



WHITEPAPER

Handling Potent Products in a Sterile Environment

BEYOND BOUNDARIES®

Introduction

In this Whitepaper, ILC Dover discusses best practices for handling potent products in sterile manufacturing processes. As containment specialists with expertise in cross-functionalities for multiple industry sectors, ILC Dover has developed innovative solutions for processing potent products in sterile environments at all levels of production volume.

Learn about today's sterile manufacturing trends, important considerations for choosing the right isolator system for your operations, and ILC Dover's newest sterile flexible-film isolator.

[Let's Dive In...](#)



Trends in Sterile Manufacturing

The frequency of handling potent products in the biopharmaceutical industry has drastically increased over the last few decades, with more companies processing potent materials than ever before. This unprecedented increase in manufacturing has caused most companies to require highly advanced equipment and additional safety protocols.

Some of these recent materials include:

- Cell and gene therapy products (ATMPs)
- Patient-specific products
- Antibody-drug conjugates (ADCs)
- Potent sterile powders

Another rising trend is pharmaceutical companies outsourcing these sterile processing operations to smaller contract manufacturers, thus creating a strong demand for custom equipment and suitable sterile environments.

Potency of Molecules in the Pharmaceutical Space

As the industry continues to leverage more innovative ways of making new medicines, we find that many commonly handled molecules have a much higher level of toxicity when compared to materials produced 30 years ago.

Back in the 1990s, a 1-mcg OEL exposure limit was considered unheard of. Today, these limits are going down into the nanograms levels, which require a much more sophisticated processing environment for effective containment. The processing of products like ADCs (Antibody Drug Conjugates) has also created industry crossover and a sharp increase in the demand for a sterile processing environment coupled with high-level containment capabilities for potent powders.

Our Involvement as Containment Specialists

ILC Dover's involvement as containment specialists has evolved substantially over the years. We have been approached by many pharmaceutical consultancy firms as well as directly by customers to establish what equipment is available and what environments we can create to suit certain processes. Determining feasibility starts with choosing the correct equipment specific to a customer's needs and having an established environment capable of safely running a particular process.

We get involved in these assessments at the earliest stage possible, e.g., 2-3 years out from product realization to address safety concerns with the operators and proposed products. Our experiences in cross-functionalities across multiple industry sectors have allowed us to develop innovative solutions for processing potent products in sterile environments at all levels of production volume.



Creating the Right Environment

ILC Dover has developed isolated technology that goes far beyond a box with positive or negative pressure. Whether working in a hard-wall system or flexible-film isolator, there is a perfect environment for every type of operation, from cell banking to ADC processing. Whenever there is a chance of putting operators at risk, especially in potent processing environments, it is crucial to create the highest level of containment possible that fits your budget.



One example is a closed-barrier system with negative pressure and a double HEPA filtration exhaust. Another example of a sterile fill and finish process is the requirement for extremely low particle counts and absolutely zero microbial growth, including decontamination and high airflow to keep particle counts low. For sterile dry powder inhalation products, the foremost requirement is very low humidity.

The wide variety of needs throughout the industry can make it burdensome to figure all of this out. ILC Dover can help with this process and create a suitable environment for any specific process and budget.

Handling Potent Molecules Inside Sterile Environments

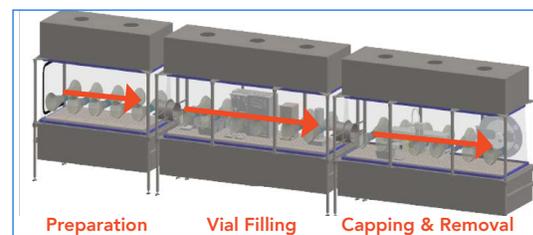
As the frequency of potent sterile processing has increased dramatically in the last 5-6 years, it is of the utmost importance to understand the adverse effects these compounds have on operators and their environment. An essential step in isolated design is looking at some of the risks associated with the process. Then, developing measures around that operation, such as safe product entry handling, double HEPA filtered exhaust, safe waste and product removal methods, and advanced features like pressure cascades.

There are multiple safe product entry methods such as the rapid transfer path, liner systems, and air lock pass boxes—all of which work very well depending on the specific process.



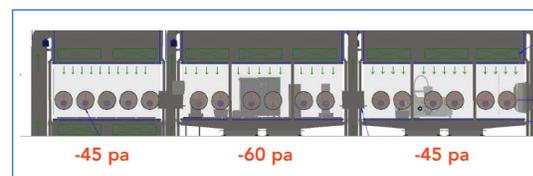
Safe Product Entry Methods Double HEPA Filtered Exhaust Safe Waste & Product Removal

Double HEPA filtration is an important mechanism to consider when dealing with potent materials, as the extra layer of filtration prevents exposure to stray particles that have accidentally passed through the primary filter.



One-Way Product Handling

Safe waste and product removal are highly overlooked parts of the process by customers, but are some of the most essential for operator safety.



Pressure Cascades

Other things to consider are the locations where the waste and finished product will go after the production run, whether into another clean space, directly to the warehouse, or onto secondary and tertiary packaging. If you are running more extensive processes, pressure cascades are important to keep in mind when assessing the correct sequence of positive and negative pressures to keep potent products from becoming increasingly contaminated as they move through the fill and finish process.

Considerations for Potent Molecules

One of the most important factors to consider when handling potent products is operator protection. If an operator were to be exposed to potent material accidentally, would it hospitalize them or make them ill for a certain amount of time, or worse?



Once you determine the adverse effects, it is essential to know the risks of them occurring during operation. Realistically, you will need to approach this question by determining what type of environment is required inside and outside the isolator system. To better understand the risks involved in your particular operations, ILC Dover will review your cleanroom setup, gowning procedures, and operator training on PPE to risk-assess the entire process from start to finish.

When comparing positive versus negative pressure systems for fill and finish operations, you are traditionally looking at a positively pressured system. In the case of a breach, the particles would transfer out of the critical zone and into the surrounding clean room, so any airborne particulates and bioburden would not get back into the isolator and affect the product. However, breaches with positively pressured systems can also expose the operators working in the cleanroom, so it could be beneficial to flip the pressure to a negative system. With a negative pressured system, you will protect your operator, and you will have an ingress into the isolator if there is ever an airborne particulate breach. Likewise, with negative pressure systems, you are potentially risking contamination to the process and product in the case of a breach.

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Considerations for Potent Molecules

So, which system should you deploy for your operation?

To determine the most suitable options in mitigating risk, there are a few review points to consider before engineering the right solution, such as:

- ✓ Having a grade in the isolator
- ✓ Further separating the operators from the process
- ✓ Changing the gowning procedure
- ✓ Adding a decontamination procedure
- ✓ Changing the PPE for the operation
- ✓ Providing additional environmental monitoring

Proven Benefits with ILC Dover Flexible Film Systems

ILC Dover has the experience and capabilities to provide an efficient and productive piece of equipment suited to your particular process and environment. One benefit of our equipment is that it can be easily transferred in and out of areas, plus has a small footprint. Another beneficial feature is its automatic control system, which eliminates manual operator involvement, increasing safety and ease of operations. Having a single-use disposable option is one of the most advantageous features of ILC Dover’s flexible-film equipment, as it helps eliminate cleaning validation and frees up cleaning and maintenance expenses you would otherwise incur with hard-wall or other traditional systems.



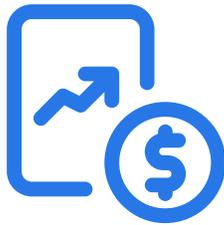
Create efficiency and maximize productivity:

- Small footprint
- Automatic control system
- Single-use disposable options eliminate cleaning validation

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Proven Benefits with ILC Dover Flexible Film Systems

Another huge advantage of ILC Dover equipment is the ability to lower your overall capital expenses. Many contract manufacturers do not have the excess funds big pharmaceutical companies do, so why pay potentially millions of dollars for traditional systems when you can achieve the same performance at a fraction of the cost with ILC Dover isolator systems? Having long lead times is a big hurdle to overcome, with some traditional equipment taking well over a year for delivery, while ILC Dover equipment takes only about 16 weeks in most cases.



Reduce costs and deliver on time:

- Lower CapEx to hard-wall alternative
- Turnkey solutions available
- Short lead time delivery
- Enabling you to bring your aseptic processing in house

The most important factor when it comes to choosing the right system is mitigating risk. With ILC Dover equipment, you can be assured of the best possible outcomes for the operator and environment with full regulatory compliance already integrated into every system.

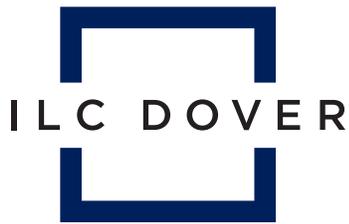


Mitigate risk and meet regulatory compliance:

- Fully compliant system
- Double H14 HEPA exhaust
- Full qualification services available
- In-built integrity testing function

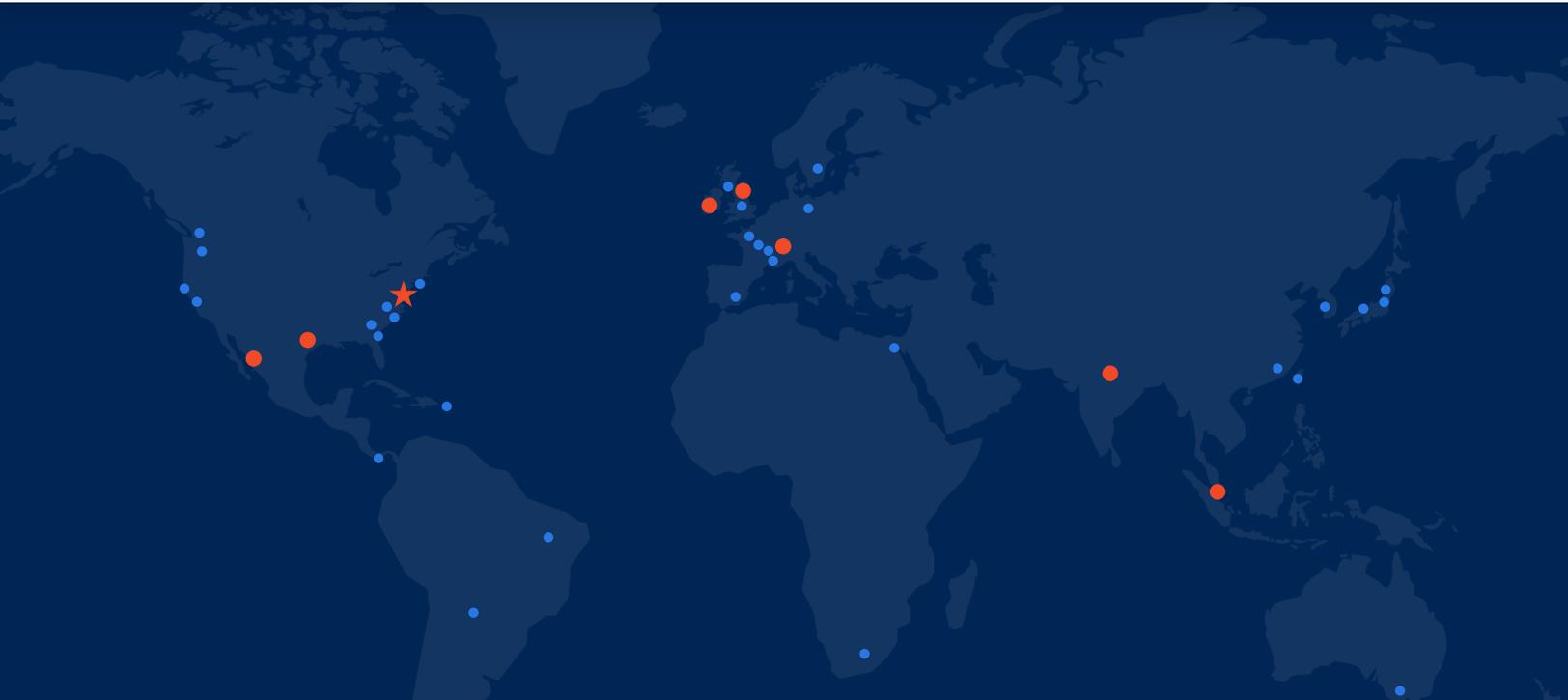
Are you ready to transform your cleanroom into a sterile manufacturing machine without the added expense?

To experience the risk-reducing power of a single-use isolator system, visit ilcdover.com.



BEYOND BOUNDARIES®

ILC Dover is a world-leader in the innovative design and production of engineered flexible protective solutions for pharmaceutical and biopharmaceutical, flood protection, personal protection, bulk packaging, and aerospace industries. Our customers will attest to our relentless dedication to high value products, advanced technology, and responsive service, as our visionary flexible protective solutions have improved efficiency while safeguarding people, product, and infrastructure in hazardous conditions since 1947.

A dark blue world map with several colored dots (red, orange, and blue) indicating global locations. A red star is placed over the United States, marking the headquarters location.

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