# Recommendation on Structural and Technical Safety Measures in BSL-3 Laboratories

## A Tool for Stakeholders

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Cover photo: BSL-3 Laboratory of the Institute for Infectious Diseases (IFIK), University of Bern. Picture: Pascal Gugler

## Client

Swiss Expert Committee for Biosafety, SECB

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# 1. Foreword

The Federal Expert Committee for Biosafety SECB is an independent expert body of the Swiss Confederation. It supports the Federal Council and the federal offices in the preparation of laws, ordinances and enforcement aids. It also advises the federal and cantonal authorities on the implementation of these regulations.

The SECB also draws up recommendations for experts working with pathogenic, genetically modified or invasive alien small invertebrates. In some cases, it consults external experts for this purpose.

This recommendation, which is of a general nature, specifies the requirements for selected structural and technical safety measures that are laid down for Class 3 activities in the Containment Ordinance (ContainO), the Ordinance on the Protection of Employees from Dangerous Organisms (PEMO), and the Major Accidents Ordinance (OMA). It specifies the state of the art in safety technology, which is constantly evolving.

It is a legally non-binding aid for all those involved in planning, construction, operating, assessing and inspecting such structural-technical safety measures in BSL3 laboratories as part of their professional activities. The recommendation is aimed on the one hand at planning and architectural offices and building owners, and on the other hand at facility and laboratory managers and persons responsible for biosafety in the laboratories, as well as at authorities responsible for enforcing the relevant ordinances. During the development of this recommendation, various persons from all target audiences were consulted as examples.

The structural-technical safety measures serve to prevent organisms from escaping into the environment. Since every BSL3 laboratory is unique, not all requirements can be implemented identically in every laboratory; instead, specific circumstances must always be considered. These include, for example, the organisms used, the type and scope of the activity and the age of the laboratory. As the state of the art in safety technology evolves, different requirements may be placed on a new building today than in the past. However, as long as organisms are still successfully prevented from escaping into the environment, there is no need for structural and technical improvements to such laboratories. In principle, technical solutions that deviate from this recommendation are also possible, as long as they meet the protection goals and measures specified in the relevant ordinances. The responsibility remains with the establishments and those who handle the organisms.

Bern, April 2022
Federal Expert Committee for Biosafety

## 2. Terms

| | |
|---|---|
| Construction, assembly | Selection of structural and engineering products and systems, and their use in the construction of the containment or in the implementation of the safety measures. |
| Workspace, containment | According to Annex 4 number 2.1 ContainO [1], the work area is the containment zone in which organisms are handled according to ContainO (laboratories, incubation rooms, etc.). Other areas are containment zones where no handling of organisms according to ContainO takes place (e.g., airlocks, corridors). It is state of the art in safety technology that the work area, personnel and material airlocks, pass-through boxes, etc., are planned, built and operated as a unit in terms of construction and building technology. In this recommendation, this unit is referred to as a safety level 3 laboratory or containment. |
| BSL3 Laboratory | Safety level 3 laboratory in accordance with the Ordinance on the Contained Use of Organisms (Annex 4 no. 2.1 ContainO [1]) and the Ordinance on the Protection of Employees from Dangerous Organisms (Annex 3 no. 2 PEMO [2]). Activities involving organisms in contained systems that pose a moderate risk to humans, animals or the environment must be carried out in a safety level 3 (BSL3) laboratory. |
| Requirement | Property, value, limit value or tolerance range in the design of a safety measure and the test with the recommended test method. In some cases, requirements may be limited to the existence of a safety measure (e.g., redundancy). The requirements in this recommendation are based on the state of the art in safety technology and on existing sets of rules. |
| Test method | Methodology or procedure to test the execution and properties of the safety measure for defects, errors or other deviations from the intended function or conformity. |
| Project-related quality management (PQM) | Aids for planning offices and construction companies to ensure quality in the execution of complex and demanding structures [7], [8]. |
| Special operation | Special operations include troubleshooting, fumigation of rooms, technical events, laboratory incidents, set-up, all maintenance work, calibrations, inspections, tests, etc. |
| User Requirement Specifications (URS) | Statement of work or requirements description for the BSL3 laboratory. The requirement specifications are written by the commissioning party. They describe in detail the intended activities, their risk assessment, structural-technical requirements including primary containment systems, or also work procedures (SOP) that affect the architectural design of the laboratory. They are considered and implemented by the planning office for the design and construction in an appropriate manner [14]. The present recommendation can be considered for the preparation of the requirement specifications. |

# 3. Introduction

Scope of application

The present recommendation is intended as legally non-binding assistance in the specification of structural-technical safety measures in BSL3 laboratories. It applies to BSL3 diagnostic and research laboratories in which microorganisms are handled and is addressed to persons who plan, build, operate, assess and inspect such structural-technical safety measures within the scope of their professional activities.

Destination

The aim of this recommendation is to specify the safety measures in order to contribute to a better understanding of the necessary structural-technical requirements, to increase planning and cost security and to improve the safety, quality and sustainability of such laboratories.

Applicable regulations and directives

The safety measures that must be observed for Class 3 activities (BSL3 laboratories) are described in the following regulations and guidelines:

_ Ordinance on Handling Organisms in Contained Systems (Containment Ordinance, ContainO [1], Annex 4)
_ Ordinance on the Protection of Employees from Dangerous Microorganisms (PEMO [2], Annex 3)
_ Ordinance on Protection against Major Accidents (Major Accidents Ordinance, MAO [3], Annex 2.3)
_ Manual on the Major Accidents Ordinance, General Part [4], associated module "Establishments with Biological Hazard Potential" [5]

ContainO and PEMO distinguish between general and special safety measures. In this recommendation, we consider only selected special safety measures from the areas of buildings and equipment (Annex 4, para. 2.1 ContainO and Annex 3, para. 2 PEMO). The module "Establishments with Biological Hazard Potential" also describes other measures that may be relevant for establishments subject to the Major Accidents Ordinance. Some of these are also considered in this recommendation.

Assistance and recommendations

Laws and ordinances always regulate a multitude of facts in theory. This is also the case with the above-mentioned ordinances, which refer to the state of the art in safety technology with regard to the requirements for safety measures that must be fulfilled.

However, the state of the art in safety technology changes over time and is very broadly defined: It includes all the technical knowledge about safety measures that exists in the professional world and is publicly available but may not yet have been generally introduced. The safety measures are also mostly explained in biosafety manuals only descriptively and not specifically, such as for the HEPA filter system or the tightness of the containment. These requirements must be defined anew for each BSL3 project.

It therefore remains a great challenge to build BSL3 laboratories according to the current state of safety technology. This is also confirmed by the experience of BSL3 laboratories commissioned in the last 10 years. This also shows the need for the present assistance.

Target audience

Planning offices should find concrete recommendations in this document on how the structural-technical measures of the ContainO, PEMO, and MAO can be implemented in a new building, renovation or alteration so that they comply with the current state of safety technology. In order to ensure planning and cost security, the safety measures should ideally be specified on a project-specific basis as early as the preliminary project phase, but at the latest as part of the construction project and the invitation to tender [6]. The descriptions of the safety measures also contain information on their concretisation, the test methods and the targeted requirements.

At the same time, this recommendation is also addressed to the persons commissioning the work, i.e., the building owners, proprietors, facility and laboratory managers and the persons responsible for biosafety (BSO).

In addition, the inspection and enforcement bodies are to be provided with a tool that makes it easier to assess whether and which safety measures and structural-technical designs meet the necessary requirements.

Teamwork, picking up experience

The commissioning parties and the commissioned planning and specialist planning offices should develop a common basis and language for the biosafety requirements and the necessary structural and technical requirements as part of a preliminary project. Joint visits to BSL3 laboratories and discussions with the persons responsible are suitable for this purpose. It is very valuable to establish such contacts in order to pick up experience. Planning offices are advised to supplement the planning team with a specialist experienced in BSL3 laboratories. Independent third-party opinions (reviews) during the planning phases can help to identify and avoid planning deficiencies and errors in good time.

Scope of the recommendation

This recommendation applies to BSL3 diagnostic and research laboratories where microorganisms are handled. It may nevertheless be applied, where appropriate, in production and animal facilities, greenhouses or invasive alien organism facilities.

Safety measures considered

The selection of safety measures taken into account is limited to those of a structural-technical nature according to Annex 4, number 2.1 ContainO [1] and Annex 2.3 MAO [3] and also considers those of the module "Establishments with Biological Hazard Potential" of the MAO manual [5]. Measures related to organisation, biosecurity, etc., are not considered if they are not of a structural-technical nature.

Project-related quality management

For the planning and realisation of a highly complex and demanding structure such as a BSL3 laboratory, the use of a PQM is necessary. The proposed requirements and test methods are part of the project-related quality management (PQM) [7], [8].

Commissioning and testing

The tests mainly take place during commissioning. This phase can take several weeks to months, depending on the size and complexity of the laboratory and the experience and competence of the planning and construction team. Validations of equipment, e.g., the autoclave, are not part of commissioning, with the exception of, for example, an automatic fumigation system, which must be set up by the supplier together with the operator for the intended fumigation process.

Continuous audit period

It is recommended that a so-called endurance test period of up to 12 months is contractually agreed after handover to the commissioning persons. During this period, the BSL3 laboratory should be used as realistically as possible, including all special operating conditions (e.g., fumigation, maintenance, etc.) [6].

# 4. Procedure in the Description of the Safety Measures

## 4.1 State-of-the-art in Safety Engineering

Requirements of the ContainO, PEMO, and MAO

The ContainO, PEMO, and MAO provide for special safety and protective precautionary measures with correspondingly different emphases.

Article 12 paragraph 2 ContainO states that the safety measures taken must consider the risk determined in each individual case and correspond to the state of the art in safety technology. According to Article 3 paragraph 1 of the Ordinance, the owner of an establishment must take all measures suitable for reducing the risk that are available according to the state of the art in safety technology, are supplemented on the basis of his experience and are economically viable. Article 8 paragraph 1 PEMO requires that to protect employees from risks to their safety and health from microorganisms, the employer must take all measures that are necessary according to experience, applicable according to the state of the art and appropriate to the given circumstances.

These safety measures are interrelated, as described in the module of the Handbook on the Major Accidents Ordinance (MAO), "Establishments with Biological Hazard Potential" [5] on page 11-12 (quote):
"The Containment Ordinance requires that the general safety measures listed in Annex 4 ContainO as well as the special safety measures required by the type and class of activity be taken. Furthermore, an operational safety concept must be drawn up. The safety measures taken must consider the risk determined for the individual case and correspond to the state of the art in safety technology. With the implementation of these provisions of the Containment Ordinance, the requirements for safety technology and protective measures according to the Major Accidents Ordinance are also covered."

Exemptions from the scope of the MAO

Establishments where an activity is carried out with genetically modified, pathogenic organisms or invasive alien organisms subject to containment that are assigned to Class 3 or 4 according to the Containment Ordinance of 9 May 2012 are subject to the Containment Ordinance. The competent, usually cantonal, enforcement authority may, under certain conditions, exclude establishments from the scope of application. This can be done for establishments which, according to Article 1 paragraph 2bis of the Containment Ordinance, only carry out Class 3 activities with organisms according to Annex 1.4 of the Containment Ordinance, where serious harm to the population and the environment can be ruled out.

State-of-the-art in safety engineering

The state of the art in safety technology is defined in the Federal Office for the Environment (FOEN) Handbook on the Major Accidents Ordinance (MAO), General Part [4], page 13, as follows (quote):

"Available according to the state of the art in safety technology are those measures that are successfully used in comparable installations in Switzerland or abroad under similar conditions and can be transferred to other installations. The state of the art in safety technology comprises all the technical knowledge about safety measures that is available in the specialist community and publicly accessible, but which may not yet have been generally introduced. The recognised rules of technology, on the other hand, comprise the generally introduced and proven technical knowledge as recorded in sets of rules, standards and manuals. The state of the art in safety technology thus goes beyond the recognised rules of technology in most cases. Information on the state of the art in safety technology is usually available in the relevant technical literature or from the relevant trade and industry associations."

Standards, regulations and manuals to specify the state of the art in safety technology

For this purpose, the following national and international standards and regulations are used to specify the state of the art in safety technology, insofar as they can be applied to BSL3 laboratories:

_ SIA standards (Swiss Society of Engineers and Architects)
_ German regulations
_ SN (Swiss norms), EN (Euronorms), and VDI standards (VDI, Association of German Engineers)
_ US, Canadian and Australian standards and guidelines
_ Biosafety manuals (e.g., WHO)

### 4.2 Focus and Content of the Recommendation

The state of the art in safety technology is always the subject of discussion, resulting in different safety standards for laboratories. This recommendation therefore describes safety measures for BSL3 laboratories according to the state of the art in safety technology as a matter of priority, if these are used successfully in Switzerland and abroad and can be transferred to Swiss conditions in accordance with Article 3 paragraph 1 MAO [3].

In second priority, the concretisation of the implementation of the safety measures according to the state of the art is explained, if these are well described in existing standards and regulations and can be applied to BSL3 laboratories.

The structural-technical measures mentioned in the module "Establishments with Biological Hazard Potential" of the Handbook of the MAO [5] on page 24 must be listed in the summary report pursuant to Article 5 of the Ordinance [3]. Legally binding for the application in BSL3 laboratories are the measures specified in Annex 4 number 2.1 ContainO [1] (analogous to Annex 3 no. 2 PEMO [2]) for safety level 3 facilities, which *must* correspond to the state of the art in safety technology. They are to be taken in addition to the general safety measures in accordance with Annex 4, para. 1 of the ContainO [1] and Article 8 as well as Annex 3 number 1 PEMO [2].

This recommendation deals with those structural-technical safety measures that require interpretation assistance, both in terms of the state of the art in safety engineering and in terms of their testing and requirements. The specified measures are listed in Table 1. Further mandatory requirements can be found in the above-mentioned ordinances [1],

[2], and additional recommendations for their implementation can be found in the module "Establishments with Biological Hazard Potential" [5].

| Chapter | Special safety measures according to Annex 4 number 2.1 ContainO [1] | Measures for establishments handling microorganisms according to Annex 2.3 MAO [2] and module "Establishments with Biological Hazard Potential" [5], page 24 |
|---|---|---|
| 5.1 | Work area sealed so that fumigation is possible (No. 11, *) | Sealable rooms that allow for fumigation |
| 5.2 | - | Ventilation system separated from the ventilation of the entire building |
| 5.3 | Exhaust air outlet from the work area via HEPA filter (no. 14*) | HEPA-filtered exhaust air |
| 5.4 | Work area under negative air pressure with respect to the immediate surroundings (No. 12*) | Permanent negative pressure in the laboratory and in the airlock (with two air pressure differentials) |
| 5.5 | Inactivation of microorganisms in contaminated material, in waste and on contaminated equipment (No. 36*) | Pass-through autoclave |
| 5.6 | - | Uninterruptible emergency power supply for selected equipment and for the control systems |
| 5.7 | - | Alarm system for equipment faults |
| 5.8 | - | Designing the floor as a catch basin for extinguishing water (or alternative measures) |
| 5.9 | Inactivation of microorganisms in the outflow of sinks, pipes and showers (No. 30*) | Waiving of discharging wastewater into the sewage system or complete inactivation of all wastewater |
| 5.10 | - | Compliance with earthquake safety standards |
| 5.11 | Rooms with easily cleanable floors and walls (No. 9, No. 10) | - |
| 5.11 | Surfaces resistant to water, acids, alkalis, solvents, disinfectants and decontaminants (No. 19) | - |

**Table 1. Safety measures for BSL3 laboratories considered in the recommendation according to ContainO [1], MAO [3] and the module "Establishments with Biological Hazard Potential" [5]. For explanations, see chapters 5.1 to 5.11.**
(*): The measure may be modified, replaced or omitted with the authorisation of the competent federal office.

# 5. Explanations of the Selected Measures

Target audience-specific information on the selected measures is given in chapters 6. and 7.

## 5.1 Sealable or Sealed Rooms

Basics

- ContainO: Annex 4 no. 2.1 ContainO, measure no. 11 [1]. This measure may be modified, replaced or omitted under certain conditions (Art.12 para. 3 let. a ContainO).
- PEMO: Annex 3 para. 2 PEMO, measure no. 11 [2]. Depending on the result of the risk assessment, deviations from the measure are possible (Annex 3.2 PEMO).
- MAO: Annex 2.3 let. c MAO [3] and module "Establishments with Biological Hazard Potential", p.24 [5].

Purpose

The purpose of sealable or sealed rooms is to prevent the escape of gaseous, vapour or mist-based chemical decontaminants during the "fumigation" of individual rooms, zones or the entire containment. This serves to protect the health of persons in the building and to maintain the required fumigation conditions. In addition, the requirement serves to check the quality of the tightness of the containment enclosure (in case of failure of the pressure cascades and the directional inward air flow).

Tightness

Tightness is a relative term. In engineering practice, a distinction is often made between "airtight" and "gastight", with higher requirements being placed on gastightness. For various structural systems or materials, i.e., ventilation ducts, dampers, ducts, HEPA filter housings, doors, etc., the tightness requirements are described in corresponding norms. The containment consists of a large number of structural systems and materials, the combination of which must be tested for leak tightness in the final construction.

Definition of containment for fumigation

For the purpose of fumigation, the containment includes not only the actual enclosure components of the work area such as walls, ceilings, floor, doors and windows, but also fumigatable personnel and material airlocks, ventilation ducts, media and cable penetrations, pass-through boxes, pass-through autoclaves and fumigatable parts of the ventilation system.

Fumigatable sections of the ventilation system

The sections of the ventilation system outside the containment that are considered for fumigation shall be designed gastight. The supply air ducts from the shut-off dampers on the supply air side to the containment and the exhaust air ducts from the containment to the shut-off dampers on the downstream side of the HEPA filter system must be gastight for reasons of durability and resistance, preferably made of welded stainless steel (for a description of the HEPA filter system and testing of gastightness, see chapter 5.3 ).

Planning and realisation

To achieve the requirements for the tightness of the containment, the mechanical durability and resistance of walls, wall panels, doors, windows and seals must be planned and executed with particular care.

Susceptibility to leakage

Particularly susceptible to leakage are the walls (wall system, wall structure, wall-floor and ceiling transitions), joints and penetrations. The mechanical robustness of the wall systems as well as the chemical resistance and porosity of the sealing materials are of particular importance in terms of value retention and maintenance costs. The walls, like all other enclosure components, can be exposed to large pressure fluctuations of up to ± 1000 Pa and can be damaged. Great attention must be paid to the choice of structural system and material as well as the installation of the walls during the realisation phase (see PQM, chapter 3. ).

Penetrations

From experience, special attention should be paid to sealing solutions for penetrations of cables, piping and ventilation ducts. The number of penetrations per room should be kept as small as possible. The concealed installation of cables, lines or pipes in the wall would be advantageous with regard to the "easy to clean" requirement but is disadvantageous with regard to the tightness requirement and later alterations or additions (see chapter 5.11 ). For the sealing of cables and pipes, multi cable and pipe transits have proven their worth, as they are used in fire protection and marine applications. With a view to later retrofitting, the multi transits are advantageously equipped with reserve installation openings.

Only cables, pipes and ventilation ducts that are required in the BSL3 laboratory may be laid (no through ducts).

Methods for measuring air tightness

There are basically two methods for measuring the air tightness of rooms:

1. Leakage air volume flow test (or pressure holding test): Measurement of the leakage flow at a constant room pressure.
2. Pressure drop and pressure rise test (pressure decay method): Measurement of the increase or decrease in pressure starting from the initial value within a period of time.

Rules and regulations

Worldwide, there are three sets of rules for measuring the tightness of BSL3 and BSL4 laboratories [9]. In North America, the pressure rise test is used for facilities with gastight doors. This method does not consider the surface area or volume of the tested space. It is well suited for leak testing of pass-through boxes or small rooms. In Australia, an air leakage volume flow test is used for BSL3 facilities, which also does not consider the surface area or volume of the tested space.

Leakage air volume flow test according to VDI 2083-19

Therefore, it is recommended to use the leakage air volume flow test of the third recognised set of rules, the VDI standard 2083-19 **Fehler! Verweisquelle konnte nicht gefunden werden.**. It considers the surface area of the room.

Testing methodology

The test is carried out for *each* door of the containment according to the "blower door test procedure" **Fehler! Verweisquelle konnte nicht gefunden werden.**, [11]. For this purpose, a wooden or metal clamping frame of variable size is inserted airtight in the door frame instead of the door. The clamping frame is covered with a firm plastic foil. Air is blown into the room through an opening in the foil with an adjustable fan until the test pressure is reached. The air volume flow or leakage flow to maintain the test pressure is measured.

In the case of airtight or gastight doors, a port for the air leakage volume flow test is required at a suitable point at the room or at the ducts.

During the test, the supply-air and exhaust-air shut-off dampers in the ventilation ducts remain closed.

Requirements

Experience has shown that test pressures lower than 125 Pa led to imprecisely measurable leakage currents in BSL3 laboratories due to the high tightness of the rooms [9]. The test for a room or a zone is passed if the limit values of leak tightness class 4 according to Table 2 **Fehler! Verweisquelle konnte nicht gefunden werden.** are met at a test pressure of +250 Pa or higher and at
-250 Pa or lower are complied with **Fehler! Verweisquelle konnte nicht gefunden werden.**.

| **Class** | **Test / reference pressure in Pa** | | | | |
|---|---|---|---|---|---|
| | **250** | **500** | **1000** | **2000** | **5000** |
| | Air permeability $qV_{, leakage, spec, \Delta p}$ in l/(m² -s) | | | | |
| 4 (BSL3) | 0,03620 | 0,05680 | 0,08913 | 0,13985 | 0,25371 |

**Table 2. Permissible air permeability of rooms. Excerpt from VDI Standard 2083 Part 19** Fehler! Verweisquelle konnte nicht gefunden werden.**. For BSL3 laboratories, the values for tightness class 4 apply.**

Pressure rise test

Active, decontamination pass-through boxes or frequently used decontamination material airlocks shall be tested with the pressure decay test due to their small volume [12]. For this purpose, air is extracted in the pass-through box or in the airlock with a blower via built-in connection pieces with a valve until the test negative pressure is reached. The valve is closed, and the pressure increase over time is recorded [12]. The test for the pass-through box or the material airlock is considered passed if the time for the pressure increase from- 500 Pa to -250 Pa or for the pressure drop from +500 Pa to +250 Pa takes at least 20 minutes [12].

Deviations

In justified cases, deviations from the proposed limit values may be made, for example if the containment is enclosed by a contamination-free safety corridor with complete exhaust air (without recirculation and with up to eight air changes per hour during fumigation). Deviations shall be supported by a risk assessment.

Leak detection

Leaks can be located and repaired with the (wet) hand, soapy water or smoke (flow tester for air). Subsequently, the tests must be repeated.

### 5.2 Ventilation System Separated From the Ventilation of the Entire Building

Basics

_ ContainO [1]: Not mentioned. Separate ventilation system is state of the art in safety engineering.
_ PEMO [2]: Not mentioned. Separate ventilation system is state of the art in safety engineering.
_ MAO: Annex 2.3 let. c MAO [3] and module "Establishments with Biological Hazard Potential", p.24 [5]. This measure concerns BSL3 laboratories that are subject to the MAO (Art. 1 para. 2, let. b, Art. 1 para. 3 let. b and Annex 2.3 MAO). Establishments that carry out an activity in accordance with Art. 1 para. 2bis let. A, and have been exempted from the scope of the MAO by the authorities, are excluded.

Purpose

This measure is an essential criterion of a BSL3 laboratory to ensure the safety, availability and reliability of the ventilation system for the following reasons (for additional information see chapter 5.4 ):

_ Maintaining the negative pressure in the containment (normal and fault operation)
_ Control of the ventilation in the individual rooms and compliance with the pressure differences in normal and special operation (prevention of reversal of the inward directional airflow).
_ Maintaining ventilation for as long as possible in the event of a fire alarm or fire outbreak in the entire building in coordination with the responsible authorities (fire police, building insurance)
_ Ensure that no unfiltered air from the BSL3 laboratory can enter the building as a whole.
_ HEPA filtration of the exhaust air from the containment; exhaust air routed via roof

Requirements; regulations

The principle of a separate ventilation system from the outside air intake to the exhaust air opening, including building automation, is state of the art in safety engineering ([12]-[17]).

The ventilation system of the BSL3 laboratory must continue to run even in the event of a fire in the rest of the building or if the heating or cooling system fails. In the event of a fire in the containment, it must continue to operate at negative pressure until the exhaust air HEPA filters block.

Outside air intake

The fresh air volume flow must not be influenced by other fresh air intakes. For general information on the fresh air intake, see [19].

Exhaust air opening

The exhaust air should be directed away from the roof in such a way that people on the roof or in neighbouring buildings are not endangered even if the HEPA filter is damaged (exhaust air velocity > 10 $ms^{-1}$; if feasible: air outlet 3 metres above accessible roof surfaces). For general information on exhaust air routing, see [19].

Structure of the ventilation system

All rooms of the containment, i.e., including personnel and material airlocks, should be ventilated with the BSL3-specific ventilation system [17]. Rooms outside the containment must not be ventilated with the BSL3 ventilation system.

The services area with all ventilation systems and components is preferably built on the floor above the BSL3 laboratory.

The supply and exhaust air ducts should be routed through the ceiling room by room. All components are set up in the services area, i.e., shut-off dampers, volume flow controllers and the HEPA filter system. The supply and exhaust air handlers can also be set up there. The shut-off dampers should be installed as close as possible to the containment boundary, i.e., from experience no further away than 1 metre (fumigation of the duct section up to the damper).

Accessibility to all components of the ventilation system must be guaranteed for maintenance and fumigation.

An exemplary sketch of a BSL3 ventilation system according to the state of the art in safety technology is shown in [17] shown.

### 5.3 HEPA-Filtered Exhaust Air, Exhaust Air of the Working Area via HEPA-Filter

Basics

_ ContainO: Annex 4 no. 2.1 ContainO, measure no. 14 [1]. This measure may be amended, replaced or omitted under certain conditions (Art.12 para. 3 let. a ContainO).
_ PEMO: Annex 3 para. 2 PEMO, measure no. 14 [2]. Depending on the result of the risk assessment, deviations from the measure are possible (Annex 3.2 PEMO).
_ MAO: Annex 2.3 let. c MAO [3] and module "Establishments with Biological Hazard Potential", p.24 [5]. This measure concerns BSL3 laboratories that are subject to the MAO (see Art. 1 par. 2bis MAO and Annex 1.4 MAO).

Purpose

The purpose of HEPA filtration of the exhaust air from the containment is to prevent aerosols and particles with microorganisms from escaping from the containment.

Requirements; regulations

There are no specific standards or norms for the construction, design and testing of HEPA filter systems in BSL3 laboratories. Therefore, established industry standards for the manufacture, installation and testing of HEPA filters are used as a basis and adapted in an appropriate way to the requirements and operation of a BSL3 laboratory (good engineering practice or state of the art safety technology: [20]-[26]).

Site

The HEPA filter system should be installed in the services area above the laboratory. An installation location in the containment is not recommended because of the difficulty of maintaining the filter system. If this variant is implemented, the exhaust air duct from the filter unit to the containment boundary must be gastight.

The exhaust air should flow horizontally through the filter housing. If, due to lack of space, a housing for vertical flow is chosen, the air must flow through the enclosure from top to bottom (position of the filter cassette seal at the top).
The space around the filter unit must be planned in such a way that access to the HEPA filter unit is guaranteed at all times (fumigation, testing, filter replacement, etc.). A space of at least 1 metre must be provided in front of the unit.

The requirements for the HEPA filter station include:
_ Filter class
_ Stainless steel filter housing
_ Pressure resistance of the filter housing
_ Gastight filter housing
_ Guarantee of fumigability in the installed state
_ Gas-tight butterfly valves and ventilation ducts
_ Tightness of the filter seat
_ Possibility to check the separation efficiency of the installed filter in *situ* during operation of the ventilation system (in operation)
_ Differential pressure indicator (protected by microfilter on the potentially contaminated side)
_ Tests

Filter classes

For BSL3 laboratories, HEPA filters of classes H13 or H14 are suitable. A pre-filter (F9) serves to protect the HEPA filter.

Stainless steel filter housing

Suitable HEPA filter housings are made of gastight welded stainless steel to ensure pressure resistance to large pressure fluctuations and fumigability with chemical decontaminants.

Pressure resistance test

The pressure resistance (mechanical strength) of the filter housing is tested before installation by the manufacturing companies at 2000 Pa according to [24], [25] or [26].

Fumigability

It must be possible to change and test the filters without contamination. For this purpose, butterfly valves and decontamination connections are necessary on the upstream and downstream sides. According to reports from the field, the use of plastic bags in *bag-in-bag-out (*BIBO) type filter housings is not recommended [27].

Gas tightness

The filter housing with the duct connections on both sides and the two shut-off dampers must be gastight. The shut-off dampers must also have a gastight test groove (see [24], [25] or [26]).

The leakage rate of the HEPA filter housing is tested after installation at 1000 Pa. It must be less than 0.1 per cent of the enclosure volume including duct sections between the shut-off dampers per minute [26].

*Nota bene*: The exhaust air ducts from the containment to the downstream shut-off damper of the HEPA filter unit must be gastight for reasons of durability and resistance, preferably made of welded stainless steel (see chapter 5.1 ).

Filter tests

HEPA filters must be subjected to a sealing seat test and a separation efficiency test after installation, annually and after a filter change. If the HEPA filter system does not have redundancy, filter changes and tests must be carried out after decontamination and decommissioning of the BSL3 laboratory, e.g., as part of laboratory maintenance. If the filter system has redundancy, the filter change and the tests can be carried out during operation after the filter system has been decontaminated.

Tightness of the filter seat

The filter seat must have a gastight test groove for the tightness test [25].

*In situ measurement of* the degree of separation

It must be possible to test the collection efficiency of the HEPA filter while the ventilation is running. Established and suitable industry standards as a basis for *in-situ measurement* are:

- SN EN 1822:2010. High efficiency air filters (EPA, HEPA and ULPA) - Part 4 (determining the efficiency of filter elements) and Part 5 (determining leakage of filter elements (scan method)) [21]; withdrawn)
- SN EN ISO 29463:2019. High-efficiency filters and filter media for removing particles in air – Part 4 (test method for determining leakage of filter elements-Scan method) – Part 5 (test method for filter elements) [22]. This standard is essentially based on the European standard EN 1822, which was withdrawn. Both EN 1822 and EN 29463 define the state of the art.
- SN EN ISO 14644-3:2020. Cleanrooms and associated controlled environments - Part 3: test methods [23].

The following points should be noted:

- The uniform application of the test aerosol to the filter surface must be ensured and, if possible, verified. The most suitable HEPA filter housings are those with integrated systems to achieve uniform exposure and distribution of the test aerosol on the filter surface [20]. Otherwise, for uniform exposure and distribution, the test aerosol must be fed into the duct at a distance of at least 10 duct diameters upstream of the filter, either via an injection port on the exhaust duct or in a laboratory room via an exhaust air opening. This usually results in sufficiently good mixing of the aerosol in the air stream.
- The particle count for measuring the separation efficiency is measured simultaneously on the upstream and downstream side. The separation efficiency can be determined in two ways:

- _ Best practice consists of a device for automatically scanning the filter surface using a measuring trolley (Part 5 of the Standards [21] and [22]).
- _ Not recommended is the so-called integral measurement at a downstream distance of at least 10 duct diameters (Part 4 of the Standards [21] and [22]). In this case, the duct section up to and including the sampling port must be built gastight (note: installation site of the filter system).

_ The cleanroom standard [23] can also be used with the scanning measurement method if uniform exposure to test aerosol is ensured.

Differential pressure indicator

The filters (including the pre-filters, if applicable) are equipped with a differential pressure indicator that determines the degree of filter loading and forwards a signal to the building automation system, if necessary. The differential pressure indicator visualises the pressure loss across both the pre-filter and the HEPA filter as a result of increasing load. With increasing pressure loss, energy consumption increases, and the performance of the ventilation system may be impaired. When the permissible final pressure loss is reached, the filter must be replaced. The pressure gauge or pressure display must be protected with a 0.45 µm filter on the potentially contaminated side.

Tests

_ Pressure resistance of the filter housing
_ Gas tightness of the filter system (in the section between the butterfly valves)
_ Tightness of the filter seat
_ Checking the filter separation efficiency: initial installation, annually and after replacement
_ Further requirements see above

### 5.4 Permanent Negative Pressure in the Laboratory and in the Airlock, Atmospheric Negative Pressure of the Work Area Compared to the Environment

Basics

_ ContainO: Annex 4 no. 2.1 ContainO, measure no. 12 [1]. This measure may be amended, replaced or omitted under certain conditions (Art.12 para. 3 let. a ContainO).
_ PEMO: Annex 3 para. 2 PEMO, measure no. 12 [2]. Depending on the result of the risk assessment, deviations from the measure are possible (Annex 3.2 PEMO).
_ MAO: Annex 2.3 let. c MAO [3] and module "Establishments with Biological Hazard Potential", p.24 [5]. This measure concerns BSL3 laboratories that are subject to the MAO (see Art. 1 par. 2bis MAO and Annex 1.4 MAO).

Purpose

To prevent aerosols and particles with microorganisms from escaping from the containment, a pressure difference is used to create a directional inward air flow from uncontaminated to potentially contaminated areas.

According to the ContainO and PEMO ([1], [2]), aerosol dispersion with microorganisms must be prevented (measure no. 22). There is not yet an established method for measuring aerosols laden with microorganisms in laboratories. Developments in this field must be followed.

Requirements; regulations

The state of the art in safety on this topic is addressed in a variety of biosafety standards, regulations and recommendations ([12]-[17]). This SECB recommendation proposes requirements that have already been implemented many times and successfully in established BSL3 laboratories in Switzerland, Europe, North America and Australia. For the HVAC specialist planning team[1] the state of safety technology in Germany is described in [18].

The requirements concern the following elements:

_ Pressure difference or cascade
_ Reference pressure
_ Maintaining the pressure differences in normal operation
_ Airlocks with lockable doors
_ Fault and special operation, alarming
_ Redundancy operation
_ Pressure displays
_ Air exchange rate
_ Alarm indicator for open doors
_ Fault messages and ventilation alarm
_ Tests

Pressure difference or cascade

In theory and practice, pressure differences between 20 and 30 Pa have proven to be effective [18], [28]. Pressure differences of less than 15 Pa or more than 60 Pa are not recommended. The necessary pressure zones are proposed by the facility and laboratory management to the HVAC planning office on the basis of a risk assessment. The latter designs the pressure cascade in such a way that there is no reversal of the air flow in either normal or special operation. The control is planned on a case-by-case basis. The quality of the control depends, among other things, on the selected pressure differences, the size and tightness of the rooms, the selected volume flow controllers and the building automation (control speed).

Reference pressure

The reference pressure is usually measured in a still place in the building, i.e., in a room without the influence of wind, ventilation systems, lifts or passenger traffic (door opening). It is also possible to measure the reference pressure above the roof with a pressure sensor that is not affected by wind and weather.

Normal operation

When doors are opened between two areas with different pressures during normal operation, the pressure difference across the door collapses and so does the inward airflow. The movement of the door leaf and people create turbulent air flows in the door opening and thus a mixing of the air between the two spaces [28].

Airlocks

For this reason, airlocks with interlocking doors must be present at the containment boundary. In combination with a high air exchange rate (see below), this minimises the probability of aerosols and particles containing microorganisms escaping from the containment.

[1] HVAC, heating, ventilation, air conditioning

The safety measure "permanent negative pressure in the laboratory and in the airlock (with two pressure levels)" mentioned in the module [5] means that there must be a pressure difference at both doors of the airlock to ensure the inward flow of air.

Fault operation and faults

Fault operation is understood as the failure or malfunction (faults) of parts of the ventilation system that lead to impermissible negative or positive pressures in the containment or individual rooms. Reversal of the air flow at the containment boundary (airlocks), or between rooms in the containment with different risks, is not permitted, even temporarily. If airflow reversal occurs between spaces of similar risk in the event of disturbances within the containment, this may be tolerated according to a risk assessment.

Possible malfunction scenarios are to be defined by the planning team in cooperation with the operator and the laboratory management in the planning for the specific facility in the description of functions (see below, operation and fault matrix). The system and its regulation and control must be planned, executed and tested accordingly during commissioning. This includes, for example, malfunctions and failure of supply or exhaust air handlers, dampers, volume flow controllers, sensors and the power supply. All faults in the ventilation system must be monitored and logged (trending).

Start-up and shut-down mode

Pressure fluctuations occur during start-up and shut-down in automatic mode. They can temporarily change abruptly into the positive (reversal of the air flow) or into the negative range. Extreme pressure fluctuations can be avoided by using suitable components (dampers, damper drives) and with the help of a suitable building automation system.

Alarms

The recording of malfunctions and alarms should distinguish between failures or malfunctions that require immediate action (e.g., fire in the containment) and those that allow work to be stopped and the BSL3 laboratory to be left (e.g., ventilation malfunction, failure of ventilation, power failure).

Failures and malfunctions must be indicated to staff in all rooms by appropriate audio and visual means. Audio alarms shall also be easily heard by employees wearing a Powered Air Purifying Respirator (PAPR) when working on a microbiological safety cabinet (MSC). In the description of functions, it must be defined which functions must be maintained in the event of a malfunction and for how long (uninterruptible power supply, (UPS), safety and backup lighting, door closure, overriding of door locks, etc.).

The alarm system must therefore be defined in coordination with the employees on a facility-specific and risk-based basis and must also be specified in the description of functions. In any case, it must be ensured that the facility can be safely evacuated in all cases of malfunction.

Redundancy operation

According to the state of the art in safety technology, the system must have redundancy operation for the failure of a supply air or exhaust air handler. It is recommended to operate the air handlers at 50 per cent of their capacity during normal operation (N+1, warm redundancy [5]).

If both exhaust air handlers fail at the same time or in immediate succession, the supply air handler(s) must be shut down immediately (hardware interlocking) to avoid a reversed, outward airflow from the laboratory. If the total ventilation failure is not due to power failure, a slight negative pressure can be maintained using a bypass emergency exhaust fan.

If one or both (if any) supply air handlers fail, the negative pressure and the pressure cascade in the containment must be secured in terms of control and regulation.

These operating faults must be defined in the description of functions and checked during commissioning.

For automatic switchover to emergency power and restoration of mains power supply, see section 5.6 .

High positive and negative pressures that could lead to damage to the enclosure components (see chapter 5.1 ) must be avoided at all costs. This operating fault must also be defined in the description of functions and checked during commissioning.

Pressure displays

Doors with pressure differentials must display the differential pressure on the entry side with an indication of the set range.

Air exchange rate

The total exhaust air volume flow from a room, together with the room cubature, defines the air change rate. During operating hours, it should be in the range of 10 to 12 per hour. Outside operating hours, the air exchange rate can be reduced to 6 per hour. Humidity and heat loads must be considered.

Cooling failure

The temperature in the containment is controlled by the air. Additional recirculating fan coil units (FCUs) are at most an option in areas outside the actual working area (discharge side autoclave). If the ventilation fails completely, temperatures will rise in rooms where equipment such as MSC, freezers, incubators, MGIT equipment[2] , etc. is present. Increased temperatures can lead to equipment damage or incorrect results. This must be considered when planning the ventilation system.

Open doors alarms

Doors with pressure differences may only remain open for a short time and must have an automatic door closer. If these doors are open, an alarm should sound after one minute. The pressure difference monitoring and control for the two connected rooms should be suspended during this time.

Fault messages and alarms

The description of functions should include an operation and fault matrix. An explanation and examples for the HVAC technical planning team are included in the appendix of [18].

[2] MGIT, Mycobacteria Growth Indicator Tube

Tests

All faults and operating states, including redundant operation, must be checked during commissioning and recorded in a results log. The choice of faults to be tested depends on the structure and design of the system according to the operation and fault matrix.

Door locks (incl. overriding in emergency situations) and door alarms are to be checked.

The pressure displays on the doors must be checked with a calibrated hand-held gauge.

The pressure differences, or the pressure cascade, as well as the alarms are recorded in accordance with [29] during normal operation, as well as for start-up and shut-down operation and redundancy operation (failure of redundant system parts, power failure). System reactions to failures of system equipment (e.g., dampers, volume flow controllers) are tested and recorded. Pressure differences should be recorded at least every 5 seconds [29].

### 5.5 Autoclave/Pass-through Autoclave; Inactivation of Microorganisms in Contaminated Material, in Waste and on Contaminated Equipment.

Basics

_ ContainO: Annex 4 no. 2.1 ContainO, measure no. 36 [1]. An autoclave must be available in the work area. If approved by the authorities, an autoclave may be used within the building or may be omitted altogether (see also Art. 12 para. 3 let. a ContainO). Other equivalent inactivation methods are permissible after validation.
_ PEMO: Annex 3 para. 2 PEMO, measure no. 36 [2]. An autoclave must be available in the work area. Depending on the result of the risk assessment, an autoclave may be used within the building or omitted altogether. Other equivalent, validated inactivation methods are permissible.
_ MAO: Annex 2.3 let. c MAO [3] and module "Establishments with Biological Hazard Potential", p.24 [5].

Purpose

To prevent the spread of pathogenic microorganisms on materials and equipment and their escape via waste, all potentially contaminated materials and equipment as well as all potentially contaminated waste[3] must be inactivated [1]. This is classically done by autoclaving, see also [30] or [31].

The autoclaving conditions to be selected must be adapted to the autoclaved material, validated, and documented [32]. Other inactivation methods are possible. Specific information on the treatment and disposal of relevant wastes can be found in the relevant SECB recommendation [32].

Requirements

With regard to ensuring BSL3 containment, the following device parameters are state of the art in safety technology:

[3] In this chapter on autoclaves, a distinction is only made between liquid and solid waste.
This differs from the definition of "waste" as used by the authorities on the ECOGEN platform. There, a distinction is made between three forms of waste: (1) liquid waste, (2) solid waste, by which is meant microbial cultures on agar plates, slant and stab cultures and other forms of microbial cultures, and (3) other contaminated waste, which includes, for example, monolayer cell cultures, 3D tissue cultures, etc.

- The choice of autoclave type (single-door autoclave in the laboratory or pass-through autoclave) is risk-based. A pass-through autoclave (see [1], [5]) has the advantage over a single-door unit that it can be unloaded, monitored, and maintained from outside the containment and no work instructions are necessary for the safe removal of the decontaminated waste.
- Vacuum autoclaves (class B with fractionated vacuum cycles) are state of the art in safety technology.
- Pass-through autoclaves:
  - Possibility of maintenance from outside the BSL3 laboratory [17].
  - Interlocking of the two doors. Door opening from outside only after trouble-free completion of the process.
  - Gas-tight installation in the containment perimeter by means of a temperature-resistant and elastic flange seal ("Bioseal" s. chapter 5.1 ) and gastight pipe penetrations.
  - Controls on both sides or on one side to be defined.
- Single-door autoclaves in the laboratory and pass-through autoclaves:
  - Safe thermal inactivation of condensate; no dead volumes. In normal operation, condensate is automatically autoclaved.
  - Exhaust air sterilisation, e.g., thermal or by means of sterile filtration [33] (select suitable particle category). In normal operation, autoclave exhaust air is automatically decontaminated.
  - Chamber burst protection (pressure relief) via safety valve or burst disc. Safety valves can also leak easily or blow off uncontrollably during normal operation. To prevent a release, the following methods are used by the manufacturing companies: For example, downstream monitored rupture disc (to detect slightly leaking safety valves), blowing off into a decontaminable pressure relief or expansion tank [35].

Device type and selection

Before selecting the autoclave, some fundamental decisions must be made that have consequences for the structural-technical planning and operation.

An autoclave with an integrated steam generator is often preferable to an autoclave with steam provided by a boiler, since the boiler creates an additional risk of failure or malfunction.

The installation of a redundant autoclave must be decided on a case-by-case basis (see below).

The autoclave must be selected so that the decontamination of the expected autoclaved material (liquid, solid, porous, thermostability of the organisms, maximum volume to be autoclaved, etc.) can be carried out safely. The state of the art in safety technology is that the autoclave has fractionated vacuum cycles which can be adapted according to the type of waste (validation required, also of predefined programme cycles).

Certification according to the Medical Devices Ordinance (MedDO, [34]) is not necessary.

Other autoclave parameters

- Suitable vacuum programmes or programmable fractionated vacuum cycles
- If required, support pressure for autoclaving large volumes of liquids and rapid cooling (observe safety measures for autoclaving liquids)
- Suitable volume
- Throughput performance: Throughput analysis considering chamber geometry, planned loads and batch times
- Suitable temperature and pressure range, often up to 140°C and 4 bar absolute pressure
- Outside temperature of the autoclave surface maximum 60°C
- Doors locked until pressure equalisation and until cooling below 60°C
- Display concerning normal, fault and special operation
- Alarm and emergency stop
- Data recording, data backup or data transfer, e.g., printer, network connection or USB

Planning

It is essential that the type of autoclave, the throughput capacity, the number and the positioning are already defined in the planning phase in order to determine the associated structural-technical specifications:

- Safe collection, storage and transport routes for the autoclaved material before and after the autoclaving process (see also PEMO Art. 8, par. 2, let. f).
- Sufficient and secured storage space for autoclaved items in containers or bags on both the potentially contaminated and contamination-free sides. Sufficient space in front of the autoclaves for manoeuvring trolleys with autoclaved goods. On the contamination-free side, a sink with a sufficiently large basin and shelf is recommended, especially if liquids are autoclaved.
- Required power supply (240 V or 400 V)
- Required compressed air
- Water connections (demineralised water for steam generation, cooling water). All water connections should have easily accessible stopcocks (or water stoppers).
- Sewage system connection on the contamination-free side
- Further technical measures, if necessary:
  - Room dehumidification and odour neutralisation on the discharge side (e.g., separate room with negative pressure, exhaust air, storm ventilation, etc.).
  - Cooling with recirculating fan coil units (FCUs) on the maintenance side (not BSL3). FCUs are not recommended in the actual work area (maintenance, dust, decontamination of the condensate).
  - If the autoclave is also intended for sterilising media etc. for use in the BSL3 laboratory, these measures must be observed both on the non-containment and on the containment side.

Redundancy operation

It is recommended to check whether a second, redundant autoclave should be installed to ensure throughput (repairs, maintenance) [14]. In normal operation, both autoclaves should be used.

The decision on this is to be made for the respective operation based on the volume of the autoclavable material that accumulates daily, the space for its safe storage and the possibility of alternative, validated inactivation methods in the event of a malfunction

and during special operation (e.g., maintenance of the autoclaves). The handling of contaminated materials, equipment and waste that arise until the malfunction is rectified, until the maintenance work is completed, or until the work is completed safely must be assessed.

The availability of a second autoclave also enables continued, possibly reduced BSL3 operation in case of failure of one unit. This is therefore also an operationally relevant decision.

Tests

All malfunction scenarios and the various operating cycles must be checked during commissioning and regular maintenance work and recorded in a results log. The choice of relevant malfunction scenarios depends on the autoclave type according to the operation and fault matrix.

Relevant examples of tests are:

- Programmes and cycles with calibrated data loggers and, if necessary, supplementary bioindicators. Special attention must be paid to their correct placement[4] .
- Display, data acquisition and securing of the programme sequence
- Alarms
- Abort and emergency stop button
- Door seals
- Door interlocking and unlocking after pressure relief and cooling below 60°C
- Outside temperature at the unit: It should not exceed 60°C over the entire operating time.
- Exhaust air system and exhaust air decontamination
- Wastewater / condensate drain and its inactivation system
- Additionally for pass-through autoclaves:
  - Opening of the doors (door interlocking, airlock function between containment and non-containment area)
  - Leak detection around wall-flange (bioseal)
    (see chapter 5.1 )

### 5.6 Uninterruptible Emergency Power Supply for Selected Units and for the Controls

Basics

- ContainO [1]: Not mentioned. Uninterruptible emergency power supply for selected units and for the controls is state of the art in safety technology.
- PEMO [2]: Not mentioned. Uninterruptible emergency power supply for selected units and for the controls is state of the art in safety technology.
- MAO: Annex 2.3 let. c MAO [3] and module "Establishments with Biological Hazard Potential", p.24 [5]. This measure concerns BSL3 laboratories that are subject to the MAO (Art. 1 para. 2, let. b, Art. 1 para. 3 let. b and Annex 2.3 MAO). Establishments

[4] When simulating the autoclaving of liquids, the test temperature logger as well as the autoclave's own load sensor must be placed in a reference vessel filled to the largest volume. The reference vessel must be made of the same material (plastic, metal) as the standard liquid waste vessels.
When autoclaving solid waste in autoclave bags, the test temperature loggers must be placed in various locations within the simulated, uncontaminated autoclave load that are difficult for the steam to access.

that carry out an activity in accordance with Art. 1 para. 2bis let. a, and have been exempted from the scope of the MAO by the authorities, are excluded.

Purpose

The uninterruptible emergency power supply is used to safeguard ongoing work with microorganisms and their storage, etc., as well as to ensure the orderly and safe termination of work and the orderly exit from the BSL3 laboratory in the event of a malfunction or failure of relevant system parts. In the event of fire in the building, the power supply shall be ensured for as long as possible. For details on the planning, commissioning and testing of the alarms and procedures, see chapter 5.7 .

Requirements; regulations

The state of the art in safety technology on this topic is covered in a large number of biosafety standards, regulations and recommendations ([12]-[17]).

The requirements concern:
_ Emergency power generator
_ Uninterruptible power supply (UPS)
_ Connected systems and devices

Emergency power supply

All safety-relevant technical equipment and devices must have an emergency power supply:
_ Ventilation system (only emergency generator)
_ Ventilation control and regulation components
_ Building automation
_ Door control
_ Pressure displays
_ Communication systems (two independent, redundant systems)
_ Fault messages and alarms for laboratory staff and management
_ Emergency call and monitoring systems
_ Safety lighting, escape door control
_ Fire control system
_ Microbiological safety cabinets and other primary containment devices

The switchover from mains power to UPS or emergency generator takes place automatically.

The power supply shall be provided at least for the duration of the orderly and safe completion of the work and the orderly exit from the BSL3 laboratory.

Emergency power generator

An emergency generator shall be provided for the emergency power supply. In the event of a mains power failure, the power supply shall switch over to the generator in less than 15 seconds. The switching operation shall be tested at least annually. The switching processes can generate abrupt and temporary strong pressure fluctuations. These must be considered when planning the system (complete failure of ventilation, start-up in automatic mode).

Uninterruptible power supply (UPS)

In Germany, a UPS system is compulsory for all technical installations and equipment, including the ventilation system [17]. As the state of safety technology in Switzerland, it

is proposed for research and diagnostic laboratories to support all technical facilities and equipment with UPS, with the exception of the ventilation system. All work with microorganisms is carried out in primary containment systems (e.g., in the MSC). In the event of a failure of the ventilation system, until it is restarted in automatic mode and normal operating conditions are restored, organisational measures must be taken (this usually takes 30 to 120 seconds). Employees shall be informed of the operating status by audible and visual alarms (alarms and alarm resets, monitoring).

Tests

_ Function of automatic switching from mains power to emergency power according to the requirements
_ Function of automatic switchover from emergency power to mains power
_ Ensuring the running times of the emergency generator and the UPS system for the required duration
_ Check for permanent maintenance of the inward air flow (see chapter 5.4 ). Reversal of air flows within the actual working area, e.g., between different pressure zones, shall be evaluated with a risk assessment.
_ The behaviour of laboratory personnel must be regulated and trained organisationally (closing doors, ending work, etc.).

### 5.7 Alarm System for Equipment Faults

Basics

_ ContainO [1]: Not mentioned. An alarm system is state of the art in safety technology.
_ PEMO [2]: Not mentioned. An alarm system is state of the art in safety technology.
_ MAO: Annex 2.3 let. c MAO [3] and module "Establishments with Biological Hazard Potential", p.24 [5]. This measure concerns BSL3 laboratories that are subject to the MAO (Art. 1 para. 2, let. b, Art. 1 para. 3 let. b and Annex 2.3 MAO). Establishments that carry out an activity in accordance with Art. 1 para. 2bis let. a, and have been exempted from the scope of the MAO by the authorities, are excluded.

Purpose

Failures, faults and malfunctions in structural-technical systems that can result in personal injury, environmental damage or damage to property are safeguarded via alarms and/or fault messages.
Based on a risk assessment, additional laboratory equipment important for operation and safety can be secured.

Alarms and fault messages are used by the staff in the containment and, if available, by a control centre to detect faults. Special operating conditions are also monitored.

Uniqueness of BSL3 laboratories

Each BSL3 laboratory is unique. The arrangement and function of airlocks and rooms in the containment, of ventilation systems, other safety-relevant technical equipment and devices as well as the building automation differ from laboratory to laboratory. The building automation must be suitable and flexibly adaptable for the control, regulation and monitoring of a BSL3 laboratory. Various suitable products are available on the market and must be adaptable to the conditions. When planning BSL3 laboratories, the corresponding requirements must be defined at an early stage.

Outline of the procedure

There are no standards or norms for the design, execution and testing of building automation and alarm systems of BSL3 laboratories. This recommendation outlines the state of good engineering practice on this subject area.

Requirements specifications

The requirements are to be written by the commissioning party in the preliminary project (programming phase, concept design) as a draft and in the detailed design phase in detail in the requirements specifications.

Signalling of the operating states

As a rule, a distinction is made between:
_ Normal operation or automatic operation
_ Malfunctions
_ Special operation

Dealing with special operating states and alarms

Muting of alarms and fault messages during special operating conditions (e.g., maintenance, fumigation) shall be regulated. Attention must be paid to resetting alarms, acknowledgement and reporting to the facility (incl. organisational measures).

Normal operating conditions

For the identification and allocation of possible faults to priorities and the resulting alarms and messages, it is imperative that building services and ICE[5] specialists, together with the laboratory management and the persons responsible for biosafety, describe the various operating states and possible faults in the aforementioned operation and fault matrix, define the processes and determine the reactions of the building automation, messages and alarms for:
_ Starting up and shutting down the system
_ Automatic operation: automatic measurement, control and regulation of all system parameters, in particular the ventilation system and all safety-relevant technical equipment and devices, both in the idle state and during work processes (door opening and closing, changing heat loads, etc.). Based on the requirement specifications, equipment for research and diagnostics is also considered (e.g., cooling equipment, microbiological safety cabinets, etc.).
_ Maintenance work, trial operation
_ Decommissioning, fumigation
_ Acknowledgement of alarms
_ If necessary, differentiation between day and night operation for the purpose of energy saving.

Setpoints, limit values, tolerance ranges

Setpoints, limit values, tolerance ranges, etc. are defined for the normal operating states. The normal state is monitored by the building automation system on this basis. The building automation must be able to automatically ensure compliance with the defined setpoints and limit values at all times.

Trending

The building automation system should continuously record the parameters over time (trending). A separate system should be set up for collecting the trending data. Extracting data from the normal management level of the building is usually difficult.

[5] ICE: instrumentation and control engineering

Priority levels

Faults and alarms shall be classified in priority levels. They shall be defined with the persons responsible for biosafety. The reaction of the employees to the alarms and messages must be regulated organisationally. Based on the alarm message, they know whether the work must be stopped and secured, whether it is possible to wait in the actual work area until the malfunction has been rectified or whether the containment must be left immediately.

Faults, alarms and messages

If a tolerance range or a setpoint is exceeded or undershot for a certain time (timer), this is a malfunction or failure. Failures mean that a system or a technical device is no longer available. It can also be only a minor malfunction (irregularity) that does not affect operation, for example the failure of a lighting unit, which is not necessarily reported automatically. It is up to the laboratory management, the persons responsible for biosafety, and the building services and I&C specialists to decide which malfunctions are minor, so that a report without an alarm is sufficient.

Alarm-based systems

According to the rules of safety engineering, at least the following systems should be alarm-supported:

_ Fire in the building or in the containment (see next section for details).
_ Ventilation system: Failure or major deviation of pressure control or volume flow rate
_ Ventilation control and regulation components
_ Heating or cooling system failure
_ Mains power failure
_ Loading of filter systems
_ Door control: Malfunctions of automatic door closures
_ Communication systems
_ Emergency call and monitoring systems (emergency button, person-down system)
_ Failure of the effluent decontamination system (EDS, if present)
_ Biosecurity: intrusion, unauthorised entry into the containment, etc.
_ Risk-based: Failure or malfunction of primary containment equipment (e.g., microbiological safety cabinets) and other laboratory equipment (e.g., refrigeration equipment)

Fire alarm system

The fire detection system and the location of the detectors on the ceiling must be coordinated with the ventilation system and the exhaust air openings in the ceiling of the BSL3 laboratory to prevent smoke from being extracted and not detected. One solution is to install additional smoke detectors in the exhaust air ducts, although the laminar flow and air velocity in the exhaust air ducts are unfavourable for smoke detection.

The delay time for alarm triggering must be weighed due to the high air exchange rate in the containment.

Alarm stations

Audio alarms: Loud signal tone for primary warning of staff. The alarm is reset after the fault has been rectified, or it can be muted by authorised personnel. Audible alarms must also be heard when working on the MSC and when wearing PAPRs (Powered Air Purifying Respirators).

Visual alarms: Enable the type of alarm and the priority to be recognised, for example by means of colours. The alarm is reset after the fault has been rectified.

The audible and visual alarms for priority 1 malfunctions are always triggered in the containment and outside at all entrances, pass-through boxes and dunk tanks. The alarm is forwarded via suitable systems to the responsible persons and, if available, to the control centre. The messages are displayed or explained on control panels with monitors in the containment and at the entrances to the laboratories. Authorized persons can follow the time sequence of the malfunction via the control panels and correct it if possible.

Signalling: Examples

- Normal/automatic operation (e.g., optical indicator on green): All functions and states are within the set range.
- Priority 2 malfunction (e.g., optical indicator on yellow, sound) includes malfunctions for which there is no immediate need for action (yet), for example:
  - Minor deviations in pressure control, but pressure cascade still adhered to, timer (permitted time period) not exceeded. If the time element is exceeded, a priority 1 alarm is triggered.
  - Fire alarm outside the containment (pre-alarm)
  - Malfunction of the automatic door closing. To be distinguished from the case door is kept open beyond the defined permitted time period (timer).
- Priority 1 includes faults for which immediate action is required, e.g.:
  - Fire in the containment
  - Failure or deviation in pressure control (pressure levels are permanently not maintained)
- Minor disturbances (irregularities) only trigger a message (e.g., to the control centre, to responsible persons or to control panels with monitors in the containment and at the entrances), but no alarm.

The aforementioned matrix describes the possible faults, failures, fire alarms, and other emergencies (e.g., medical) for the BSL3 laboratory in question for all operating conditions, as well as the building automation system responses and prioritisation.

The availability of all safety-relevant technical equipment and devices (see chapter 5.6 ) must be ensured in the alarm state.

Tests

All fault messages and alarms must be tested.

### 5.8 Design of the Floor as a Catch Basin for Extinguishing Water (or Alternative Measures)

Basics

- ContainO [1]: Not mentioned.
- PEMO [2]: Not mentioned.
- MAO: Annex 2.3 let. c MAO [3] and module "Establishments with Biological Hazard Potential", p.24 [5]. This measure concerns BSL3 laboratories that are subject to the MAO (Art. 1 para. 2, let. b, Art. 1 para. 3 let. b and Annex 2.3 MAO). Establishments that carry out an activity in accordance with Art. 1 para. 2bis let. a, and have been exempted from the scope of the MAO by the authorities, are excluded.

Purpose

The spread of potentially contaminated extinguishing water from the containment must be prevented by retaining the extinguishing water [37]. For this purpose, laboratories and airlocks are designed as catch basins with sufficient retention volume in water-based extinguishing concepts, so that the resulting extinguishing water can be completely collected during manual firefighting or, if available, during the use of water-based automatic extinguishing systems.

Requirements; rules and regulations

The areas affected in each case must be kept as small as possible and the use of water must be minimised as far as possible [37]. The fire protection concept includes the extinguishing systems and the retention of extinguishing water. Afterwards, the extinguishing water must be inactivated *in situ* with appropriate protective measures, pumped out or diverted[6] and subsequently inactivated.

Catch basin concept

Retention of the calculated extinguishing water volume [37][7] is realised in the design of the respective room as a catch basin with an upstand corresponding to the extinguishing water volume calculation over the coving at the floor-wall connection and with extinguishing water barriers (doorway water barrier) at the same height in the door areas.

If a swing-over bench is used in the airlock, it can be used as an extinguishing water barrier.

The extinguishing water volume and the height of the side upstands and door barriers are lower for high-pressure spray systems than for low-pressure spray systems [38]. Upstands and water barriers must be significantly higher for sprinkler systems. In the case of manual extinguishing by the fire brigade (lance or fire extinguisher), the volume of extinguishing water is usually rather low, but in individual cases, large volumes of extinguishing water can also occur in the containment area.

A low, solid door threshold is usually sufficient for spray systems, a higher solid threshold is necessary for sprinkler systems, which should be sloped on both sides to prevent uneven threshold conditions (trip hazard). Higher expected volumes of extinguishing water, for which doorway water barriers would have to be set manually or automatically, should be avoided.

When using automatic extinguishing systems, consider whether the airlock should be planned with further raised upstands and an automatic doorway water barrier. This way, in the event of unexpectedly high volumes of extinguishing water, the airlock can prevent it from escaping into the non-BSL3 area and, conversely, the doorway water barrier blocks the flow of extinguishing water into the BSL3 area when a sprinkler system is triggered in the non-BSL3 area.

Suitable extinguishing systems for BSL3 laboratories include:

[6] Discharge, for example, into a dedicated BSL3 extinguishing water collection tank with subsequent wastewater decontamination. For the discharge, the floor must slope towards a floor drain (fire-resistant, tight-closing and only to be opened for discharge in the event of fire extinguishing).

[7] The required extinguishing water retention volume can be calculated using the Guide to Practice 'Extinguishing Water Retention [37] (Appendix A).

_ Spray extinguishing systems [39] extinguish by cooling and oxygen extraction, no danger to persons, good extinguishing effect; as a rule, for even thresholds conditions, slopes (trip prevention) should be used as a barrier.
_ Special extinguishing systems with pentanone compounds [38] extinguish via cooling, no danger to persons, good extinguishing effect; interruption of operation comparatively short, no water damage.

Test

Visual inspections for damage and maintenance of the upstands, doors thresholds and/or doorway water barriers must be carried out regularly, at least annually.

### 5.9 Waiving of Discharging Wastewater Into the Sewage System or Complete Inactivation of all Wastewater; Inactivate Microorganisms in the Outflow of Sinks, Pipes and Showers.

Basics

_ ContainO: Annex 4 no. 2.1 ContainO, measure no. 30 [1]: Inactivation of microorganisms in the outflow of sinks, pipes and showers. This measure may be modified, replaced or omitted with the authorisation of the competent federal office (Art.12 para. 3 let. a ContainO).
_ ContainO: Annex 3 para. 2 PEMO, measure no. 30 [2]. Depending on the result of the risk assessment, deviations from the measure are possible (Annex 3.2 PEMO).
_ MAO: Annex 2.3 let. c MAO [3] and module "Establishments with Biological Hazard Potential", p.24 [5]. This measure concerns BSL3 laboratories that are subject to the MAO (see Art. 1 par. 2bis MAO and Annex 1.4 MAO).

Purpose

This measure serves to prevent organisms from escaping from the containment via possibly contaminated wastewater.

Dry lab

Ideally, a microbiology or cell culture BSL3 laboratory should be designed as a dry laboratory, i.e., without sinks in the actual work area and in the potentially contaminated area of the airlock, and without a shower.

Any liquid waste generated must be inactivated and discharged via autoclaving or alternative suitable and validated methods.

Small amounts of liquid (residues in tubes, multiwell plates, etc.) can be autoclaved with the solid waste.

Reusable materials should first be autoclaved, discharged and then washed in a non-BSL3 area. The use of non-shatterproof reusable materials, especially glass, is not state of the art safety technology in BSL3 laboratories for research and diagnostics because of the risk of injury.

There should be no floor drains. An exception, if defined accordingly in the fire protection concept, are permanently closed floor drains exclusively for the discharge of extinguishing water.

Emergency systems

As a rule, self-contained eye-washers according to DIN EN 15154 without a water connection are suitable as emergency device [40]. This must be determined in advance in

the risk assessment. The use and collection measures of the liquid used (often sterile physiological saline solution) must be defined and trained.

Emergency safety shower stations with water connections in the work area and the airlocks should be avoided as far as possible based on the risk assessment. The use of emergency safety showers (drench showers) to shower off biologically contaminated persons is contraindicated.

If systems with a water connection have to be used, they should be tested regularly and standing water must be prevented. Collection and decontamination measures for leaking water must be tested, defined and trained for both testing and use.

Shower system in the airlock

If required, an emergency shower cubicle with wastewater collection tank can be installed on the potentially contaminated side of the airlock, based on risk. The contents of the wastewater tank can then be manually chemically inactivated or has an integrated thermal inactivation system. The capacity of the tank should be sized according to the needs of a suitable shower cycle.

Such showers can also be useful when dealing with organisms that are particularly easy to carry and survive for a long time. Here, showering at the end of work can also make sense on a risk-based defined standard basis. In such cases, the shower can also be designed as a "shower airlock" to be used as needed in the airlock area next to the normal changeover area from the potentially contaminated to the non-contaminated side. The shower water must be fed to an inactivation system with appropriate throughput capacity.

Hand basin

A hands-free disinfectant dispenser must be provided on the potentially contaminated side of the airlock, ideally in such a way that it can also be used before crossing over to the non-contaminated side.

A hand-washing basin should only be provided on the non-contaminated side of the airlock near the exit door. Here, a thermal inactivation system under the washbasin could be used for wastewater decontamination. With the authorisation of the competent federal office, however, a decontamination system at the hand-washing basin can be dispensed with, since no further contamination is to be expected if a double-glove concept is adhered to and, if necessary, hand disinfection is carried out beforehand when washing hands.

Wet laboratories

If water connections, wash basins and drainage systems (e.g., from bioreactors) are nevertheless to be installed in the containment, any wastewater that arises must be decontaminated. This can be done via individual autonomous wastewater collection tanks with chemical and/or thermal inactivation systems (in the case of bioreactors, possibly *in situ* inactivation) or via a central effluent decontamination system.

Drinking water protection

Drinking water supply lines into the containment must be protected against backflow (system separation of class 5 in accordance with [41]).

Effluent decontamination system, EDS

As soon as contaminated wastewater is fed into a central effluent decontamination system, it must be decided whether this should be designed as a continuous system (thermal) or as a batch system with thermal and / or chemical inactivation.

An effluent decontamination system must have sufficient tank and throughput capacity and, if required, additional, redundant tank capacity for maintenance and repair. Pressure relief valves with exhaust air filtration, an electronic control system, level indicators and an alarm system are state of the art.
Tanks, piping and fittings must be tightly welded, regularly inspected and accessible from outside. The piping must be decontaminable in sections [42]. Non-return valves must be provided.

It is essential to pay attention to the suitability (pressure development, reactivity) and material compatibility (chemical resistance, even at elevated temperatures) of decontamination agents used in the laboratory.

The tank system itself is to be installed as a primary containment in a containment located under the BSL3 laboratory conforming to the corresponding specifications for safety level 3 laboratories. In the event of leaks from tanks, piping and fittings or potentially non-contamination-free maintenance work, appropriate measures are already to be taken into account in the planning of the effluent decontamination system (e.g. catch basins, decontamination, enclosure of the work site, use of personal protective equipment) [36].

Siphons

Discharges of potentially contaminated wastewater into central collection tanks must have devices for decontamination of the piping (e.g., siphon solutions), connections and shut-off (stopcocks for maintenance work).

The water column in siphons must be sufficiently high for the possible air pressure fluctuations (static pressure of the air handlers, incl. safety factor). Ventilation lines from the containment, equipped with a moisture-resistant sterile filter, can be discharged via the roof (separate line from other systems in the building) or into the collection tank of the effluent decontamination system [42].

Tests

_ Gas and liquid tightness of piping, fittings and containers
_ Calibrations, functional tests, acceptance tests according to the manufacturer's company
_ Display, data acquisition and securing of the programme sequence
_ Alarms
_ Abort and emergency stop button
_ Support of the operation by the manufacturing company in the validation of the effluent decontamination system
_ Outside temperature at thermal systems: It should not exceed 60°C over the entire operating time.
_ Exhaust air system (vent lines) and exhaust air decontamination

### 5.10 Compliance with Earthquake Safety Standards

Basics

_ ContainO [1]: Not mentioned.
_ PEMO [2]: Not mentioned.
_ MAO: Annex 2.3 let. c MAO [3] and module "Establishments with Biological Hazard Potential", p.24 [5]. This measure concerns BSL3 laboratories that are subject to the MAO (Art. 1 para. 2, let. b, Art. 1 para. 3 let. b and Annex 2.3 MAO). Establishments that carry out an activity in accordance with Art. 1 para. 2bis let. a, and have been exempted from the scope of the MAO by the authorities, are excluded.

Purpose

Earthquake-compatible planning of structures aims at protecting people, limiting damage and guaranteeing the functionality of the structure when affected by the design earthquake.

Requirements; regulations

Structures are divided into three structural classes (BWK, building class) based on their significance ([43]-[45]). BSL3 laboratories that are subject to the MAO are classified at least in BWK II because of the possibility that the population or the environment may be harmed. According to [45], the following applies (quote, paragraph 9.1.7): "For structures that are subject to the Major Accidents Ordinance and for which a risk assessment is required, the degree of protection shall be determined on the basis of the risk assessment. All other structures posing a risk to the environment must meet the requirements of structure classes BWK II, BWK II-i or BWK III in relation to the environmental hazard they pose."

Test

The planning or specialist planning office must provide proof of structural safety for the load-bearing elements of the building and for the actual containment ([5], [43]-[45]). The containment comprises the enclosure components of the BSL3 laboratory such as walls, ceilings, floor, doors and windows as well as the components of the ventilation system and, if present, the effluent decontamination system that can potentially become contaminated.

### 5.11 Rooms With Easily Washable Floors and Walls and Surfaces and Resistant to Water, Acids, Alkalis, Solvents, Disinfectants and Decontamination Agents

Basics

_ ContainO: Annex 4 no. 2.1 ContainO, Measures no. 9, 10 and 19 [1]
_ PEMO: Annex 3 para. 2 PEMO, measures no. 9, 10 and 19 [2]
_ MAO: Annex 2.3 MAO [2] and module "Establishments with Biological Hazard Potential", p.24 [5] not mentioned.

Purpose

The purpose of these measures is the cleanability of surfaces in containment with commercially available detergents and their resistance to chemical decontaminants. The use of hydrogen peroxide ($H_2O_2$, concentration up to 35 per cent), chlorine-containing compounds and other chemical agents for surface decontamination shall be considered.

Definition of containment for surface decontamination

For the purpose of decontamination, the containment of a BSL3 laboratory includes not only the actual enclosing components of the work area such as walls, ceilings, floor, doors and windows, but also personnel and material airlocks, ventilation ducts, media

and cable penetrations, pass-through boxes, pass-through autoclaves that may become contaminated and, if present, the effluent decontamination system, in particular the piping carrying the wastewater.

Surfaces

Surfaces are understood to include floors, ceilings, walls, supports, but also laboratory furniture, microbiological safety cabinets, pipes, luminaires, fittings, etc.

Requirements

Easily washable means "easily accessible", i.e., surfaces should be fully accessible by hand or aids (e.g., ladders, wipers/mops with sticks). All surfaces must be smooth and non-porous (no raw concrete surfaces). Joints must be filled completely and evenly. The joint filling must be durable and resistant to chemical decontamination agents.

Floors and walls

Floors must be tight, closed, wear-resistant and as joint-free as possible. Resistance to point loads (e.g., heavy transport trolleys, furniture) must be considered. Wall connections must be made with coved profiles with an upstand of 5-10 cm (height depends on the type of firefighting, i.e., water retention for sprinkler and extinguishing water).

Floors must be resistant to the acids and alkalis used in the laboratory and to chemical decontamination agents [46]. For the slip resistance of the floors, the specifications in Table 314-6 of the SECO guidelines apply [47] (R10). Proof of resistance and slip resistance must be requested from the supplier or the manufacturer.

Laboratory trades

Concealed-mounted lines, cables and pipes are advantageous from the point of view of easy-to-clean, but disadvantageous with regard to the tightness of the containment and the flexibility for later alterations or additions (see chapter 5.1 ). It is recommended that lines, cables and pipes are generally surface-mounted at a distance of at least 2.5 cm in front of the wall to allow cleaning or surface decontamination by hand. Pipes, cable ducts or equipment mounted on the surface must be sealed against the wall.

Installation and cable trunkings do not have to be airtight. Suspended ventilation ducts, cable platforms, etc. along ceilings and walls should be avoided if possible (dust deposits).

All laboratory technical trades shall be arranged in such a way that they are easily accessible and easy to clean and decontaminate.

Laboratory furniture and equipment

Surfaces of laboratory furniture, especially worktops and tabletops, should be durable and scratch-resistant. The materials of tabletops must be resistant to the acids and alkalis used in the laboratory as well as to chemical decontamination agents.

In norms on laboratory furniture, the relevant safety requirements are only stated in descriptive terms [48]. An overview of suitable materials for laboratory furniture is given in [49]. Laminated laboratory furniture and other equipment with a wooden core are not recommended. Specifications are usually provided qualitatively by the supplier or manufacturer.

Supply air ducts from the supply air side shut-off dampers to the containment and exhaust air ducts from the containment to the exhaust air side shut-off dampers of the HEPA filter station must be resistant to the selected surface decontamination process (corrosion-resistant, fumigatable; see chapters [5.1 and [5.3 ).

Dangerous surfaces

There must be no sharp or rough edges or surfaces that could cause injury or damage the gloves used.

Diagnostic and research equipment

Equipment and facilities for diagnostic and research activities are the responsibility of the facility but must also be washable and decontaminable.

Tests

_ The responsible specialist planning office must take the requirements for the condition of surfaces into account in the project planning, tendering and award of contract [6]. Certificates or proof of the suitability of surfaces, such as their chemical resistance, slip resistance, etc., must be requested.
_ If no resistance data is available, for example corrosion resistance to hydrogen peroxide or other chemical decontamination agents, the supplier, manufacturer or the responsible planning office carry out appropriate material tests.
_ To test for sharp edges and roughness during construction, the surfaces are wiped by hand with a fine latex glove and with light pressure. The test is considered passed from experience if the latex glove is not damaged.

## 6. Notes for Commissioning Parties

The following information and advice are intended for the building owner, the owner, the facility and laboratory management as well as the persons responsible for biosafety (BSO). They are not exhaustive and should be supplemented or adapted on a case-by-case basis.

_ As part of a preliminary project (concept design), the commissioning persons and the commissioned planning and specialist planning offices should develop a common basis and language for the biosafety requirements, the processes in a BSL3 laboratory and the necessary structural-technical requirements. Joint visits to BSL3 laboratories and discussions with the owners and the facility are suitable for this purpose. Establishing contacts is very valuable in terms of gathering experience. Planning offices are recommended to complement the planning team with a specialist experienced in BSL3 laboratories.
_ Draw up comprehensive requirements specifications (statement of work, requirements description) as early as possible [14]).
_ For reasons of planning and cost security, specify the structural and technical requirements in detail in the preliminary project (schematic design; incl. tests and applicable norms and test methods).
_ Obtaining independent third-party opinions (reviews) during the planning phase
_ Early contact in the planning phase with supervisory authorities (biosafety, fire protection, NBC protection, etc.)
_ Support of the planning office in the preparation of the PQM [7] [8]

_ Check which measures are necessary for the planned activities, or whether they can be modified, replaced or omitted (authorisation by the competent federal office, if necessary). These considerations must be considered during the planning phase (schematic design). In the case of later changes of use, retrofitting/retrofitting may no longer be feasible or may be very costly.
_ List test methods and requirements in the summary report in accordance with Article 5 of the MAO if the installation is subject to the MAO ([4], [5]). The summary report is usually not written before the end of the construction phase (detailed design/installation).
_ Substantiate deviations from the requirements in the summary report in accordance with Article 5 MAO with a risk assessment
_ The responsible planning office must take the requirements into account in the project planning, tendering and awarding of contracts [6] and reports on the progress of construction at regular intervals.
_ Planning, execution and testing must be carried out by qualified and experienced specialists.
_ Construction site reports are to be inspected by the persons placing the order and defects are to be reported.
_ Keep a list of defects and an inspection plan (considering the warranty periods and the continuous inspection period).
_ Check test reports for the methods used, confirmations of conformity, and results within the scope of commissioning and completion [6].

## 7. Guidance for the Inspections by the Enforcement Bodies

According to Article 23, paragraph 2, letter a ContainO [1], the inspections of the safety measures are carried out by the specialist body designated by the canton (Art. 18 ContainO). Pursuant to Article 8b of the OMA [3] the (cantonal) enforcement authority carries out regular on-site inspections and determines their frequency depending on the hazard potential, the type and complexity of the establishment and the results of previous inspections.

The following points can serve as hints and advice for checking the structural-technical safety measures. They are not exhaustive and can be supplemented or adapted on a case-by-case basis.

For the first inspection, it is recommended to pay attention to the notes on individual measures listed below. For repeated inspections, the instructions in chapter 8. (maintenance) will also be useful.

_ Examination of the summary report in accordance with Article 5 MAO [3] if the establishment is subject to the MAO
_ Reviewing and assessing the risk assessments, especially in the case of deviations from the requirements
_ Checking of test reports with the methods used, conformity confirmations and results, which have been prepared [6]

Tightness of the containment

_ Standard and method used (pressure holding test, pressure drop test and pressure rise test), test pressure used
_ Consideration of sections of the ventilation system that may have to be fumigated with the room (e.g., up to the shut-off dampers)
_ Indication of the leakage rates for each individual fumigatable room of the containment (incl. airlocks, pass-through boxes) in the floor plan
_ Gas tightness and materials of fumigatable ventilation duct sections
_ In case of deviations from the requirements: Assessment of the risk-based justifications
_ In case of repeated inspections: Proof of the maintenance work carried out [36]

Ventilation system

_ Separate ventilation system for the containment; see ventilation schematic for the building and the containment.
_ Type of exhaust air ducting (via roof if possible)
_ Control of BSL3 ventilation operation in the event of fire in coordination with the responsible authority (fire police, building insurance).
_ Shut-off dampers available for each room or fumigation zone (check in ventilation scheme)
_ In case of repeated inspections: Proof of the maintenance work carried out [36]

HEPA filter system

_ Filter class used
_ Stainless steel filter housing
_ Pressure resistance test of the filter housing
_ Ensuring fumigation of the system in the installed state (arrangement of the shut-off dampers, fumigation connections)
_ Gas tightness test of the filter housing
_ Gas-tight butterfly valves and ventilation ducts
_ Leak test of the filter seat
_ Possibility to check the separation efficiency of the installed filter in *situ* during operation of the ventilation system (in operation)
_ Differential pressure indicator (protected by microfilter on the potentially contaminated side)
_ In case of repeated inspections: Proof of the maintenance work carried out [36]

Permanent negative pressure, pressure cascade

_ Pressure differences or cascade (in the range 20 to 30 Pa): Directional air flow from non (less) contaminated to potentially (more) contaminated areas.
_ Location of the reference pressure sensor (still room)
_ Compliance with the set pressure differences in normal operation (stability)
_ Door lock functions (incl. emergency override) and door alarms
_ Control of fault and special operation, alarming
_ Control of redundancy operation
_ Pressure displays present on the doors, calibrated
_ Air exchange rate in the range 10 to 12 per hour, or justified deviations
_ Concept of fault messages and ventilation alarm (description of functions; operation and fault matrix available and tested)

_ Performance of the ventilation system in the event of the malfunctions and special operating states designated as relevant in the description of functions with regard to maintaining the inward directional airflow (also in the event of malfunctions, special operation, redundant operation incl. automatic switchover to emergency power and the restoration of the mains power supply). Recording of pressure differences at least at the airlock doors and at doors between different pressure zones in the containment.
_ Pressure fluctuations during start-up and shut-down of the system (automatic operation; recording and assessment of pressure differences (see above).
_ In case of repeated inspections: Proof of the maintenance work carried out [36]

Autoclave

_ Proof of the requirements
_ Proof of professional installation, commissioning and functional testing
_ In case of repeated inspections: Proof of the maintenance work carried out [36]

Power supply

_ Emergency power supply (UPS and emergency generator) for all safety-relevant technical facilities and equipment. An emergency power generator is sufficient for the ventilation system, a UPS is not required.
_ Proof of automatic switchover to emergency power and restoration of the mains power supply
_ Maintaining the inward air flow during the changeovers. Recording of pressure differences at least at the airlock doors and at doors between different pressure zones in the containment (recording and assessment of pressure differences (see above).
_ Coordination of the running times of the emergency generator and the UPS system with SOP "orderly and safe termination of work and orderly exit from the BSL3 laboratory" available

Alarm system

_ Concept in place for alarms, usually based on a tolerance, target or threshold value with prioritisation
_ Alarm concept and means for the case of fire in the laboratory and building (in consultation with the fire police or the building insurance)
_ Signalling priority 1 and 2 to employees by means of audio and visual alarms
_ Consideration of faults and malfunctions that may result in personal injury, environmental damage or damage to property in accordance with the list of alarm-supported systems in chapter 5.7

Fire water retention

_ Catch basin concept according to extinguishing strategy (fire protection concept in coordination with fire police/building insurance)
_ Execution of extinguishing water retention
_ Method of extinguishing water decontamination
_ Visual inspection of upstands, door thresholds, and of floor drains if necessary

Wastewater decontamination

_ Dry or wet laboratory concept
_ Drinking water protection in wet laboratories
_ Handling of liquids and inactivation methodology
_ Type of eye-washer station
_ Emergency shower and wastewater decontamination strategy

_ Hand hygiene, hand wash basins and wastewater
_ Effluent decontamination system: Installation below the containment and compliance with the corresponding specifications for safety level 3 laboratories.
_ In case of repeated inspections: Proof of the maintenance work carried out [36]

Earthquake safety

_ If applicable: Verification of the structural safety according to BWK II (building class II) for the load-bearing elements of the building and the enclosing components of the containment and components of the ventilation system, and, if present, the effluent decontamination system, which can potentially become contaminated.

Surfaces

_ No materials made of wood or with wood core (laminated surfaces) available
_ Laboratory furniture, especially worktables and tabletops suitable for microbiological laboratories (chemical resistance, scratch-resistant, durable; verification by the supplier or manufacturer).
_ Slip resistance, washability and chemical resistance of the floors (verification by the supplier or manufacturer).
_ Visual inspection for accessibility of all surfaces for easy cleaning and chemical decontamination
_ Visual inspection of the finish: closed surfaces, absence of pores, no sharp and rough edges and surfaces

## 8. Notes for Maintenance

The SECB recommendation on the Maintenance of Laboratories and Facilities of Safety Levels 2 and 3 in accordance with the Swiss ContainO and the Swiss PEMO [36] contains information and aids for planning and carrying out maintenance.

Predictive and preventive maintenance can be carried out either on an ongoing basis during operation, or annually during a shutdown after the facility has been decontaminated, or as a combination of both [36]. The choice of maintenance strategy depends on the role and size of the laboratory.

Tightness of the containment

The tightness of the ventilation systems and the condition of the containment's enclosure components should be checked regularly: e.g., annually by a visual inspection for damage and, if necessary, by leak detection (hand, soapy water, smoke). In the event of major modifications and interventions, as well as at longer intervals to be determined on the basis of risk, it is recommended that the leak tests be repeated.

Ventilation system

Maintenance of the ventilation system is complex. According to the SECB recommendation on the Maintenance of Laboratories and Facilities of Safety Levels 2 and 3 in Accordance with the Swiss ContainO and the Swiss PEMO [36], a detailed maintenance and inspection log for the maintenance of ventilation systems and building automation is useful.

HEPA filter system

There are no standards or regulations that specify how long a HEPA filter can be used. Filter replacement is only necessary if the pressure drop exceeds the differential pressure values recommended by the manufacturer. In some companies, it has been possible to wait up to 10 years before replacing the filters.

If necessary, change the pre-filters (F9) more frequently.

In GMP facilities, depending on the cleanroom classification, testing the filter efficiency is mandatory every 6 or 12 months. For filter systems in BSL3 laboratories, annual testing of the efficiency is recommended. If the filter system has an automatic scanning device or redundancies, the filter efficiency can be tested during operation.

Permanent negative pressure, pressure cascade

It is recommended to check the following requirements annually:

_ Door locks/interlocking (incl. overriding in case of an emergency) and door alarms
_ Pressure displays on the doors with a calibrated hand-held gauge, adjust if necessary
_ Compliance with set pressure levels; recordings of pressure differences according to [29] during normal operation and for start-up and shut-down operation, redundancy operation (failure of redundant facility components, power failure; control of alarms).
_ Testing the building automation system for failures of system components (e.g., dampers, air volume flow controllers)
_ During the tests of the ventilation system and the building automation, pressure differences in the rooms should be logged at least every 5 seconds [29]. If necessary, in large laboratories the measurements can be limited to risk-relevant rooms (e.g., airlocks, internal corridor, rooms where microorganisms are handled).

Autoclave

In normal BSL3 laboratory operation, it is essential to be able to rely on the proper functioning of the autoclave and the reliable decontamination of contaminated materials, equipment and waste. Validations and checks must be carried out for this purpose.

The validations of the selected autoclaving programmes must be demonstrated with simulated standard batches of exemplary autoclaved goods by using bioindicators, if necessary, in combination with temperature loggers. They must be placed at suitable locations. The bioindicators used are ampoules for liquids and strips with *Geobacillus stearothermophilus* spores for solid autoclaved goods. Further guidance and detailed test protocols are given in the standards ISO 17665 Part 1 [50] and Part 2 [51] and the use of bioindicators in DIN 58949-4 [52] is described.

A number of routine checks should be carried out regularly at each facility:

_ Visual inspection of the seals, the displays, the placement of the temperature sensor and the correct programme selection before starting operation.
_ Monitoring the autoclaving process e.g., with chemical indicators [53] or heat-sensitive test strips
_ Monitoring the correct, trouble-free programme run on the display
_ Custody of the data for documentation
_ Provision of a clean autoclave for the next use

_ Weekly vacuum test of the cold and dry autoclave to determine the steam leakage rate, if the autoclave provides a corresponding integrated programme
_ Annual or regular testing / validation with bioindicators
_ Annual maintenance and inspection by service technicians incl. testing of exhaust air and condensate decontamination and submission of report

Power supply

Switching from mains power to emergency power should be tested annually.

Alarm system

The alerting for priority 1 and 2 alarms should be tested annually.

Fire water retention

Upstands and door thresholds should be visually inspected at least once a year.

Effluent decontamination system

For the maintenance of piping, fittings and tanks, appropriate protective measures must already be considered in the planning of the effluent decontamination system, especially for potentially non-contamination-free work (e.g., decontamination, enclosure of the work site, personal protective equipment) [36].

If potentially contaminated wastewater is produced, the respective decontamination system and the inlets and outlets must be visually inspected regularly (e.g., daily) for leaks and their displays checked for correct settings.

Maintenance, inspection, testing of the exhaust air decontamination, and data logging, should be carried out annually by a specialist.

Earthquake safety

Without structural changes or damage to the building, the containment enclosure, the ventilation system and, if available, the effluent decontamination system, annual visual inspections of the aforementioned systems are sufficient.

Surfaces

The condition of all surfaces incl. joints should be visually inspected in regular intervals (at least annually).

## 9. References

Note: Some references are available only in German(D), French (F), or Italian (I)

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