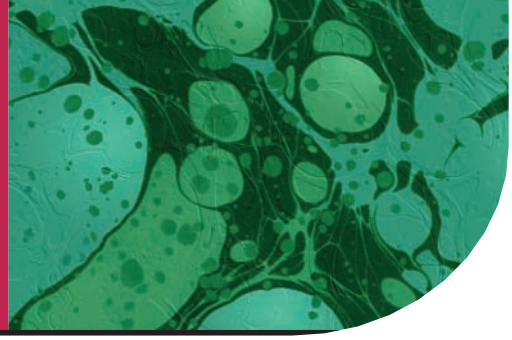

WHICH IS THE BEST CONTAINMENT EQUIPMENT FOR THE LABORATORY?

Many systems offer chemical or biological protection for personnel, environment and product. These systems are generically referred as safety barriers and, according to the risk level of the product to be handled, one or more safety barriers should be used.

> ***"In order to choose suitable containment equipment that meets the needs of the user, whether a biological safety cabinet or a laboratory isolator, it is essential to know the applications, use and nature of the products that will be handled inside it."***

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Primary Safety Barriers are those designed to eliminate or reduce exposure to biological and/or chemical materials. This category notably includes biological safety cabinet classes I, II and III, isolators, protective suits, respirators, masks, and safety goggles.

Several types of containment equipment are currently available for any given application, so it is ultimately up to the laboratory manager to decide on the preferred equipment or the one that best adapts to its work method and protocol for risk assessment and prevention.

This article aims to offer the decision makers purchasing this type of equipment an insight into the key factors that allow them to choose the system that best meets their needs.

HOW CAN USER KNOW WHICH CONTAINMENT EQUIPMENT IS BEST SUITED TO THEIR NEEDS?

In order to choose suitable containment equipment that meets the needs of the user, whether a biological safety cabinet or a laboratory isolator, it is essential to know the applications, use and nature of the products that will be handled inside it.

Before deciding on the equipment they require, users must ask themselves a number of key questions:

Nature of the products to be handled and their risk level

For biological samples, several containment levels are applicable according to the virulence of the pathogenic agent being handled. In order to select the containment

Table 1: Summary of biohazard levels

BSL	Risk of infection to the human being*	Risk of propagation to the collective*	Prevention & Treatment*
BSL1	**No or low individual risk** A microorganism that is unlikely to cause human or animal disease.	**No or low community risk**	Not necessary
BSL2	**Moderate individual risk** A pathogen that can cause human or animal disease but is unlikely to be a serious hazard to laboratory workers, the community, livestock or the environment.	**Low community risk**	Laboratory exposures may cause serious infection, but effective treatment and preventive measures are available and the risk of spread of infection is limited.
BSL3	**High individual risk** A pathogen that usually causes serious human or animal disease but does not ordinarily spread from one infected individual to another.	**Moderate community risk**	Effective treatment and preventive measures are available.
BSL4	**High individual risk** A pathogen that usually causes serious human or animal disease and that can be readily transmitted from one individual to another, directly or indirectly.	**High community risk**	Effective treatment and preventive measures are not usually available

**Definitions done by the WHO (World Health Organization) in the Laboratory biosafety manual. Third edition.*

Laboratory isolator with positive pressure for handling sterile material

system correctly, it is essential to know the risk level of the biological agents that will be handled inside it. These are classified into groups, according to their different infection risk levels.

These risk levels condition individual and collective preventive measures, the handling of biological material, the installation of the laboratory, protective measures and laboratory techniques.

If the samples are of chemical origin, basically substances that are carcinogenic or cancerous, mutagenic or toxic for reproduction (all other chemical substances are normally handled in a gas hood), they cannot be easily neutralised, for which reason they must always be handled with a third-filter system, or others safe enough alternative, under the work surface of the cabinet, to protect personnel during maintenance operations.

What is it necessary to protect?

According to that, a specific pressure system will be set up inside the work chamber of the cabinet.

Product protection:

If the cabinet is being used to deal with products with no biohazard that require conditions of absolute sterility, it is advisable to use positive-pressure isolators. In this case, the work chamber of the isolator is at a higher pressure than the rest of the room. The material pass-through is also under positive pressure, although slightly lower than the work chamber to guarantee aseptic conditions inside the cabinet. This kind of equipment not only provides a high level of containment against external contamination, but avoids the risk of cross-contamination because of laminar flow of the work chamber.

If the product handled inside the chamber does not pose any chemical or biological risk but requires a sterile laminar flow without conditions of extreme asepsis, it is advisable to work with vertical or horizontal laminar flow cabinets instead of with isolators, since there is easier to work in and the equipment is less expensive. A vertical or horizontal flow chamber is chosen according to the user's application and the instruments to be placed inside it. When the user requires easy access to material inside, it is advisable to use horizontal laminar flow cabinets, but if the user is handling samples that can splash or release bad smells, or simply needs to place large objects such as CO2 incubators inside the cabinet, it is advisable to use vertical laminar flow cabinets.

User protection:

When it is necessary to handle microbiological agents with Biosafety Level 4 (BSL-4) it is essential to guarantee the protection of the operator. In these cases, it is necessary to use a Class III Biosafety Cabinet. These cabinets provide a completely enclosed, sealed working area, ensuring the user is completely separated from the product by a physical barrier, handling the sample with mechanical gloves attached to the sealed window of the cabinet. A HEPA H-14 filter located on the side or at the rear of the cabinet provides a continuous supply of filtered air to the work chamber, and the evacuated air is passed through a HEPA-14 filter to prevent the release of microorganisms into the environment. The HEPA H-14 supply filter provides a turbulent flow inside the cabinet. Materials are introduced in and removed from the cabinet through one or two material pass-through with interlocking door

Class III Biosafety Cabinet

system, which can be decontaminated between uses.

To handle pathogenic agents of groups BSL-1, BSL-2 and BSL-3 with the sole aim of protecting the users in cases where the samples do not require protection, a class I biosafety cabinet can be used, although this is not a very common solution, and always requires the use of additional protection means.

Class II Biosafety Cabinet

Protection of the user, product and environment:

When working with microorganisms of Biosafety Levels 2 and 3 (BSL-2 and BSL-3) it is important to guarantee the protection of the user, the product and the environment. In these situations, it is advisable to use class II biosafety cabinets, which provide a ISO 4 (class 10) or 5 (class 100) sterile laminar flow inside the work chamber. Another option is to use negative-pressure isolators with laminar flow inside the work chamber. While the cabinet protects the user by means of an air barrier, the isolator is a closed system which protects the user by means of a sheet of glass. It is important for the user to be aware of the current standards and regulations governing these devices before choosing one correctly. Biological safety cabinets have been regulated for decades by strict legal regulations, initially local (such as BS-5726 in the UK, NF X44-201 in France or DIN 12950 in Germany) and later by a single European standard: EN 12469. Several entities, such as TÜV or LNE are authorised to issue the relevant certification, with TÜV in Hamburg

having the best reputation since it conducts strict inspections not only on the equipment, but also on the traceability of the production process.

As regards isolators, in Europe there is no standard to regulate their design and production, so that each manufacturer applies the quality and control systems it deems most suitable, meaning that their use for laboratory purposes is highly incipient and requires the user to have a high level of experience and only to deal with companies that have proven technical skills in this field.

Protection of the user, product, environment and maintenance personnel:

When the product to be handled inside the equipment is a hazardous chemical substance, such as, for example, cytostatic and cytotoxic drugs (substances that are cancerous or carcinogenic, mutagenic or toxic for reproduction), it is important to protect the operator as well as the service and maintenance personnel responsible for changing the filters of the equipment when required.

In these occasions, it is advisable to use a Class II Biological Safety Cabinet with a third filter stage under the work surface or a negative pressure isolator, also with its corresponding filter stage under the work surface. The two devices have negative pressure and laminar flow inside the work chamber. The only difference is that, while the cabinet sets up a protective barrier for the user by means of the air intake flow, the isolator places a physical glass barrier between the user and the sample. The two systems, according to best practices for laboratory work and equipment handling, are equally efficient and effective for protecting the user against the toxicity of the handled samples, and it is up to the user to select the type of device required for everyday work. It is important to consider that the user's ergonomics, access to the working material and cleaning are always much more limited in an isolator than in a biological safety cabinet, given the simple fact that the user has less mobility. It should also be stressed, as mentioned previously, that class II biological safety cabinets are regulated by a clearly defined European standard, while isolators are not.

Class II Biological Safety Cabinet with third filtering stage for handling cytostatics

Laboratory isolator with third filtering stage for handling cytostatics

How many samples will be handled simultaneously?

If the user of the device intends to handle several samples or products simultaneously, it is important to choose a device operating with sterile laminar flow, to minimise the risk of cross-contamination between samples. In these cases it is advisable to use class II biological safety cabinets or isolators. If only one type of sample will be handled in the cabinet, laminar or turbulent flow can be selected.

Preference for a certified system

Biological safety cabinets are regulated by European Standard EN-12469. This standard describes the materials to be used to manufacture a cabinet, its design and production, as well as its requirements in terms of tightness, cleaning capacity or sterilisation capacity. It also describes the tests to be performed on the cabinets, from type testing to production, installation and maintenance tests (for example, assessment of the front opening latch, tightness of the casing, testing the filters after installation, speed of the laminar flow, extraction rate, luminosity, noise level). If, in addition, the cabinet is independently certified by a prestigious entity such as TÜV or LNE, this guarantees the quality and safety of the equipment. In the USA, standard NSF 49 has been in force since 1976.

At this respect to mention that only a third part well reported certification can guarantee the compliance of the standard.

European standard EN 12469 defines the following classification for biological safety cabinets:

For the isolators, there is no European standard to govern their design, production and methods for testing their key values, so that if the user requires certified equipment, an isolator is a more complex option which requires specific validation protocols approved at least by the user, the manufacturer and the body approving the laboratory.

It must be taken in account that EN-12469 standards not only certifies compliance. Aditionally, certification companies as TÜV provides not only testing but treacability.

Table 2: The main characteristics of each cabinet class are defined in European standard EN 12469.

CLASS	Front intake speed to protect the user	Vertical laminar flow speed to protect the product
I	> 0.7 – 1.0 m/s	Not applicable
II	≥ 0.4 m/s	> 0.25 m/s – 0.50 m/s
III	≥ 0.7 m/s with one glove outside	Not applicable

OTHER ASPECTS TO BE CONSIDERED:

Secondary Safety Barriers

When handling pathogenic agents, the design of the laboratory is obviously an important factor to be taken into account according to the biohazard level in question. This refers to secondary protection barriers. This type of barrier is intended to provide the required level of separation between lab areas and public-access areas, as well as to contain the suitable decontamination equipment.

Laboratories can be classified as follows according to their design characteristics, construction and containment barriers:

- Basic laboratory covering levels P1 and P2;
- Containment laboratory corresponding to level P3; and
- Maximum containment laboratory corresponding to level P4.

Given the characteristics of the microorganisms handled in the P4 containment laboratories, which require highly specialised facilities and personnel, few sites around the world have maximum-containment facilities. Laboratory managers are faced with common problems during the design and construction of P3 containment laboratories.

In a laboratory with biological safety P3, in addition to good laboratory practices and procedures (GLP), care should be taken to ensure the correct design and construction of the facilities, paying special attention to the installation of all the containment barriers of the P3 integrated design. The aim of the above is to ensure that the biological barrier that maintains the safety of the worker and the environment and the containment of the unit are not broken at any time, guaranteeing the quality of the facilities and equipment.

Tertiary and Quaternary Safety Barriers

We speak of tertiary barriers when the actual building requires a special design, or even of quaternary barriers, which relate to the location of the building, for example in areas that are isolated from urban centers.

CONCLUSIONS

Work with pathogenic germs, unknown high-risk microorganisms or cytostatic/cytotoxic drugs has forced R&D labs, hospitals and the pharmaceutical industry to work under increasingly strict safety conditions to guarantee the protection of their personnel and the environment. These bodies have defined increasingly widespread, global protocols for assessing and preventing risks associated with exposure to biological and chemical agents, to avoid contamination due to contact with these agents.

It is important, when selecting biological and chemical protection equipment, to perform a correct assessment of the risk level and to assign it correctly to the various operations of the process, remembering that the best protection is the one that also makes the user's work easier.

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