft^3
Total leaked concentration	43.64 ft^3	0.51 ft^3	0.02 ft^3

6 Discussion

It is generally accepted that flow differentials necessary to minimise or eliminate AVM during entry/exit are unreasonable high. Increasing the flow differentials could potentially affect the integrity of the building envelope and place an unnecessary amount of stress on the engineering system components in addition to having a high operating cost. Therefore, increasing flow differentials is neither the most 'green' approach nor is it cost effective or necessary if reasonable options and safety measures are considered as part of the risk assessment.

The design team, including occupational health and safety personnel, engineers and users, should however take into account the very real possibility that some leakage will occur in the event of a power failure unless extreme measures such as increasing the flow differential are incorporated into the design or retrofit of the facility. To minimise the use

of costly extreme measures, the design team would be better served to perform a proactive risk assessment that will include the probability of an event and provide more latitude to less probable events such as total exhaust failure with the supply running, i.e., The risk assessment will guide the facility design interactively with SOPs and examine the possible agents to be used in the facility, the design of the primary barriers and the HVAC system capacity, redundancy and capabilities.

It is important to note that the ultimate goal in design and operation is to achieve sustained directional airflow such that under failure conditions the airflow will not be reversed. However, the proposed methodology should be applied when, and only when, all other measures to achieve zero tolerance have been ruled out. Only upon completion of due diligence to achieve zero tolerance, should the model be employed when performing the facility health and safety risk assessment in order to determine the reverse airflow tolerance in a BSL-3 facility.

In any case, the early development of draft SOPs is necessary to advance the building design documents confidently. It is necessary to address the safest achievable solution that will prevent contamination of the lab occupants prior to and upon exiting the lab and to protect contamination of the rest of the facility. There are specific measures that should be taken to reduce potential contaminant leakage before exiting the defined containment area. Although they may appear to be 'common sense', it is important to include them as part of BSL-3 operational procedures. For instance, upon becoming aware of a power outage, occupants should:

1 Stop all experimental work and procedures.

2 NOT REMOVE personal protective equipment that is being worn at the time of the outage except for gloves at the time of exit. The risk assessment should determine if gowns/lab coats should be removed.

3 Cover open biological material in the BSC and place used pipettes in disinfectant within the BSC or in a discard bag and tightly close discard bag.

4 Perform normal BSC and surface wipe down decontamination procedures.

5 Leave all materials in the hood rather than moving them and risking a spill.

6 NOT OPEN centrifuges, lyophilisers or other sealed equipment that creates aerosols.

7 NOT OPEN tissue culture incubators.

8 NOT OPEN refrigerators, freezers, LN_2 dewars.

9 NOT REMOVE lids to animal holding cages except to return animals in use to respective cage.

10 NOT DISTURB used bedding in clean up process.

11 Remove dirty gloves prior to exiting containment room and replace with clean gloves; remove other personal protective equipment as determined by risk assessment.

By using the proposed methodology to determine AVM through the door gap versus when the door is opened and closed to exit the contaminated area, they can assess the risk of infectious disease transmission that might occur using currently accepted design parameters for differential room pressure and flow rates rather than to try to minimise or

eliminate AVM during entry/exit. Additionally, considerable time would be lost in the project schedule by making changes to go from an excursion that is commensurate with a person exiting (probably on the order of 30 seconds) to one that is less than that when the total difference in annual air exchange difference is less than 0.3%. Both increasing flow differentials unnecessarily and delaying a project have high price tags and in most cases can be avoided.

Although, the behaviour of aerosolised infectious particles is important to understand in the transmission of disease, this topic is covered extensively elsewhere. Suffice it to say that transmission of infectious particles is dependent on particle size, trajectory, dose, infectivity and pathogenicity, force of expulsion, air currents, temperature, and humidity all of which may also have a role in the concentration of contaminants that leak across a door gap if normal operations are arrested for any reason. All the elements of the lab design perform in a finely tuned interacting fashion. The use of an anteroom adjacent to the lab will definitely reduce the amount of contaminant escape but further research into the role of each of these parameters is needed.

When considering how to reduce the risk of infectious disease transmission from a BSL-3 or otherwise negatively pressured area such as a biocontainment patient care facility, a number of other concerns come to mind that are worth further study. Among these are answers to the following questions:

- How are the boundaries of containment defined?
- What if there is no shower-out requirement for the suite? If sustained airflow is providing the protection between clean and dirty areas, should ‘shower out’ be a requirement in all airlocks?
- What constitutes an acceptable lag time before directional airflow and proper pressurisation are restored?
- What might constitute an acceptable leakage value?

7 Conclusions

In this paper, the author proposes a practical mathematical approach that not only validates Hayden’s et al. (1998) premise but takes it a step further. The proposed model calculates how much air displacement and contaminant leakage occurs during a power outage that may result in a momentary positive pressure reversal and compares the degree of contaminant leakage that would occur through door gaps before opening the door during momentary pressure reversal versus the contaminant leakage that would occur when the door is opened to exit the area. Hayden’s data illustrated that leakage areas were dominated by leakage through the doorway during entry/exit. The result of the proposed methodology concludes mathematically that if there is a pressure reversal, there is significantly less contaminant leakage through the door gap than from opening and closing a door. Incorporating a mathematical approach in the risk assessment allows the design team to adjust the variables to the specific system outputs and capabilities of the facility. For example, a 6.2 second lag time is used in this model for purposes of demonstration but may be adjusted based on the circumstances.

It is highly recommended that engineers use a combination of tools at their disposal to properly design BSL-3 laboratories so that they perform as intended and are as fail safe as possible. Once again, it is important to emphasise that the ultimate goal in design and operation is to achieve sustained directional airflow such that under failure conditions the airflow will not be reversed, per the BMBL, 5th ed. However, the proposed methodology should be applied when, and only when, all other measures to achieve zero tolerance in a BSL-3 facility have been ruled out. Only upon completion of due diligence to achieve zero tolerance, should the model be employed when performing the facility health and safety risk assessment to determine the reverse airflow tolerance in a BSL-3 or AII environment.

The proposed methodology may be adapted to the unique criteria of the facility in question to calculate how much air displacement and contaminant leakage occurs through the door gap and other leakage points compared to leakage from opening and closing the doors of the BSL-3 area if there is egress during a power outage that results in a positive pressure reversal. The methodology is one useful tool to be used as part of the risk assessment for a BSL-3 lab or ABSL-3 animal facility when sustained directional airflow cannot be realistically achieved by the existing backup systems. The methodology may also be used to quantify contaminant migration across a boundary for other room types, such as AIIs and PPEs), that use sustained differential air pressure as one means to prevent infectious particle transmission.

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Nomenclature

Q	Airflow rate, cfm
P	Pressure, inH_2O
f	Flow coefficient, cfm/inH_2On
n	Flow exponent, dimensionless
V	Room Volume, ft^3
Δt	Time step, s
c	Room concentration, dimensionless
C	Leaked contaminant, ft^3
M	Mass of the room, kg
R	Air constant, 287 J/kg/K
T	Temperature of room, F
v	Displaced volume by door
H	Door height
W	Door width
θ	Angle that door opens

Subscript

o	Operational condition
lab	Animal holding room, lab
pass	Passage room
ante	Anteroom
t	Time step t
$t + \Delta t$	Time step $t + \Delta t$
open	Door open
close	Door close
leak	Leaked