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Airtightness in Belgian high biocontainment facilities

Overview of four BSL-3 facilities and recommendations for optimal airtightness

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Contents

1. Foreword

Following a discussion in 2011 at the meeting of the European Joint Enforcement Group of Contained Use & Deliberate release of GMOs (EEP2011) about the current situation on airtightness in high-containment facilities throughout Europe, the Biosafety and Biotechnology Unit (SBB) of the Belgian Scientific Institute of Public Health (WIV-ISP) decided to survey the biosafety officers of institutions with facilities of biosafety level 3[1] (BSL-3) in Belgium, and offered the possibility to measure the airtightness of their high-containment area by means of a blower-door test (norm NBN EN 13829:2001).

Four institutions, representing different construction types, were selected. These were a newly built and state-of-the-art facility, a box-in-a-box renovation, a thorough renovation with conventional building techniques, and a superficially renovated animal facility. The present report summarises the main fumigation techniques commercially available for decontamination and the techniques that were used for measuring the airtightness, as well as the results of the airtightness tests obtained in the different facilities, and provides some recommendations to achieve optimal airtightness.

1 See glossary

2. Introduction

2.1. Rules, norms and guidelines on airtightness in biocontainment facilities

European Directive 2009/41/EC on the contained use of GMMs[2], implemented in the regional Belgian decrees and extended to the contained use of GMOs and pathogens for humans, animals and plants, states that a laboratory of containment level 3 or 4, and optionally (as determined by the technical expert) large-scale facilities and animal housing facilities of containment level 2, should be sealable (made airtight) for decontamination by fumigation (Annex IV of Directive 2009/41/EC). Decontamination by fumigation is necessary in biocontainment facilities in several cases, amongst which: (1) after a bio-incident with possible release of aerosols[3] containing highly infectious agents (genetically modified or not), (2) at the end of any activity where contamination of the biocontained area with highly infectious agents could not be avoided (eg. large animal housing, greenhouses), (3) before maintenance, or (4) in context of release for other purposes (decommissioning) of the facility and/or its equipment.

While the European legislation doesn't contain any required minimal numerical values for airtightness, the Australian and Canadian norms do. Norm AS/NZS 2243.3 (2010) from Australia and New Zealand recommends an air leakage rate of 10^{-5} m^3/Pa.s, measured at an overpressure of 200 Pa. The Canadian Biosafety Standards and Guidelines (2015) prescribe - depending on the work to be performed in the facility - a pressure decay test as a part of the commissioning (first certification) procedure for high biocontained facilities, whereby the criteria for acceptance include two consecutive tests with a maximum of 250 Pa loss of pressure from an initial 500 Pa over a 20 minutes period. Subsequent certifications, if no major modifications were performed to the envelope, include visual inspection of the integrity of the containment barrier and tests with a smoke pencil or a tracer gas (CBS, 2015).

2.2. Decontamination by fumigation

Fumigation is the method of choice in order to achieve a broad-spectrum decontamination of a room or enclosure, including surfaces which might be difficult to reach, as well as the air of the room which might contain airborne pathogens. Several options are available for decontamination by fumigation, with formaldehyde, hydrogen peroxide (HP) and chlorine dioxide (CD) being the most prevalent fumigants. The choice of the fumigant is often site-specific because of the infrastructure itself (the facility is too spacious to maintain temperature and humidity, the equipment/devices are sensitive to certain fumigants,…), because there is potential organic soiling that cannot be fully cleaned in advance, or because of cost considerations.

Formaldehyde is the cheapest, easiest to set up and was the most used fumigant in the past. This is a true gas, which evenly spreads within the available volume without the need for active circulation, contrary to HP or CD. This makes HP and CD much more expensive fumigants: HP is used as a vapour, is non-diffusive and therefore requires the use of a specific apparatus to circulate and monitor it, while CD very easily breaks down in sunlight, also requiring a dedicated system to generate it *in situ*. Hydrogen peroxide is the most sensitive to organic soiling, and thus a thorough clean-up of all surfaces with detergent before decontamination is required. While formaldehyde and CD still maintain some efficacy in the presence of organic matter such as blood or faeces, a pre-cleaning step is nevertheless

2 See glossary

3 Examples of bio-incidents with possible release of aerosols: spills, splashes, breaking of container, technical failure of biosafety cabinet, see http://www.biosafety.be/CU/Bioaerosols/bioaerosols.html

always recommended.

An important down-side of formaldehyde is its toxicity and carcinogenicity, highlighting the importance of a high level of airtightness/sealability of the facility in which it is to be used during fumigation. A recent change in classification of this substance to “Carcinogen category 1B: presumed human carcinogen” by the European Chemical Agency has resulted in stricter rules and conditions for the use of formaldehyde, as well as increased protective measures against exposure to the substance in the work place (with possible derogations for life science laboratories). Other downsides to the fumigation with formaldehyde are the formation of toxic residues which have to be additionally rinsed with water, and all chlorine-releasing agents should be removed in advance to prevent a potential reaction and release of carcinogenic products.

Whatever the chosen method, it is important to validate the decontamination protocol for every area prior to its first use, by using biological indicators. The most resistant organisms to the fumigation method, like spores of *Geobacillus stearothermophilus,* are generally used as indicators and are often commercially available on easy-to-use strips that were specifically developed for the validation of decontamination procedures through fumigation (Gordon *et al*., 2012).

2.3. Measuring the airtightness: the blower-door test

In addition to preventing the escape of harmful fumigants to adjoining rooms, with risk of exposure of the occupants, a certain level of airtightness is also required for the effectiveness of the fumigation process, in case some specific levels of humidity and temperature must be met and maintained. Therefore it is important that the rooms, which are to be decontaminated by fumigation, can be made airtight up to a certain level. Although this legal obligation can be interpreted as being required only at the moment of the preparation for and during the fumigation, it is advisable to achieve this airtightness as much as possible through the infrastructural quality of the building/facility. The room’s external envelope is hereby especially important, together with the perfect fit and sealing of the windows, doors or other openings through this envelope such as electrical outlets. In addition to the necessity for biosafety reasons, a high level of airtightness benefits the energy-efficiency of maintaining the negative pressure, required for a BSL-3 lab.

The airtightness of a room can be quantified by means of a blower-door test (norm NBN EN 13829:2001), during which a pressure difference is created between the volume to be tested and the outside, by a calibrated fan that is hermetically fitted in a (door) opening (Figure 1). This fan (de)pressurizes the room for a multi-point test to a series of pressure differences up to ~ 75 Pa[4] (measured by a calibrated manometer) and the required airflow to maintain a stable pressure difference is recorded. This is the leaked volume of air per hour, which is inversely proportional to the airtightness of the room. In order to effectively compare rooms of different sizes, the leaked volume of air per hour at the chosen pressure (V_{50}) is converted to the amount of air-changes per hour (= n_{50} in unit h^{-1} in case of 50 Pa pressure difference), by normalizing against the total volume of the tested room.

Figure 1: Blower-door with fan fitted in a lab door opening

The blower-door tests in the present study were performed by a

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certified control firm both at negative and positive pressure, while biocontained facilities are designed for operation at a negative pressure difference with the uncontained area. This construction mode might be slightly different in some aspects compared to facilities built for positive pressure (e.g. clean room under ISO norm 14644-1), and the calculated air exchange rates at negative and positive pressure are indeed often somewhat different. An example of the construction differences are window seals, which might be installed in such a way that a negative pressure inside the lab pulls them more tightly to the inner sealing, while a positive pressure, i.e. a force applied in the opposite direction, might slightly push the seals apart. Integrity of the seals and the containment envelope at the levels of pressure difference of normal lab operation can be ascertained during the blower-door test, by the linear output of a graph plotting (on log-scales) the required airflow to keep a certain pressure (m³/h) vs. the applied pressure difference (Pa).

3. Results of airtightness measurements of the tested BSL-3 facilities

The airtightness at a pressure difference of 50 Pa (negative and positive, n_{50} (neg) and n_{50} (pos) respectively) of the four high containment facilities of biosafety level 3 (BSL-3) was measured by the blower-door test in accordance with the requirements of NBN EN 13829:2001; n_{50} (mean) is the calculated mean of both values with a deviation of 10%. One of the tested facilities was a newly built, state-of-the-art laboratory, while the others were renovations. Of the three renovations, one concerned a box-in-a-box setup, another a research lab totally renovated with conventional building techniques, and the last was a superficially renovated large-animal facility.

3.1. Newly built laboratory

The facility consists of an anteroom, 4 labs (a main lab of 163 m³ and three smaller ones of 82 m³), a corridor and an autoclave area. It was built in 2010 according to the state-of-the-art, with pneumatic door seals, conventional outer building materials and inner walls based on sandwich panels[5] and additional acrylic glass in front of the outer windows. The BSL-3 area is maintained and monitored at a constant negative pressure (clean and dirty anterooms: -20 and -30 Pa; autoclave area: -30 Pa; labs: -50 Pa) by means of an HVAC[5] system, which is independent from the adjacent zones and coupled to an emergency power supply. The initial airtightness test in the largest lab, with the ventilation system switched off and water in the siphons, revealed some air leakage via the perforations in the sandwich panels for electrical outlets. Following this first test, the observed air leaks were addressed by installing airtight fittings for electrical plugs. A second airtightness test was performed two years later in the same lab as well as in the three smaller labs (table 2), again with the ventilation system switched off and water in the siphons.

Additional issues with the airtightness were detected during the second day at several defined spots in the labs, again at various openings performed in the walls for utilities such as electricity, tubing for compressed air or the fire extinguishing system (Figure 2), but they were of lesser magnitude than measured on day 1. The hatch in the wall between two labs also seemed to be a source of air leaks. Nevertheless, the second test in the largest lab indicated a significant improvement in airtightness (see table 1).

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Figure 2: Air flow measurement showing air leaks at the fire extinguishing outlet

#	Day	Lab	Volume (m^3)	n_{50} (neg) [h^{-1}]	n_{50} (pos) [h^{-1}]	**n_{50} (mean) [h^{-1}]**	**V_{50} (mean) [m^3/h]**
1	1	A	163.3	0.44	0.44	**0.44**	72
2	2	A	163.3	0.38	0.36	**0.37**	60
3	2	B	81.9	0.25	0.22	**0.23**	19
4	2	C	81.9	0.32	0.21	**0.27**	22
5	2	D	81.9	0.30	0.27	**0.28**	23

Table 1: Measured and calculated values of the air-changes per hour at 50 Pa in the four different labs.

3.2. Box-in-a-box laboratory

This box in-a-box-facility of 126 m^3 was constructed in 2005 inside a building dating from the 1950's and is made out of sandwich panels. This BSL-3 facility consists of a double anteroom (clean and dirty) with interlock, one common lab area and three smaller dedicated labs, each with a window allowing for visual contact with the surrounding, uncontained areas. The common room has a double door autoclave, and the decontaminated waste is retrieved outside of the BSL-3 containment box. The BSL-3 area is maintained and monitored at a constant negative pressure (anterooms: +10 and -20 Pa; common room: -40 Pa; labs: -50 Pa) by means of an HVAC system independent from the adjacent zones and coupled to an emergency power supply.

The airtightness in this L3 facility was initially measured in three different operation modes: (1) with both the HVAC system and the double door autoclave sealed; (2) with a sealed HVAC system and the double door autoclave not sealed; (3) with both the HVAC system and the double door autoclave in standard working condition. In all instances the siphons were filled with water and in the present case, sealing off the autoclave meant it was completely covered with plastic foil, fastened to the wall; no distinction was made between sealing off the door and the connection between the autoclave body and the wall. The airtightness test revealed that the double door autoclave accounts for a total air leak of 13m^3/h (difference between #2 and #1, table 2), and infrared imaging revealed further air leaks at perforations made in the walls to install the electrical outlets (Figure 3) and the emergency alarm box.

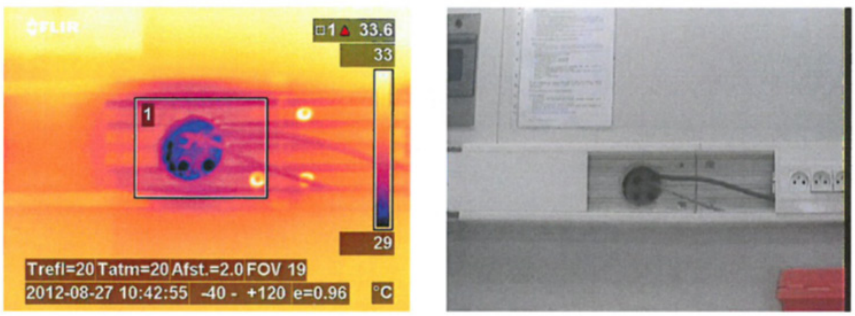

Figure 3: Thermal image (left) and white light image (right) of an electric fitting showing air leaks

Figure 4: Injected silicone for the sealing of the perforation for electric cables

After attempting to fix the detected air leaks by application of silicone (Figure 4), the airtightness test was repeated twice separately one year later with the HVAC system and autoclave in normal operation mode. During the second and third tests air leaks were still observed at perforations in the containment barrier for the passage of cables.

Overall, the additional (second and third) airtightness tests did not indicate a significant gain in airtightness, suggesting that the initially detected leaks at the level of the wall perforations were not primarily responsible for the detected air losses or were not tackled well. A thorough analysis based on infrared imaging and air velocity measurements could be helpful to identify more air leaks, but is outside the scope of this project.

#	Day	HVAC	Double door autoclave	n_{50} (neg) [h^{-1}]	n_{50} (pos) [h^{-1}]	**n_{50} (mean) [h^{-1}]**	**V_{50} (mean) [m^3/h]**
1	1	Off and sealed	Sealed	0.68	0.66	**0.67**	84
2	1	Off and sealed	Normal	0.80	0.73	**0.77**	97
3	1	Normal	Normal	0.83	0.82	**0.82**	103
4	2	Normal	Normal	0.83	0.84	**0.83**	105
5	3	Normal	Normal	0.79	0.76	**0.78**	98

Table 2: Measured and calculated values of the air-changes per hour at 50 Pa in three different operation modes and on three different days

3.3. Completely renovated laboratory with conventional building techniques

This BSL-3 facility of 152 m³ was newly renovated in 2014 inside a building dating from the 1960's, and consists of a double anteroom (one clean and one dirty anteroom) with different pressures (respectively: 0 and -15Pa) and a lab area which is maintained at -30 Pa. The tests were performed before the first use of the lab, and during all the tests the HVAC system was switched off.

To test the airtightness of both the autoclave and the room, blower-door tests were performed on two different days. Three tests were performed on day one: (1) with the autoclave's door and the junction between the autoclave frame and the wall sealed off (Figure 5); (2) with only the junction between the autoclave and the wall sealed; (3) with all sealing on the autoclave removed (operation mode) (table 3, #1, 2 and 3).

Comparison of the mean n_{50} -values of condition 1 and 2, where the only difference is whether or not the autoclave door is sealed, shows that the door and its sealing does not contribute to any air leaks, while

the frame (condition 3) is responsible for a possible air leak of 24m³/h (difference between #3 and #2, table 3). Visual inspection of the autoclave at the “clean” side revealed a gap between the top edge of the autoclave and the wall (Figure 6). During the (de)pressurisation of the lab for the blower-door test on the first test day, two additional important sources of air leaks were discovered. The first one concerns the electric switches, situated in the wall between the lab and the clean anteroom, where improper sealing of the holes performed by the building contractor was the root cause. The second important air leak was found above the dropped ceiling tiles, where the wooden panel that forms the outer envelope did not reach the concrete ceiling, leaving a sizeable gap that was only partially filled with mineral wool insulation (Figure 7), a material which is unsuitable for airtightness purposes.

The detected air leaks from day 1 were fixed by injection of silicone in the gap between the autoclave frame and the wall; the gaps in the outer envelope, above the dropped ceiling, were filled with PUR

Figure 5: Double door autoclave sealed off with tape (table 4, #1)

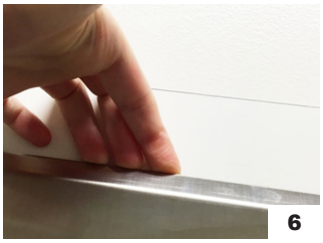

Figure 6: Gap between the top of the autoclave (metal) and the wall through which it is fitted (white)

Figure 7: Big gaps between the rock wool insulation and the refurbished wall, leading to air leaks

(polyurethane) expanding foam. During the blower-door test performed on day 2, the autoclave was not taped off anymore, and the impact of the HVAC tubing integrity was assessed by comparing the values obtained when the intake and blowing vents were taped off with plastic foil or not (table 3, #4 and #5), while the HVAC system was switched off in all instances.

The results obtained on day 2 show the HVAC to be responsible for a possible air leak of 41 m³/h (table 3, #5). The overall airtightness of the room only improved marginally, especially considering the renovations that were performed with the explicit aim of improving the airtightness. Visual inspection indicated that the PUR foam didn’t fill all the gaps, which could be explained by the fact that this material shrinks when drying after its expansion during application.

#	Day	HVAC	Frame autoclave- wall	Autoclave door	n_{50} (neg) [h^{-1}]	n_{50} (pos) [h^{-1}]	**n_{50} (mean) [h^{-1}]**	**V_{50} (mean) [m^3/h]**
1	1	Sealed	Sealed	Sealed	4.10	4.06	**4.08**	**622**
2	1	Sealed	Sealed	Normal	4.05	4.11	**4.08**	**622**
3	1	Sealed	Normal	Normal	4.26	4.22	**4.24**	**646**
4	2	Sealed	Normal	Normal	3.63	3.76	**3.69**	**563**
5	2	Seals removed	Normal	Normal	3.83	4.10	**3.96**	**604**

Table 3: Measured and calculated values of the air-changes per hour at 50 Pa in three different modes of sealing of the autoclave

3.4. Superficially renovated large-animal facility

This large-animal housing facility of biosafety level 3 is located in a building dating from the 1950's and renovated in 2011. The renovation included new high-standard windows, pneumatic seals on anteroom doors, the application of a washable resin on the joints between the wall tiles, refurbishing of floors and existing walls with epoxy coating, and a new HVAC system. The biocontained area comprises a slaughter hall, a stable of 941 m³, anterooms, several lab and feed areas, as well as technical and waste management rooms. The BSL-3 area is maintained and monitored at a constant negative pressure with regards to the adjacent zone (anterooms at -30 Pa; corridors at -35 Pa; BLS-3 lab and stables at -50Pa, technical areas for waste water collection and effluent decontamination station at -60 Pa) by means of multiple independent HVAC systems coupled to an emergency power supply.

The airtightness was measured twice over the course of 3 years, under conditions of sealed HVAC, filled siphons and doors to adjacent rooms sealed by means of the pneumatic seals, as would be the situation during decontamination by fumigation. Air leaks were detected through infrared imaging and air velocity measurements during the blower-door tests. The first airtightness measurement brought some air leaks to light at the level of window and door frames, perforations for cables, light fittings and water drains. Analysis of the difference in air change rate between condition 2 (stable, lab and feed rooms) and condition 3 (stable, lab, feed room + small corridor), where the only difference is the inclusion of a small corridor in the measurement, shows this corridor of 10 m³ to be extremely leaky (V_{50} = 168 m³/h and n_{50} = 16.8). This was probably due to the presence of a flexible joint running throughout the whole building, a necessity for its stability due to the wetland nature of the building site.

#	Day	Measured rooms	Volume (m³)	n_{50} (neg) [h^{-1}]	n_{50} (pos) [h^{-1}]	**n_{50} (mean) [h^{-1}]**	V_{50} (mean) [m³/h]
1	1	Anteroom	34	2.58	2.82	**2.70**	**92**
2	1	Stable, lab, feed room	1177	0.33	0.31	**0.32**	**380**
3	1	Stable, lab, feed room **+ small corridor**	1187	0.46	0.46	**0.46**	**548**
4	2	Stable, lab, feed room	1177	0.37	0.41	**0.39**	**460**
5	2	Stable	941	0.45	0.49	**0.47**	**444**

Table 4: Measured and calculated values of the air-changes per hour at 50 Pa in different (combination of) spaces on two different days

Air leaks were addressed after the first airtightness measurements by application of silicone and sealing foams. The second measurement, performed three years later and after extensive use of the research facility, which included cleaning and decontamination of the stable walls and floors with potentially non-compatible products (harsh or abrasive), showed a decreased airtightness of the facility (small increase in air leaks of 80 m³/h, difference between lines #2 and #4 in Table 4).

Additional airflow measurements during pressurisation identified air leaks at the sealed-off doors, at the electrical outlets, around window frames, at wall joints and angles, between wall-tile joints and also at the plugs used to seal off the ventilation outlets, suggesting some degradation of the airtightness of the room over the course of three years.

4. Discussion

The facilities tested for this report – apart from the lab which was renovated with conventional building techniques – showed very good performance in airtightness, with air-change rates of 0.8 h^{-1} or better. For comparison purposes only, the airtightness requirement for a passive house is set at n_{50} = 0.6 h^{-1}.

While the European legal obligation of sealability is in the context of decontamination by fumigation and in particular to avoid the spread of harmful fumigants outside of the contained area during the decontamination procedure, it is in case of a bio-incident not advisable for the airtightness to depend completely on a manual sealing prior to the decontamination procedure, as opposed to a high level of intrinsic airtightness of the facility. Moreover a certain level of airtightness is necessary to ensure the decontamination by fumigation is effective, since it facilitates attaining the required levels of different parameters such as humidity, concentration of fumigant and room temperature.

The role of airtightness to prevent the escape of hazardous (micro-)organisms during routine manipulations is less up for discussion, as the biological agents of biological risk class 3 or higher should always be contained within primary containments (tubes, vials, plates, etc.) and are manipulated in 'open' phase only in a biosafety cabinet. Only in case of a bio-incident with release of a pathogen, or during infection assays with large animals, is the air in a BSL-3 facility considered to be contaminated. The risk of spread into the environment is therefore mitigated by working under conditions of negative pressure, with sufficient ventilation and HEPA filtration of the circulated air. Moreover, the HVAC system includes several mandatory safety features, such as the prevention of accidental positive pressure because of malfunction (McGurk, 2009), or an emergency power supply system to prevent power cuts. Those considerations are also necessary when opting for a fire extinguisher system with gas (to protect expensive electronic equipment), which must be coupled to the HVAC system in order to maintain the negative pressure during its use, as the sudden release of the gas is accompanied by a large increase in air pressure.

Air leaks can be easily detected when the room is pressurised during a blower-door test, with infrared imaging or airflow measurements. The issues most often detected in the labs tested for this report were due to perforations in the external envelope of a high biocontained area for the passage of utility cables or ducts. These air leaks could easily be avoided if the airtightness obligation was taken into account from the start of the (renovation) project, by designing it in such a way that the amount of perforations in the outer envelope of the biocontained area is kept to a minimum. And where-ever perforation are made, they must be filled and sealed carefully and in a sustainable way before the first use of the lab.

Since the impact of an air leak depends on the total volume of the room, a smaller room makes it even more important to pay particular attention to all the details of airtightness. For comparison with other rooms it is therefore not recommended to quantify the air loss due to a specific leak as a percentage. Although there are no legal objections to rendering an area (more) airtight only prior to a decontamination by fumigation, this situation is not always desirable, e.g. in the case of a bio-incident. Moreover, many identified air leaks are not accessible anymore for manual sealing once the construction or renovation works are completed and the lab is in use.

Important devices in a high biocontainment facility to consider in context of airtightness are the HVAC system and the double door autoclave. The HVAC system is mandatory in a high level biocontainment facility and must be equipped with airtight gas valves and tubing. In this project we observed air leaks of the HVAC system from 6 m^3/h up to maximum 41 m^3/h at 50 Pa, suggesting variability in the quality of the HVAC system's seals and valves. Double door, pass-through autoclaves are recommended in

high biocontainment areas, as they minimize the transport of highly pathogenic waste and avoid the necessity to access the high containment area to collect the inactivated waste. On the other hand, they could hamper the overall airtightness when not installed carefully enough, or if inadequate sealing materials were used. The perforation in the wall to install the autoclave, but also the autoclave itself, may be responsible for air leaks. It is therefore very important, when installing a double door autoclave in the outer wall of the containment area, to seal off carefully and in a durable way the junction between the frame and the wall, but also the perforations for any pipe and cable, which are necessary for the operation of the autoclave. The integrity of the seals of the doors of double door autoclaves, as well as the seals of the ducts of the HVAC system, should be checked on a regular basis, as autoclaves generate a lot of heat and pressure, causing extra stress to those seals (McGurk, 2009).

5. Conclusions and recommendations

Although the in Belgium regionally implemented Directive 2009/41/EC states that biocontained facilities must be sealable in the context of decontamination by fumigation, this obligation is best attained as much as possible by the building itself and without external intervention prior to decontamination. Moreover, a certain level of airtightness is necessary for the efficient day-to-day operation of a lab of high biological containment, with a higher airtightness of the lab resulting in a lower cost of operation.

Throughout the tested high biocontainment facilities, **similar causes for air leaks** were found repeatedly: the electrical outlets and switches, as well as barrier penetrations for the passage of cables or ducts. Despite these recurring and similar issues, big differences in airtightness were observed in the high biocontainment facilities in this study, which could not be correlated with the age of the building or method used for the building or renovation. We suspect that these differences are rather related to the attention and care paid to the optimal airtightness requirements. It is therefore important to **make the building contractors aware of the particular airtightness requirement from the start of the project**, such as the need to place (window) sealings in an adequate manner in the context of underpressure with regards to the adjacent areas, or that the **outer shell of the biocontained area must be as intact as possible**, keeping perforations and tube junctions/connections to the minimum and sealing the perforation that are made with the **necessary care** and with **long-lasting materials**. It is also important to keep the number of (tube) junctions of the HVAC system to a minimum, and more generally to design the HVAC system with airtightness of the facility in mind, since HVAC systems are known sources of potential air leaks. Additionally, the **durability** of the materials and their **compatibility** with the intended use and maintenance of the facility are of prime importance. It is therefore recommended to perform a blower-door test (with associated detection of air leaks during pressurisation) on a regular basis to take possible **time-dependent degradations** into account.

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Figures 2, 3 and 7 by the certified control firm, all other figures by SBB.

7. Glossary

BSL-3: Biosafety level 3, set of containment measures for the use of pathogenic (micro-)organisms. One of the characteristics of BSL-3 is the requirement for the contained area to be at a negative pressure to the surrounding area.

GMM: Genetically modified micro-organism

GMO: Genetically modified organism, an organism in which the genetic material has been altered in a way that does not occur naturally through fertilisation and/or natural recombination. GMOs may be plants, animals or micro-organisms, such as bacteria, parasites and fungi.

Pa: Pascal, unit of pressure, defined as 1 Newton per square meter.

HVAC: heating, ventilation, airconditioning

Sandwich panel: A prefabricated panel used as walls and that is a layered composite formed by attaching two thin (aluminium) facings to a thicker insulating core.