NKP isotec

Flexible Film Isolators
A solution for biocontainment

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Introduction

Biocontainment Class 2, 3 and 4 is quickly developing into a more relevant field of study, thanks to the current climate. The need for additional research into viruses, vaccines and many more applications, is now relevant, even for small research groups.

The question arises; are Flexible Film Isolators safe or suitable to use for these applications.

The short answer is YES.

Flexible Film Isolators are completely gas tight and have been proven to reliably keep pathogens out. They are, therefore, just as suitable at keeping pathogens IN; thereby, protecting the user in the best possible way.

The purpose of this brochure is to highlight and explain the features and protocols necessary. Thus, demonstrating why and how Flexible Film Isolators are used for this purpose.

Please note, this is not a substitute to requirements and regulations which must be adhered to, in accordance with any local laws. These rules and regulations can differ from country to country. We hope, however, that this brochure will explain how containment can be achieved.

Should you require further information please do not hesitate to contact us.
service@nkpisotec.com

Working with Flexible Film Isolators Under Negative Pressure Conditions

General Considerations

Flexible Film Isolators, by their design are a very safe way to avoid exposure and contain infectious material, minimizing “human error”. Which is usually one of the most common causes of exposure or contamination. When containing pathogens, this is of paramount importance, as there is no room for errors. Procedures must be followed to guarantee long-lasting success.

Over the course of this document, we will explain the definitions, regulations, practical procedures and any considerations which apply to biocontainment applications in different classes.

All information has been gathered from existing pamphlets and information material:

World Health Organisation, Geneva 2004 - Laboratory Safety Manual Third edition
BBSRC - Standards for containment level 3 facilities - Version I - 2014
HSE Guidance document on the use, testing and maintenance of laboratory and animal isolators for the containment of biological agents

Classification of Biological Hazards

Risk Group 1 (no or low individual and community risk)
A microorganism that is unlikely to cause human or animal disease.

Risk Group 2 (moderate individual risk, low community 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. Laboratory exposures may cause serious infection, but effective treatment and preventive measures are available and the risk of spread of infection is limited.

Risk Group 3 (high individual risk, low community risk)
A pathogen that usually causes serious human or animal disease but does not ordinarily spread from one infected individual to another. Effective treatment and preventive measures are available.

Risk Group 4 (high individual and community 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. Effective treatment and preventive measures are not usually available.

Lists of pathogens and their classification can be found in the EU directive or other documents provided by the legal authorities or on the website of the Robert Koch Institute.

Legal Requirements General

In general, the requirements state that wherever possible the use of agents presenting a risk to human health must be avoided. However, for the purpose of this document, the reasons for your use of these agents have already been established. Therefore, little detail is required here.

From a legal point, according to EU Directives and several other Entities the following general rules will apply for class 2 and 3:

- Restriction of access
- Limiting amount of personnel
- Risk assessments to be carried out
- Hygiene measures and individual protection established
- Training of personnel
- Special health surveillance, if applicable
- Notification of the competent authority
- Special building features have to be adhered to (e.g., the room is not allowed to have a physical drain in the floor, special surfaces for flooring needs to be adhered to
- For each biohazard, the disinfectants required for decontamination must be published

Legal requirements for Class 4

To give you an indication of the maximum stringency, please find below the requirements for working with class 4 pathogens.

Workplace/ Building requirements

- The workplace is to be separated from any other activities in the same building
- Input air and Extract air to workplace is to be filtered using HEPA or likewise
- The workplace is to be sealable to permit disinfection
- Specified disinfection procedures
- The workplace is to be maintained at an air pressure negative to atmosphere
- The workplace is to be adequately ventilated to minimise air contamination
- Efficient vector control, for example rodent and insects
- Surfaces impervious to water and easy to clean
- Surfaces resistant to acids, alkalis, solvents, disinfectants
- Effluent from sinks and showers should be collected and inactivated before release
- Safe storage of a biological agent
- An observation window or alternative is to be present so that occupants can be seen
- A laboratory is to contain own equipment
- Incinerator for disposal of animal carcases on site
- Biohazard signs to be posted
- Closed systems should be located within a controlled area

Personnel requirements

- Access is to be restricted to nominated workers only - via airlock
- Personnel should wear protective clothing
- Decontamination and washing facilities for personnel
- Personnel to shower before leaving the controlled area

Closed system (Isolator)

1. Viable organisms have to be handled in a system which physically separates the process from the environment
2. Infected material including any animal is to be handled in a safety cabinet or isolation or suitable containment
3. Exhaust gases from the closed system should be treated so as to prevent release
4. Sample collection, addition of materials to a closed system and transfer of viable organisms to another closed system should be performed so as to prevent release
5. Seals should be designed to prevent release
6. The closed system needs to contain spillage of the entire contents

Further information regarding local and national regulations can be found through your country's government and Health and Safety bodies.

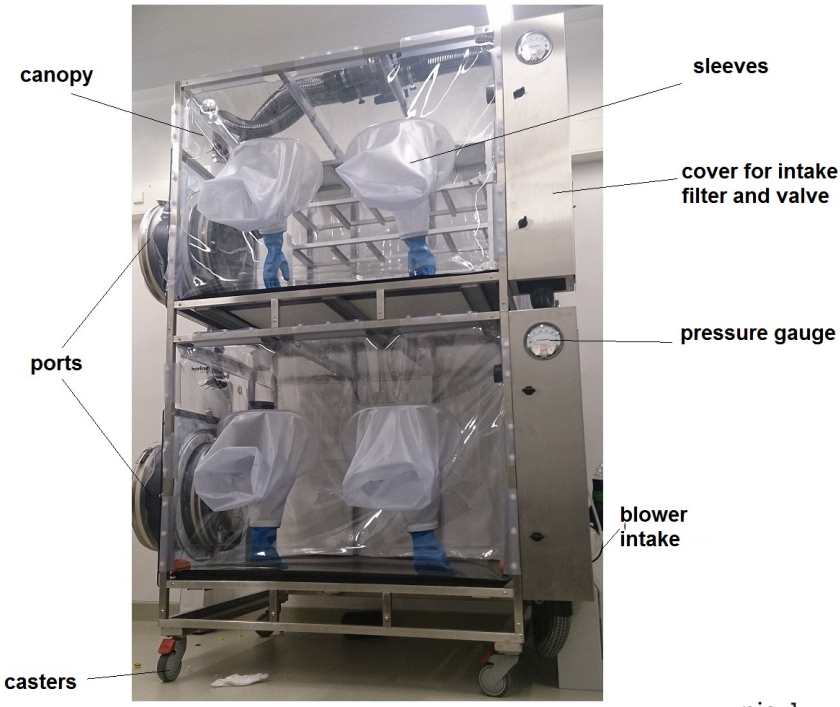
How Flexible Film Isolators Comply

Isolators are specially designed to protect the user or personnel (negative pressure operation).

The Flexible Film Isolator is manufactured as one air-tight "bubble". A single unit with minimal access points to reduce the possible entry/ exit points (weak points) from the outside to an absolute minimum. Even in the case of a complete power failure, the environment internally is protected due to the HEPA filter system on the inlet and outlet parts. Due to the large size of an Isolator, it reduces the risk to animal death due to suffocation in such an incident as compared to smaller containment units. Nonetheless it is highly important to have an independent power backup and alarm system to ensure that the situation can be rectified within 2-3 hours and provide continuous protection.

Additionally, if the Flexible Film Isolator is connected to the room's ventilation system, that is drawing air. It is almost impossible for the Flexible Film Isolator to lose pressure or inflate as a positive pressure Isolator. Therefore, providing the highest possible protection to the personnel involved.

In the following sections, the separate articles of the legal requirements will be corroborated with protocols and procedures of using the Isolator to demonstrate how protection is achieved.



pic-1

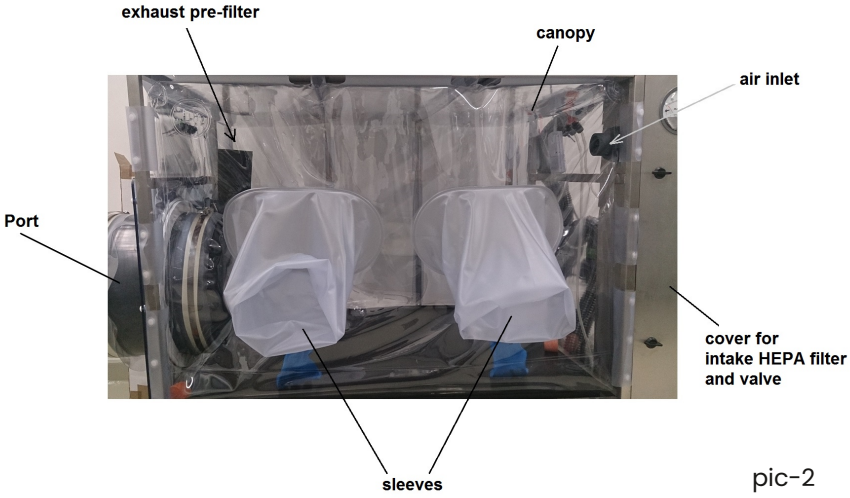
1. /2. Viable Organisms, Infected Material and Samples Have to be Handled in a System Which Physically Separates the Process from the Environment

A Flexible Film Isolator presents the best way of separating the specimen and work from the User and other Personnel. Illustrated above, the following features ensure the separation of contents from the User is achieved.

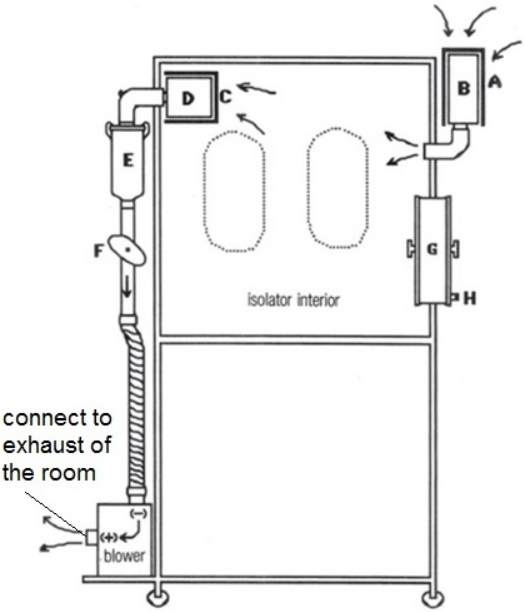
- Fully welded integrated PVC Canopy which is sufficiently pressure tested to ensure safe use
- Glove access
- Entry and Exit ports with airtight inner and outer doors
- All entry points are gas tight fixings
- Extremely durable PVC material which has a very high chemical and physical resistance
- Gloves available in a variety of materials to ensure the best protection for the application
- Easy to perform pressure tests of the integrity of the Isolator at different intervals - even whilst in use
- Mandatory 6-month intervals to perform these tests; without the need to move or stop the procedures
- Flexible Film Isolators typically run between 30-50 pascals at negative pressure

3. Exhaust Gases from the Closed System Should be Treated so as to Prevent Release

- Every Isolator has certified HEPA filters fitted to the inlet and exhaust of the Isolator
- For negative pressure applications it is recommended to use the double HEPA method, in order to ensure highest possible safety. (pic 2 - "exhaust pre-filter" shows where the HEPA filter is on the inside - protected again with a pre-filter)
- One HEPA filter is placed on the inside of the Isolator and the second one on the outside
- The exhaust air is then ideally connected to a room exhaust, which also has a filtration system in HEPA quality or similar
- The Inlet typically has one HEPA filter fitted - but also here it would be possible to use two in-line filters for extra safety
- With the above setup, it is guaranteed that the Air leaving the Isolator is free of any pathogens.
- Safe filter change can be performed while the Isolator is in use, due to possible access ports for testing and decontamination



pic-2



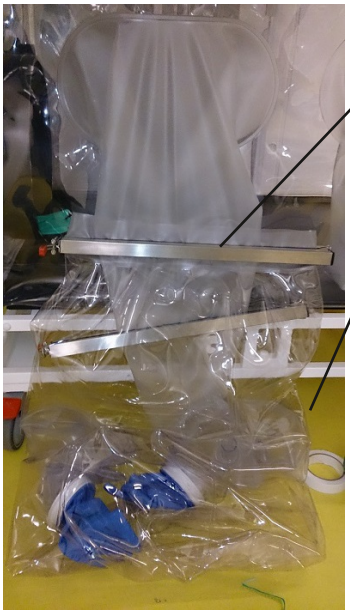
A- Pre-filter
B- HEPA fiter
C- Pre filter
D- HEPA filter
E- HEPA filter
F- Gas tight valve
G- Port with solid doors

pic-3

4. Sample Collection, Addition of Materials to a Closed System and Transfer of Viable Organisms to Another Closed System Should be Performed so as to Prevent Release

Everything which enters or leaves the Isolator needs to be sterilised or decontaminated. With the Flexible Film Isolator, it is very easy to achieve this for any pathogens which can be decontaminated with the help of designated chemical disinfectants or via fumigation.

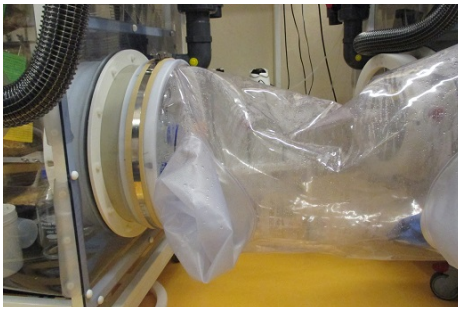
- The double port doors, allow for decontamination of every item which enters, or is removed from the Isolator
- Flexible Connection Sleeves allow removal or entry of larger items with glove access and decontamination ports
- Large autoclavable cylinders can be connected via flexible sleeves to allow decontamination of porous items which are not able to be chemically decontaminated but need to be autoclaved. These are connected and then closed off with silicon or Viton caps. The interim space is also a smooth plastic surface which allows chemical decontamination
- Gloves can be changed in a similar way using our specially designed Glove Change Bag. This allows the removal of gloves and replacement without any pathogens escaping
- NKP provides all protocols and training. Thus, allowing the User to be able to perform these tasks independently



Sleeve Clamps seal the connection to the Isolator

The glove-change-bag ensures that no particles can escape whilst glove change is performed

Access points allow decontamination of the bag prior to removal



Flexible sleeve connection with gloved access.

This way any items can be transferred into the Isolator or from the Isolator into a decontamination cylinder without risking exposure

5. Seals Should be Designed to Prevent Release

Pressure and Leak Tests

A pressure and leak test can be performed to establish if the canopy and all of its connections are gas tight. This test should be done prior to first use, and every time the Isolator is used for a new project or experiment. It is possible to perform this test even while in use [with animals inside] to allow for regular maintenance. These tests are possible to perform in positive as well as negative pressure.

Once a successful pressure test has been performed, a leak test must follow. If the pressure test is not satisfactory, leaks can be found using smoke indicators around the canopy to locate possible entry points. In case of damaged PVC material, a high-quality fixing patch must be applied to seal the damaged area.

A pressure test should be performed after any repair. If successful, and due to the nature of a negative pressure Isolator, no pathogens are able to escape. Deeming the Isolator fully functional, presenting no danger to the user. Once the experiment is over and the Isolator decontaminated, the areas should be examined by service engineers, who can advise about longevity and possible replacement needs.

NKP is able to provide all training necessary for the user to perform necessary test independently and to evaluate the integrity of the equipment

6. The Closed System Needs to Contain Spillage of the Entire Contents

As Flexible Film Isolators are made from one welded part without any manual connections to the base, containment of spillages can be guaranteed. Any airborne particles are contained via the double HEPA filter system.

Additionally, Flexible Film Isolators are able to combine many useful features, such as electrical equipment. Especially useful are the plannable connections to the outside. These are a benefit, in the fact that a lot of electrical equipment, or parts of the equipment, can be kept outside of the Isolator. Therefore, they are not directly exposed to any pathogens.

The enclosure also allows decontamination/fumigation of the entire contents without any exposure to the outside. This fulfils the requirement of collection and inactivation of any materials and supplies which have been in contact with the pathogens.

The following section, briefly lists the decontamination methods possible for Isolators.

NKP is happy to provide guidance and training in how these processes are performed with all of our equipment supplied.

Possible Sterilisation/Decontamination Procedures

Prior to first use, the Isolator will need to be cleaned and sterilised, in order to receive the first supplies and experiments. In addition, all tests ensuring the integrity of the Flexible Film Isolator should be performed. Along with any other relevant tests.

There are many methods of sterilisation for isolators, described below are two general descriptions:

a) Using a liquid sterilisation solution in conjunction with a compressor and atomising gun.
b) External Gas sterilisation connections (connection of your VHP equipment via standard Camlock fittings)
c) MINI VHP - the complete Equipment is placed inside the Isolator (in case of negative pressure operation only useful for first sterilisation / for final decontamination after the procedures are completed it is not recommended as the complete equipment needs to be imported into the Isolator.)

The agent for decontamination used is defined by the pathogens which will be used inside the Isolator. The User must contact relevant authorities or Health and Safety officers to ensure the correct Chemical, Gas or Liquid is used, and the correct application procedures are in place.

PROTECTIVE CLOTHING / MASK MUST BE WORN

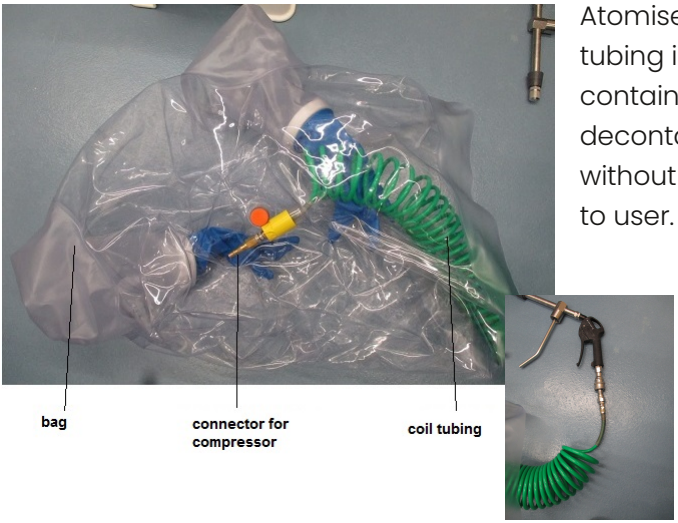
Examples for a Mini VHP

Manufacturer :

http://devea-environnement.com/en/

https://www.airinspace.com/en/surface-disinfection/rhea-compact

https://www.kugel-medical.de/en/latest-news/kugel-medical-news/news-detail/article/cleancube-classic-ihr-neues-allround-talent-fuer-die-flaechendesinfektion.html



Atomiser and pressure tubing in flexible containment bag for decontaminatin without any exposure to user.