

*examining
new methods*



*yields
new discoveries*

DoverPac®

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Why Do Our Customers Value ILC Dover?

- ▶ We keep the cost of making drugs down
- ▶ We make the medicine people take safer by protecting the drug product from contamination
- ▶ Lower cost of ownership with disposables vs. capital
- ▶ No cross contamination eliminates need for dedicated facilities
- ▶ We keep the people who make medicine safe
- ▶ Life critical softgoods that are the key to the system
- ▶ ILC's products do what they claim and we are there to support our process after the installation



DoverPac®

Our flagship product that offers the capability to offload and charge potent compounds



Continuous Liners

Multiple size continuous liner packs designed to support contained drum loading



DoverPac®SF

Charging system designed to interface with split butterfly valves or sanitary flanges



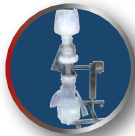
Flexible Enclosures

Standard and custom enclosures designed to provide containment for a range of process equipment



Drum Transfer System

For offloading drummed materials in a safe and efficient manner at fixed and varying heights



Mill Containment System

Critical safety and cross contamination avoidance during particle size reduction operations

One of our major customers says it best,
"You guys provide the only containment that works!"

As the pioneer of flexible containment systems, ILC Dover has collaborated with our customers in the pharmaceutical industry to develop a range of validated API containment solutions that interface with a wide variety of process equipment. All of our products are designed to be safe, effective and user friendly. The same knowledge of flexible film and fabric systems and attention to detail that allows us to be NASA's sole supplier of spacesuits, uniquely qualifies us to design and produce unparalleled containment systems.

Some of the key benefits offered by using flexible containment:

- ▶ Ability to rapidly upgrade existing equipment to handle potent compounds
- ▶ Reduced capital costs
- ▶ Increased throughput when compared to other systems
- ▶ Improved ergonomics
- ▶ Faster project start-up
- ▶ cGMP through nanogram processing

*Providing Flexible Containment Solutions
to the Pharmaceutical Industry since 1997*

Why DoverPac® Containment System?



Multiple O-Ring Technology

Our patented system of progressively advancing to a new clean zone on a canister allows multiple powder transfers without breaking containment.



Contained Separation

Crimps: The use of DoverPacs® and Continuous Liners is enhanced by this ILC innovation. Our crimps permit reliable, repeatable one-person contained separation of sample sleeves and charging and discharging necks.



Flexible Enclosures

We know that existing pharmaceutical plants are sometimes cramped and many times not originally designed to support the processing of potent compounds. Our custom flexible enclosures permit safe, contained operation with a wide range of processing equipment.



Engineering, Systems, Service Capability

Custom engineered hardware interfaces with your specific processing equipment. On-site surveys to engineer your application offered. Product performance testing and customer training at ILC's containment processing suite or on site provided. Personal and proactive customer service representatives available. Seasoned professional engineering team supports standard and custom containment solutions. We are the first to validate flexible containment.



Manufacturing

Each DoverPac® is manufactured in a clean working environment using custom sealing equipment designed and manufactured by ILC. This approach allows us to control the manufacturing quality of the product and to add design features that improve the overall reliability of the product. One such example is the fact that all DoverPacs® employ strong overlap seams even in 3-dimensional intersection areas (e.g., where the fill neck enters the main body of the liner). It's this attention to design and manufacturing detail that makes DoverPac® the first and only choice for containment.

ArmorFlex® Family of Compliant Static Dissipative Films




One of the key elements of our DoverPac® line of products is the ArmorFlex® material. These films are custom formulated by ILC to deliver superior elongation performance (nearly 500%) for ruggedness and high strength. This feature coupled with a unique blend of safe and effective anti-static additives allows all of the DoverPac® products to deliver reliable high-level containment.

From the original ArmorFlex®104 to the most recent film, ArmorFlex®114, we pioneer the advancement of flexible materials. This is evidenced by the introduction of ArmorFlex®114, the first permanent, non-blooming static dissipative film to meet the 2002/72/EC (and amendments) Directive and EP 3.1.3.



ArmorFlex® 104 Film

- » Passes incendivity testing
- » Designed and manufactured using only FDA compliant materials
- » Verified quality and reliability
- » No animal-derived components
- » Complies with USP Class VI
- » No halogenated compounds and safe for incineration

- 
- » ArmorFlex® 104 was developed in 1997 and has been in use by pharmaceutical manufacturers globally ever since. Proven in myriad applications, ArmorFlex® 104 supports processes from wetcake to dry powder storage and transfer.

ArmorFlex® 104 Film



Solvent Contact Resistance

Chemical	Resistance
Acetone	Very Good
Acetonitrile	Excellent
Anisole	Very Good
Butyl Acetate	Excellent
Cyclohexane	Very Good
Cyclohexane – Ethyl Acetate (50/50)	Very Good
Dichloromethane	Fair
Diethylether	Very Good
Dimethylacetamide	Very Good
Ethanol	Excellent
Ethyl Acetate	Excellent
HCL (37.4%)	Very Good
Heptane	Excellent
HMDS	Fair
KOH (50%)	Excellent
Methanol	Very Good
2-Methoxyethanol	Excellent
n-Methylpiperazine	Excellent
n-Methylpyrrolidone	Excellent
Mineral Oil	Very Good
NaOH (50%)	Excellent
Reagent (3A) Alcohol	Very Good
Tetrahydrofuran	Very Good
Toluene	Fair


Criteria

% Change in Physical Properties	Resistance
0 - 10	Excellent
10 - 20	Very Good
20 - 30	Good
> 30	Fair

Physical Property Data

Property	Test Method	Results
Puncture Resistance	Fed Std 191-5120	11 lbf
Tear Strength	ASTM D 624-91 Die C	470 ppi (min)
Tensile Strength	ASTM D 412-97	5500 psi (min)
Elongation	ASTM D 412-97	490% (min)

European Norm Data

EN Number	Test	Results
EN 388: 1994	Protection against mechanical risks	
EN 420: 1994, Paragraph 4.4.42	Determination of pH value	Pass

CFR Conformance

21 CFR 177.1520
21 CFR 178.3130
21 CFR 182.90

USP Conformance

Conforms to USP 24 <661> for buffering capacity, heavy metals, non-volatile residues, residue on ignition, thermal analysis, and IR (ID identity). Passes USP Class VI (7 day implant) testing.



- ▶ At ILC Dover we “create what’s next” by listening to our customers. In response to operators’ input we’ve developed a new addition to the ArmorFlex® family of films – AF 113. The clarity of the product makes this the clear film of choice for flexible enclosures and flexible isolators.



ArmorFlex® 113 Film

- ▶ Superior visual clarity, ideal for Flexible Enclosures and Flexible Isolators
- ▶ Polyethylene base film provides excellent solvent resistance
- ▶ Permanent antistat provides better than 1×10^{11} Ohms per square surface resistivity
- ▶ 5 year shelf life
- ▶ No animal derived components
- ▶ No incineration off-gassing concerns

ArmorFlex® 113 Film

ArmorFlex® 113 Solvent Resistance Solvent Contact Recommendations

Chemical	Resistance
Acetone	Excellent
Acetonitrile	Excellent
Anisole	Good
Butyl Acetate	Very Good
Cyclohexane	Fair
Cyclohexane – Ethyl Acetate (50/50)	Good
Dichloromethane	Very Good
Diethylether	Excellent
Dimethylacetamide	Excellent
Dimethylformamide	Excellent
Ethanol	Excellent
Ethyl Acetate	Very Good
HCL (37.4%)	Excellent
n-Heptane	Good
HMDS	Excellent
Isopropanol	Excellent
KOH (50%)	Excellent
Methanol	Excellent
2-Methoxyethanol	Excellent
n-Methylpiperazine	Very Good
n-Methylpyrrolidone	Excellent
Mineral Oil	Very Good
NaOH (50%)	Excellent
Reagent (3A) Alcohol	Excellent
Tetrahydrofuran	Excellent
Toluene	Very Good
Water, Distilled	Excellent

Criteria

% Change in Physical Properties	Resistance
0 - 10	Excellent
10 - 20	Very Good
20 - 30	Good
> 30	Fair



Mill impeller and screen change out

The superior visibility provided by AF113 lets you see inside the enclosure as if looking through glass.



Processing drums

Providing Flexible Containment Solutions to the Pharmaceutical Industry since 1997



ArmorFlex® 114 Film

- » At ILC Dover we are always “*creating what’s next*” by listening carefully to our customers. In response to customer input and emerging regulations, we’ve developed a robust new film to support our DoverPac® Containment Systems. This revolutionary film, ArmorFlex® 114, delivers permanent static dissipative properties while meeting FDA and 2002/72/EC requirements for food contact and EP 3.1.3 test conditions.

- » Complies with FDA 21 CFR
- » Fully compliant to 2002/72/EC and amendments
- » Meets test parameters of EP 3.1.3
- » Passes USP <661> Physicochemical Tests for Plastics
- » Passes USP <88> Class VI (7 day implant)
- » Passes <87> biological reactivity, in vitro
- » No animal derived components
- » 5-year shelf life
- » Permanent antistat replaces migrating additives
- » Passes Chilworth incendivity tests
- » Tested for solvent resistance
- » DMF filed with FDA

ArmorFlex® 114 Film

ArmorFlex® 114 Solvent Resistance Solvent Contact Recommendations

Chemical	Resistance
Acetone	Excellent
Acetonitrile	Excellent
Anisole	Good
Butyl Acetate	Good
Cyclohexane	Excellent
Cyclohexane – Ethyl Acetate (50/50)	Excellent
Dichloromethane	Excellent
Diethylether	Excellent
Dimethylacetamide	Excellent
Dimethylformamide	Excellent
Ethanol	Excellent
Ethyl Acetate	Excellent
HCL (37.4%)	Very Good
n-Heptane	Very Good
HMDS	Excellent
Isopropanol	Excellent
KOH (50%)	Very Good
Methanol	Excellent
2-Methoxyethanol	Excellent
Methylethylketone	Excellent
n-Methylpiperazine	Excellent
n-Methylpyrrolidone	Excellent
Methyl-tert-butylether	Excellent
Mineral Oil	Very Good
Reagent (3A) Alcohol	Excellent
NaOH (50%)	Excellent
Tetrahydrofuran	Very Good
Toluene	Fair
Water, Distilled	Excellent

Criteria

% Change in Physical Properties	Resistance
0 - 10	Excellent
10 - 20	Very Good
20 - 30	Good
> 30	Fair



Charging mills with DoverPac® and offloading to IBC with transfer sleeves.



Bag in-bag out sleeves



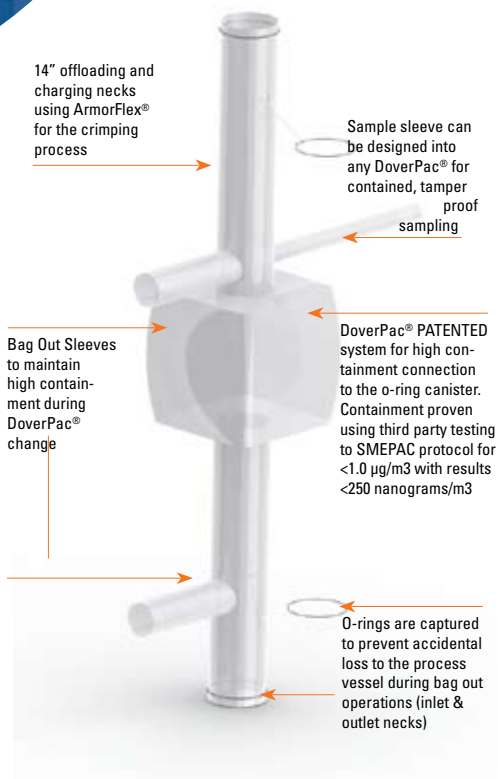
Continuous liners

Providing Flexible Containment Solutions to the Pharmaceutical Industry since 1997

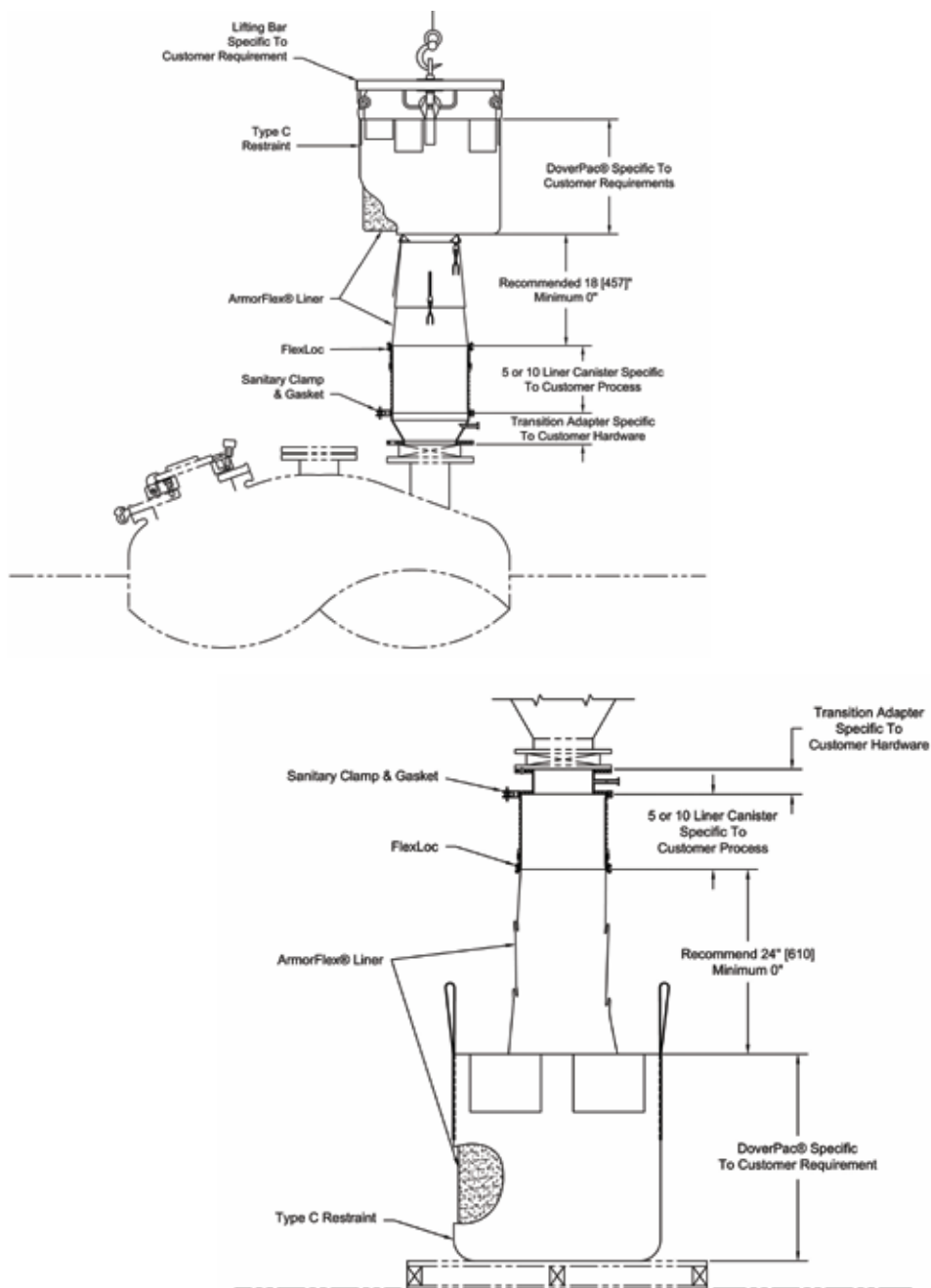


Benefits

- ▶ Verified containment as a system
- ▶ Proven to be lowest cost of ownership
- ▶ ArmorFlex® 114 film is Static Dissipative with a permanent antistat, confirmed to 2002/72/EC and amendments, FDA CFR 21, and test requirements of EP 3.1.3
- ▶ Standard and custom installations
- ▶ CE Marked configurations
- ▶ UN DOT approved configurations
- ▶ Lowest carbon footprint in a complete containment process



Proven DoverPac® Attachment





Offloading Using the Individual DoverPac® System

- » Contained processing to protect the operators
- » cGMP processing in a completely closed operation to protect the product
- » Available in sizes ranging from 20L to 2000L
- » 100% inflation tested
- » CE Marked
- » Significant capital cost savings over rigid isolation systems
- » Significant reduction in cleaning time, waste, and validation expenses
- » Integral sampling sleeve
- » Static dissipative film with groundable restraint (type c)

» System Description

This easy-to-use system has been proven effective in containing active pharmaceutical ingredients and other hazardous compounds. Its use assures a safe and effective transfer of powders, an operational requirement that cannot be achieved with a standard FIBC or big bag. The DoverPac® contained powder transfer system includes a flexible ArmorFlex® liner with restraint for containing powders and a set of hardware that fits the flange of a vessel.

While specific powders react differently due to their particle size, OEB 5 (<1.0 µg/m³) levels have been demonstrated on a task basis with results in the nanogram range. This is based on proven applications, third party testing to the "SMEPAC" protocols on similar designs, and the 100% inflation tests performed on the delivered systems.

Uses ILC Dover's Patented Technology

Basic Offloading Process Steps



Attach



Bag out stub



To sample, extend sleeve and fill



Place crimp cap on crimp body

Materials

ArmorFlex® is ILC Dover's proprietary family of films used exclusively in the DoverPac® family of high potency flexible containment products. Details are available in a databook upon request.

Offloading Canister and Transition Adapter

The canister pictured at the right shows the set up on a straight transition adapter at ILC's test facility. While canisters typically are 316L stainless steel, Hastelloy® canisters also are available. This unit has an initial groove for the canister end cap, additional grooves for liner attachment (typically 5 or 10 grooves depending on process requirements and available height), and 1 groove for the cleaning sleeve or clean-in-place (CIP) sleeve attachment.



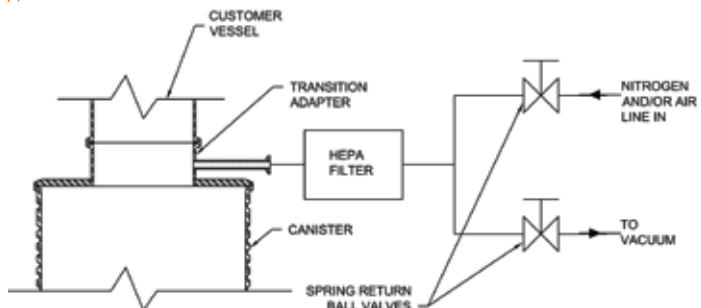
Canister and Transition Adapter Attached to ILC Dover Test Rig.

The canister is supplied with a 12" sanitary flange on each end. This allows for a common design for attachment to vessel specific transition adapters and our CIP tundish.

The custom transition adapter is fitted with a flange on one end that interfaces with the vessel flange (or valve that is in-line on the vessel flange). The opposite end is a 12" sanitary flange that interfaces with the canister. For flanges smaller than 12", a conical transition adapter is used to allow powder flow directly into the vessel without accumulation on the hardware. The adapter also is fitted with a vacuum flange port with a 1/2" sanitary flange for attachment to the vacuum and nitrogen sources to allow inert processing.

This hardware is supplied with a 240 grit (15RA) internal finish and a 180 grit (32 RA) external finish. Other materials and finishes can be quoted separately.

Purge/Vacuum Arrangement



Note: Common vacuum/purge supply connection to HEPA filter provides backwash function to extend filter life.

FlexLoc Clamp

The FlexLoc clamp is used to secure the neck of the liner to the canister. Construction of the molded clamp is of FDA compliant elastomer with integrated stainless steel band clamp. The clamp has a molded ridge along one surface to help install it in the correct orientation.

The FlexLoc functions to prevent powder from going between the inside of the liner and the outside of the canister to minimize cleaning operations. The clamp is designed to operate in the offloading and the charging operations.



FlexLoc Clamp

Crimp Separation Kit

Contained separation between vessels and DoverPacs® is achieved through a Crimp Separation Kit, using ILC's uniquely designed crimp system.

Crimps are color coded to assure that the right crimp is selected for the right product. Red crimps are used for the 14" necks, blue crimps are for the 23" diameter continuous liners, and yellow crimps are for the 4" diameter sample sleeve on the DoverPacs®.

A Crimp Separation Kit includes:

- 200 Crimps
- 1 Crimp Hand tool
- 1 Cutter
- 100 Cable Ties (7" Nylon)
- 1 User's Manual

Additional spare items can be ordered separately by their individual model/part numbers.

The crimps have been designed and tested to compress the standard diameters liners made with ArmorFlex® film. Use on any other system will preclude the crimps from closing correctly, which could result in operator and product exposures.

The hand tool applies two crimps at once. The cutter is used to cut between the two crimps, and then the cap is slid onto the closed crimp body.

ILC crimps have been designed and tested to compress standard diameter liners and sleeves made with ArmorFlex® film



Load crimp into installation tool



Position crimp



Squeeze tool until crimps are engaged -- then release tool

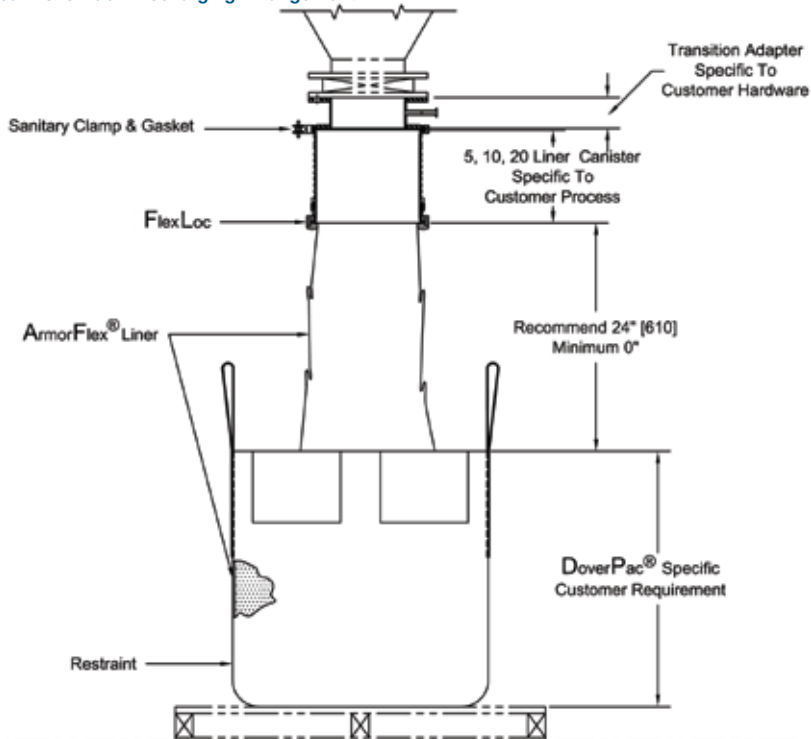


Cut and separate



Install crimp cap on crimp body

Typical DoverPac® Discharging Arrangement



Other System Components and Accessories

Other system components and accessories developed by ILC Dover to support contained pharmaceutical ingredient processing include:

- Wash In Place Enclosure
- Clean In Place System
- In Line Filter Kit



Charging Using the Individual DoverPac® System

- » Contained processing to protect the operators
- » cGMP processing in a completely closed operation to protect the product
- » Available in sizes ranging from 20L to 2000L
- » 100% inflation tested
- » CE Marked
- » Significant capital cost savings over multiple rigid isolation systems
- » Significant reduction in cleaning time, waste, and validation expenses
- » Static dissipative film with groundable restraint (type c)

» System Description

This easy-to-use system has been proven effective in containing active pharmaceutical ingredients and other hazardous compounds to assure a safe and effective transfer of powders, an operational requirement that cannot be achieved with a standard FIBC or big bag. The DoverPac® contained powder transfer system includes a flexible ArmorFlex® liner with restraint for containing powders and a set of hardware that fits the flange of a vessel.

While specific powders react differently due to their particle size, OEB 5 ($<1.0 \mu\text{g}/\text{m}^3$) levels have been demonstrated on a task basis with results in the nanogram range. This is based on proven applications, third party testing to the "SMEPAC" protocols on similar designs, and the 100% inflation tests performed on the delivered systems.

Uses ILC Dover's Patented Technology

Basic Process Flow of a Contained, Flexible Charging System



Lift over vessel



Attach liner then bag out stub



Empty



Crimp

Materials

ArmorFlex® is ILC Dover's proprietary family of films used exclusively in the DoverPac® family of high potency flexible containment products. Details are available in a databook upon request.

Charging Canister and Transition Adapter

The canister pictured at the right shows the set up on a straight transition adapter at ILC's test facility. While canisters typically are 316L stainless steel, Hastelloy® canisters also are available. This unit has an initial groove for the canister end cap, additional grooves for liner attachment (typically 5 or 10 grooves depending on process requirements and available height), and 1 groove for the cleaning sleeve or clean-in-place (CIP) sleeve attachment.

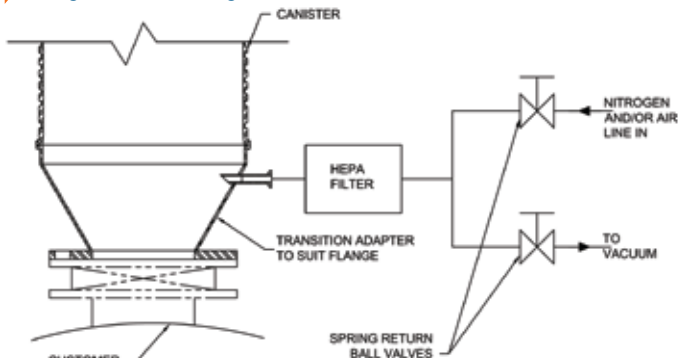


Canister Attached to ILC Dover Test Rig

The canister is supplied with a 12" sanitary flange on each end. This allows for a common design for attachment to vessel specific transition adapters and our CIP tundish.

The custom transition adapter is fitted with a flange on one end that interfaces with the vessel flange (or valve that is in-line on the vessel flange). The opposite end is a 12" sanitary flange that interfaces with the canister. For flanges smaller than 12", a conical transition adapter is used to allow powder flow directly into the vessel without accumulation on the hardware. The adapter also is fitted with a vacuum flange port with a 1/2" sanitary flange for attachment to the vacuum and nitrogen sources to allow inert processing.

Purge/Vacuum Arrangement



Note: Common vacuum/purge supply connection to HEPA filter provides backwash function to extend filter life.

This hardware is supplied with a 240 grit (15 RA) internal finish and a 180 grit (32 RA) external finish. (Other materials and finishes also can be provided.)

Please note that for vessels that normally operate under pressure, a valve is required to isolate the liner from the vessel while the vessel is under pressure. This pressure-rated valve is normally supplied by the customer and installed between the vessel and the transition adapter.



FlexLoc Clamp

» FlexLoc Clamp

The FlexLoc clamp is used to secure the neck of the liner to the canister. Construction of the molded clamp is of FDA compliant elastomer with integrated stainless steel band clamp. The clamp has a molded ridge along one surface to help install it in the correct orientation.

The FlexLoc functions to prevent powder from going between the inside of the liner and the outside of the canister to minimize cleaning operations. The clamp is designed to operate in the offloading and the charging operations.

ILC crimps have been designed and tested to compress standard diameter liners made with ArmorFlex® film



Load crimp into installation tool

» Crimp Separation Kit

Contained separation between vessels and DoverPacs® is achieved through a Crimp Separation Kit, using ILC's uniquely designed crimp system.

Crimps are color coded to assure that the right crimp is selected for the right product. Red crimps are used for the 14" necks on the DoverPacs®.

A Crimp Separation Kit includes:

- 200 Crimps
- 1 Crimp Hand tool
- 1 Cutter
- 100 Cable Ties (7" Nylon)
- 1 User's Manual

Additional spare items can be ordered separately by their individual model/part numbers.

After filling, the liner is twisted and crimped closed. The hand tool applies two crimps at once. The cutter is used to cut between the two crimps, and then the cap is slid onto the closed crimp body.



Position crimp



Squeeze tool until crimps are engaged -- then release tool



Cut and separate



Install crimp cap on crimp body

Use of Lifting Bar



Attaching the restraint to lifting bar

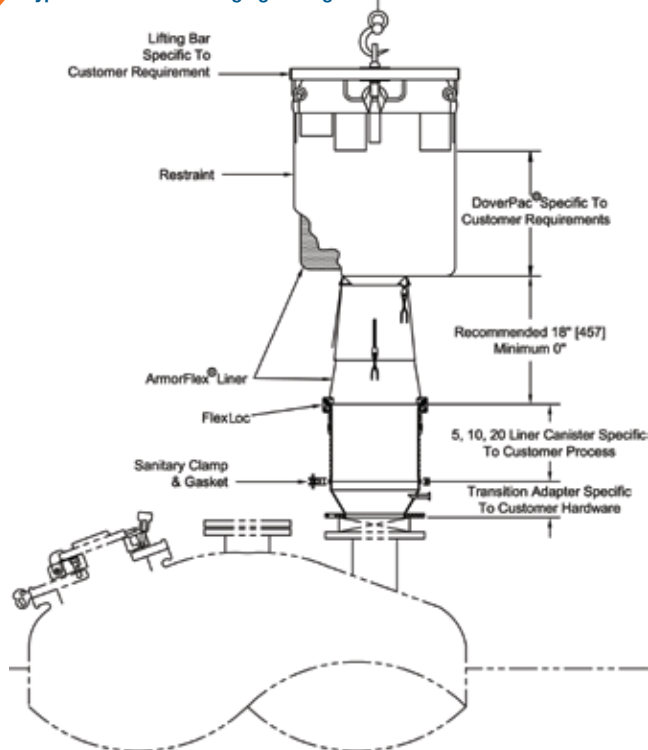


Securing the liner neck

» Lifting Bars

A lifting bar and hoist are used in order to position the DoverPac® restraints over the vessel interface for charging. The lifting bar comes in two sizes to accommodate DoverPac® sizes. Hoists typically are supplied by the customer.

» Typical DoverPac® Charging Arrangement



» Other System Components and Accessories

Other system components and accessories developed by ILC Dover to support contained pharmaceutical ingredient processing include:

- Wash In Place Enclosure
- Clean In Place System
- In Line Filter Kit

OVERVIEW

The Coaxial neck DoverPac® was originally designed to allow secondary containment to be used with a DoverPac® in the late 1990's for charging and offloading vessels through isolators. Given the increase in highly potent API manufacturing, the use of this system with either rigid isolators or flexible enclosures is a complimentary processing option.

The Coaxial Neck DoverPac® serves the dual function of contained transfer and storage system. These are available in standard 45, 185, 400, and 700Liter volumes. Custom sizes can also be accommodated.

HOW DOES IT WORK?

This system is designed to provide containment to the OEB 5 (less than 1 µg/m³ with a goal of below 200 nanograms/m³ on a task basis). To achieve this, the secondary containment (i.e. flexible enclosure and the outer neck) at the primary connection points are applied. Figure 1 shows the offloading set up during exposure monitoring trials.

The installation sequence follows:

- The top of the enclosure is attached to the first canister on the vessel outlet.
- The bottom of the enclosure is attached to the canister on the support frame.
- The external neck on the DoverPac® is then attached to the outlet point of the canister on the frame.
- The internal neck of the DoverPac® is pulled up through the lower canister and is attached to the groove on the vessel canister by using the integral glove sleeves on the flexible enclosure.



Figure 1

Once the vessel is offloaded, the internal neck is crimped off and pushed back down through the canister on the frame by using the enclosure to access the neck area. The operator then extracts his/her arms from the enclosure and crimps off the external neck.

The crimping process, Figure 2, is employed for the contained separation operations. This process consists of installing two injection molded crimps into the hand tool, twisting the liner neck, ratcheting the crimps closed, cutting between the two crimps, and installing the protective cap.

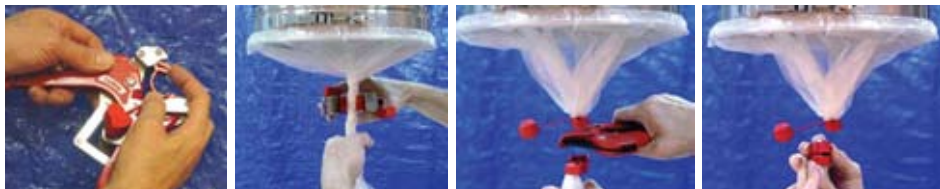


Figure 2

Coaxial DoverPac® - Nanogram Powder Transfer

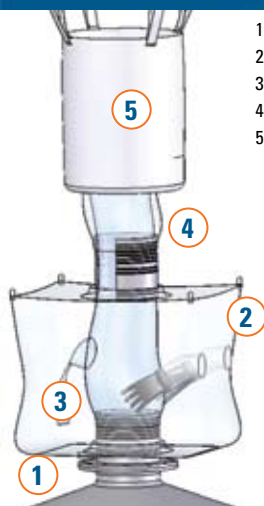


Figure 3

1. Vessel Inlet
2. Flexible Enclosure
3. Inner Neck Attachment
4. Outer Neck Attachment
5. DoverPac®

In addition to offloading vessels, the system can be applied to charging processes as shown in Figure 3. The flexible enclosure design is either supported by a frame or bungee cords.

FEATURES

- Standard DoverPac® hardware interfaces
- Standard and custom sizes
- Two barriers for containment
- Product contact with regulatory compliant materials

BENEFITS

- Uses a broad range of solutions depending on containment level needed
- Tailored to specific batch sizes
- Provides nanogram levels of protection without high capital costs
- Eliminates risk to product

WHAT CONTAINMENT LEVEL PROVIDED?

OEB 5 in the nanogram levels. The table below outlines a summary of the results achieved.

Sample Set	N	Mean	Range Lowest	Range Highest	Standard Deviation	Standard Error	Coefficient of Variation	95% Confidence Interval for Population Mean
Personal Sample Breathing Zone PSBZ – with outlier event	12	0.077 µg/m ³	0.014 µg/m ³	0.50 µg/m ³	0.136 µg/m ³	0.039	1.8	-0.00980 to 0.163 µg/m ³
PSBZ – without outlier event	10	0.032 µg/m ³	0.014 µg/m ³	0.084 µg/m ³	0.023 µg/m ³	0.0074	0.72	0.0156 to 0.0490 µg/m ³

WHY USE THIS OVER OTHER TECHNOLOGIES?

The cost of ownership, ergonomic advantages, and speed of delivery benefits of this flexible solution far outweigh those of rigid isolation systems

OTHER POTENTIAL APPLICATIONS

This technology is applicable for charging and offloading most vessels. This includes, but is not limited to, reactors (charging only), dryers, blenders and granulators.

Uses ILC Dover's Patented Technology

G2Pac - <100µg/m³ Containment Powder Transfer

G2Pac

The Smart FIBC

Features:

- ▶ Durable ArmorFlex® liner with groundable restraint (type C)
- ▶ Individual necks with bag-out sleeve to support charging and offloading operations
- ▶ Secure, dust-free hardware interface to process equipment
- ▶ Sized to interface with standard pallet
- ▶ Interfaces with ILC contained separation crimps

Benefits:

- ▶ Economical containment
- ▶ Supports dust-free operation
- ▶ Reduced cross contamination risks
- ▶ Protects operator
- ▶ One-person operation

- ▶ Eclipsing the traditional FIBC, the **G2Pac** is engineered to address the issues that arise from uncontrolled processes, including compromised facility cleanliness, cross contamination risks and employee exposure to unnecessary hazards. **G2Pac** supports cGMP operations.

Feature	G2Pac
Restraint and Liner	Yes
Charge/Offloading Neck	Yes
AarmorFlex® 104	Yes
Sizing	700L, 560L, 185L
Integral Bag-Out Sleeves for Contained Changeover	Yes
Interfaces with Contained Separation Crimps	Yes

DoverPac® Continuous Liner 23" Dia - Contained Powder Discharge to Drums

FLEXIBLE CONTAINMENT TECHNOLOGIES



23" (584 mm) Diameter Continuous Liner Systems

- » Contained processing to protect the operators
- » cGMP processing in a completely closed operation to protect the product
- » One person operation
- » Pre-loaded liner material minimizes processing time
- » Inert atmosphere offloading of products.
- » Significant reduction in cleaning time, waste, and validation expenses

» System Description

This easy-to-use system has been proven effective in containing active pharmaceutical ingredients and other hazardous compounds to assure a safe and effective transfer of powders – an operational requirement that cannot be achieved with a standard drum liner. The 23" (584 mm) diameter continuous liner system is designed to allow continuous offloading of powders into drums. This contained powder transfer system consists primarily of a set of hardware that fits the flange of a vessel and a factory packed kit of liners that are delivered in a pack ready to install on the canister. Standard systems are supplied in continuous sleeves. Sample sleeves are often added as custom applications.



The system is available in the following sizes:

Pack Length	Number of Drums per Pack*
50'	10
100'	20
150'	30

** assumes 5' of liner per drum to accommodate drum height and crimping. Actual usage will depend on the drum height*

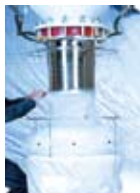
DoverPac® Continuous Liner 23” Dia - Contained Powder Discharge to Drums



The basic steps for operating this easy to use system are shown in these continuous liner process steps



Versatile hardware easily mounts to vessel discharge port



Continuous liner pack is installed



Sleeve is pulled into drum and filled



Unique DoverPac® crimping system is used to separate filled drum



Next sleeve is pulled into drum

Materials

ArmorFlex® is ILC Dover's proprietary family of films used exclusively in the DoverPac® family of high potency flexible containment products.

These films pass incendivity testing and are designed and manufactured using FDA & EU compliant materials.

Continuous Liner Kit

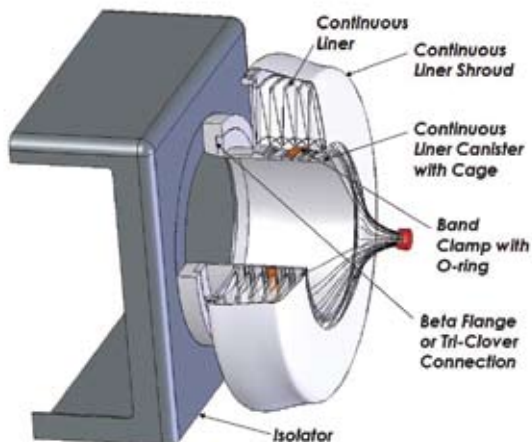
The Continuous Liner Kit includes:

- Canister
- Cage
- Shroud
- Pack Protector
- 12” Band Clamp
- Sanitary Clamp and Gasket
- FlexLoc Clamp
- 23” Crimp Kit
- Turn Table
- Continuous Liner Pack

The canister will attach to the vessel using a transition adapter. The transition adapter has a nitrogen purge/vent to discharge into an inert atmosphere (if required).

Continuous Bag-in/Bag-out System

This system can be supplied with an alpha/beta port interface to allow attachment to an isolator as depicted in the drawing. This allows the contained removal of product containers, samples, or waste from the isolator.



▶▶ Crimp Separation Kit

The 23" crimp separation kit is used to separate the filled drum from the unused pack. The 23" Crimp Separation (start-up) Kit includes:

- 200 Crimps
- 1 Crimp Hand tool
- 1 Cutter
- 100 Cable Ties (7" Nylon)
- 1 User's Manual

Additional spare items can be ordered separately by their individual model/part numbers.

The crimps have been designed and tested to compress the standard 23" diameter liners made with ArmorFlex® film. Use on any other system will preclude the crimps from closing correctly, which could result in operator and product exposures.

The hand tool applies two crimps at once. The cutter is then used to cut between the two crimps, and the cap is slid onto the closed crimp body.

ILC crimps have been designed and tested to compress standard diameter liners made with ArmorFlex® film



Load crimp into installation tool



Position crimp



Squeeze tool until crimps are engaged -- then release tool



Cut and separate



Install crimp cap on crimp body

▶▶ FlexLoc Clamp

The FlexLoc clamp is used to secure the neck of the liner to the canister. Construction of the molded clamp is of FDA compliant elastomer with integrated stainless steel band clamp. The clamp has a molded ridge along one surface to help install it in the correct orientation.



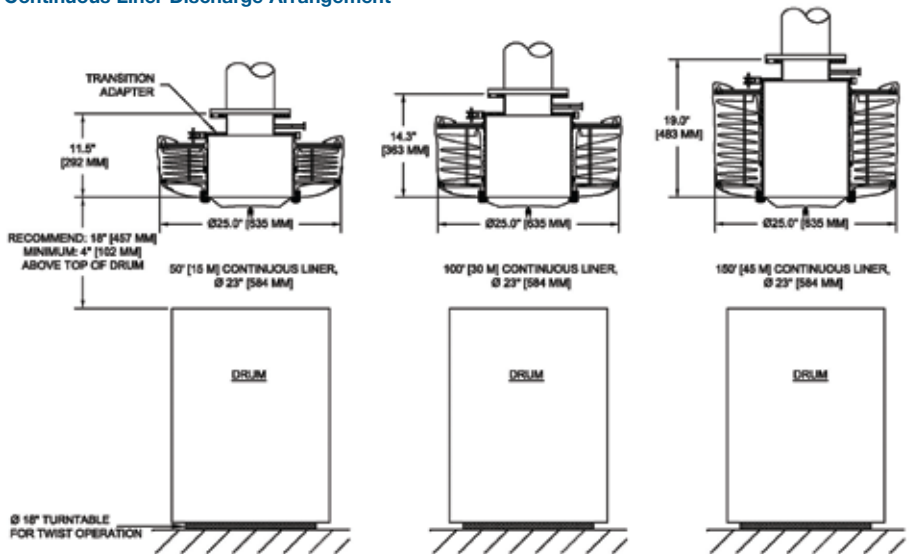
FlexLoc Clamp

The FlexLoc functions to prevent powder from going between the inside of the liner and the outside of the canister to minimize cleaning operations. The clamp is designed to operate in the offloading and the charging operations.

▶▶ Containment Levels

While specific powders react differently due to their particle size, customer testing has shown that these systems are capable of providing containment levels to below 1 µg/m³ in applications around the world.

Continuous Liner Discharge Arrangement



Other System Components and Accessories

Other system components and accessories developed by ILC Dover to support contained pharmaceutical ingredient processing include:

- Wash In Place Enclosure
- Clean In Place System
- In Line Filter Kit

Applications

- Product offloading from sifters, mills, blenders, centrifuges, dryers and other process equipment.
- Bag-in/Bag-out



14" (355.6mm) Diameter Continuous Liner Systems

» $<1\mu\text{g}/\text{m}^3$ contained processing to protect the operators with results in the 250 nanogram/ m^3 range

» cGMP processing in a completely closed operation to protect the product

» One person operation

» Inert atmosphere offloading of products

» Significant reduction in cleaning time, waste, and validation expenses

» System Description

This easy-to-use system has been proven effective in containing active pharmaceutical ingredients and other hazardous compounds. This system uses a five-liner canister, which will allow up to five contained changes of the 30' packs before cleaning or canister recovery is required. This system also provides the 30' liner packs pre-bundled, which reduces operator time. Its use assures a safe and effective transfer of powders, tablets, vials, tools, and trash.

Uses ILC Dover's Patented Technology

DoverPac® Continuous Liner 14" Dia - Contained Powder Discharge to Drums



Attach neck of continuous liner to canister

Install a band clamp

Slide the pack onto the canister

Install the outer shroud

Unsnap the retaining snaps on the pack



Pull down liner material to start processing

Materials

ArmorFlex® is ILC Dover's proprietary family of films used exclusively in the DoverPac® family of high potency flexible containment products.

These films pass incendivity testing and are designed and manufactured using FDA & EU compliant materials.

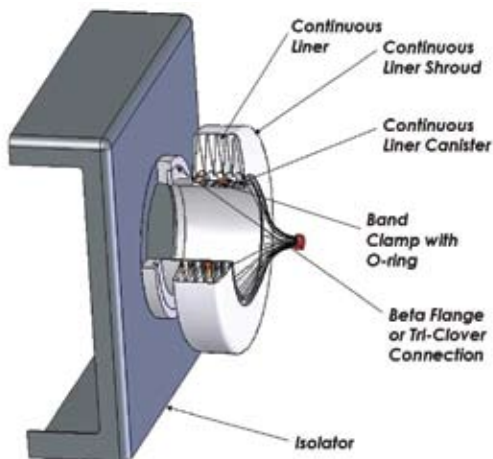
System Components

The system components for contained discharging as pictured here consist of:

- 8" Sanitary Flange Five Liner SS Canister (used to make contained connection of DoverPacs®)
- 30' Continuous Liner Pack
- Fabric Outer Shroud
- Pack Protector
- 8" Stainless Steel Band
- 8" Sanitary Clamp
- 8" Sanitary Gasket
- 14" Crimp Kit
- 8" FlexLoc Clamp

This system can be supplied with an alpha/beta port interface to allow attachment to an isolator as depicted in the drawing. This allows the contained removal of product containers, samples, or waste from the isolator.

Continuous Bag-in/Bag-out System



» Crimp Separation Kit

The 14" crimp kit is used to separate the filled drum from the unused pack. The 14" Crimp Separation (start-up) Kit includes:

- 200 Crimps
- 1 Crimp Hand tool
- 1 Cutter
- 100 Cable Ties (7" Nylon)
- 1 User's Manual

Additional spare items can be ordered separately by their individual model/part numbers.

The crimps have been designed and tested to compress the standard 14" diameter liners made with ArmorFlex® film. Use on any other system will preclude the crimps from closing correctly, which could result in operator and product exposures.

The hand tool applies two crimps at once. The cutter is then used to cut between the two crimps, and the cap is slid onto the closed crimp body.

This system has been proven effective in containing active pharmaceutical ingredients and other hazardous compounds to assure a safe and effective transfer of powders, tablets, vials, tools, and trash – an operational requirement that cannot be achieved with a standard drum liner.

» Containment Levels

While specific powders react differently due to their particle size, customer testing has shown that these systems are capable of providing containment levels to below 1 µg/m³ on a task basis in applications around the world.

ILC crimps have been designed and tested to compress standard diameter liners and sleeves made with ArmorFlex® film



Load crimp into installation tool



Position crimp



*Squeeze tool until crimps are engaged
-- then release tool*



Cut and separate



Install crimp cap on crimp body



FlexLoc Clamp

»» FlexLoc Clamp

The FlexLoc clamp is used to secure the neck of the liner to the canister. Construction of the molded clamp is of FDA compliant elastomer with integrated stainless steel band clamp.

The clamp has a molded ridge along one surface to help install it in the correct orientation.

It functions to prevent powder from going between the inside of the liner and the outside of the canister to minimize cleaning operations. The FlexLoc clamp is designed to operate in the offloading and the charging operations.

»» Other System Components and Accessories

Other system components and accessories developed by ILC Dover to support contained pharmaceutical ingredient processing include:

- Wash In Place Enclosure
- Clean In Place System
- In Line Filter Kit

»» Applications

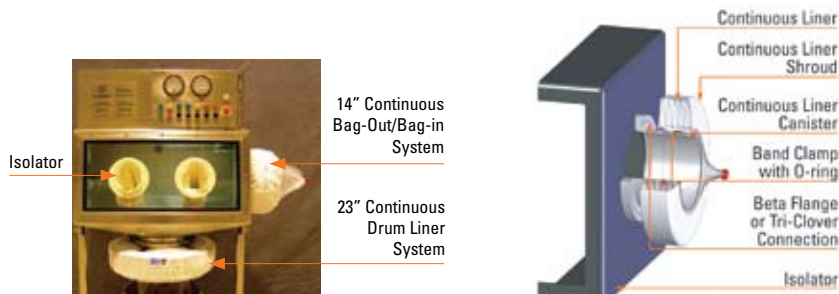
- Product offloading
- Tablet offloading
- Bag-in/Bag-out

Continuous Liner Bag in Bag out - Contained Transfer



OVERVIEW

The DoverPac® Bag In/Bag Out (BIBO) system is a family of contained transfer designs for multiple processes. The primary components for this validated operation consist of multiple groove canisters, docking interface hardware, and softgoods in either continuous liner form or discreet liners as illustrated below in the continuous liner application.



This system can be applied to any rigid isolator. The use of multiple size canisters allows a broad range of needs to be met, systems can be retrofit to existing assets, and the BIBO system requires a low capital outlay.

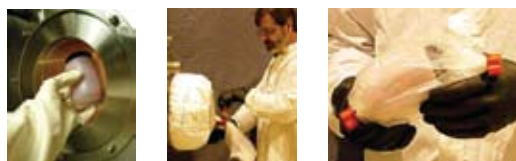
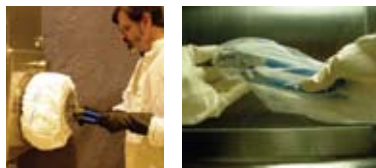
OPERATION

By utilizing the patented multi o-ring and flexible containment techniques developed by ILC Dover, this system builds on proven DoverPac® designs. The hardware is docked to the containment enclosure either by using the existing alpha/beta port hardware or bolting directly to the wall of the rigid isolator. The liner is then extended over the item to be introduced or removed from the enclosure and then crimped off to complete the contained transfer.



◀ Continuous Liner being attached to isolator

Operator shown "bagging in" a tool ▶▶



◀ Operator shown "bagging out" a sample

Uses ILC Dover's Patented Technology

Continuous Liner Bag in Bag out - Contained Transfer



Accessories and support equipment include a lifting stand to help support the larger canister size, crimps and the FlexLoc™.



▲ Crimping tool/crimps



▲ FlexLoc™



◀ Lifting Stand

APPLICATIONS—CURRENT AND POTENTIAL

Current applications: tool pass through on 22 rigid isolators at one international Pharma manufacturer's site, trash bag out, sample bottle transfer, tablet transfer for testing/analysis, pre-packaged seed/API processing after tare weight process

Other potential applications: document transfer, gamma irradiated for sterile transfer operation, wall mounted in process suite for contained pass thrus.

CONTAINMENT LEVEL

Nanogram containment levels demonstrated during task based operations – see data below.

Sample*	Location	Duration of Operation (mins.)	Measured Airborne Concentration (µg/m3)
Source Sample (AS-0BH)	At Bagout Port	31	<0.017
Operator #1 (PSBZ)	On Shoulder	31	0.017
Operator # 1 (PSBZ)	On Shoulder	30	<0.017
Operator # 2 (PSBZ)	On Shoulder	30	<0.018
Source Sample (AS-0BZ)	At Bagout Port	30	<0.017

* Finished Product, raw materials, cleaning materials, waste materials

FEATURES

- Validated system
- Proven and tested softgoods
- Disposable
- Bolt on or RTP Interfaces available

BENEFITS

- Minimizes risk during operation
- ArmorFlex films are regulatory compliant
- Eliminates concern of cross contamination due to "pneumatic" effect of low end films leaking
- Reduced cleaning and cleaning validation costs
- Reduced process time and cost by eliminating multiple RTP canisters
- Eliminates RTP seal maintenance



Static Dissipative Drum Liners

Features

- ▶ Clear durable film
- ▶ Chilworth tested– passes incendivity testing
- ▶ Available in all ArmorFlex® films
- ▶ Up to 5 year shelf life based on film selected

- ▶ DoverPac® static dissipative drum liners provide you with the confidence to safely transfer and store a wide range of API's and other powders. As the pioneer of flexible containment systems for the pharmaceutical industry, ILC Dover offers drum liners constructed from our durable ArmorFlex® film—the same material used in our DoverPac® API containment system.



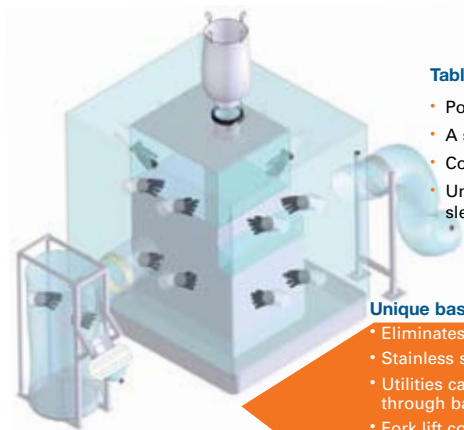
Flexible Enclosures

- » Allows operators to work in shirt sleeve environment – increases efficiency
- » 3rd party validated Nanogram containment levels using SMEPAC guidelines
- » Economical
- » Fast turnaround/installation
- » Compatible with a wide range of existing equipment for retrofit
- » Design makes use of existing DoverPac® containment details such as crimps, bag/out sleeves, and o-ring interface canisters
- » Ergonomics are improved with an increased range of motion
- » Designs support separation of process and technical areas
- » Where applicable, entire piece of equipment can be contained



*Fit check on lab scale
fluid bed dryer*

- » ILC Dover's flexible enclosures take the concept of a traditional flexible glove bag to a new level. Using the same reliable fabrication techniques and proven containment design features found on our DoverPac® family of products, we've produced a line of flexible enclosures adaptable to a wide range of existing equipment. These enclosures save time and money by allowing you to retrofit existing processing equipment while achieving nanogram containment levels. All materials meet FDA standards and the design accommodates cGMP as well as operator ergonomics.



Tablet Press/Deduster Flexible Enclosure

- Powder added using a DoverPac® and canister interface
- A series of glove sleeves permit easy press operation
- Continuous bag-out sleeve supports tablet sampling/analysis
- Unexpected maintenance can be performed using bag out sleeve and gloves

Unique base design/interface

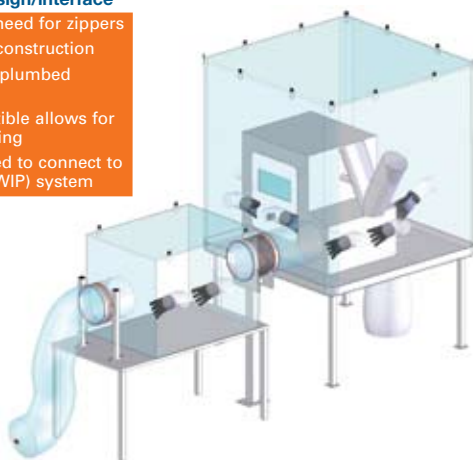
- Eliminates the need for zippers
- Stainless steel construction
- Utilities can be plumbed through base
- Fork lift compatible allows for easy repositioning
- Base can be used to connect to wash-in-place (WIP) system

Enclosures designed to work with:

- Blending
- Milling
- Tableting
- Weighing
- Subdividing

More cost effective than:

- Rigid isolators
- Downflow booths
- New equipment



Lab Scale Analytical/Blending Process Train

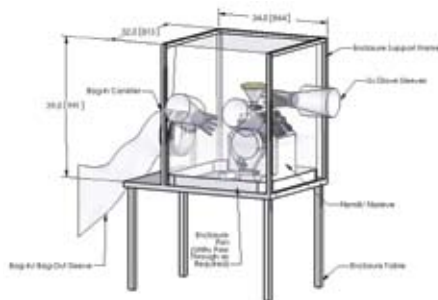
- Product enters through bag-in sleeves
- Operation of equipment accommodated via glove sleeves
- Integration of process steps through ILC Dover canister interface
- Process train can be expanded to include sub-dividing, milling, tableting, etc.

Contained Processes - Flexible Enclosures / Glovebags



Weighing and Dispensing

- Utilities through pan
- Used with standard lab equipment



L1A Fitzmill

Mill Flexible Enclosures

- Powder added at top using DoverPac® addition technique or scooped in by hand
- Milled powder discharged into DoverPac®, IBC or vessels



Granulator

- Mobile frame allows use in multiple suites
- Clear film and bungee attachments optimize ergonomics

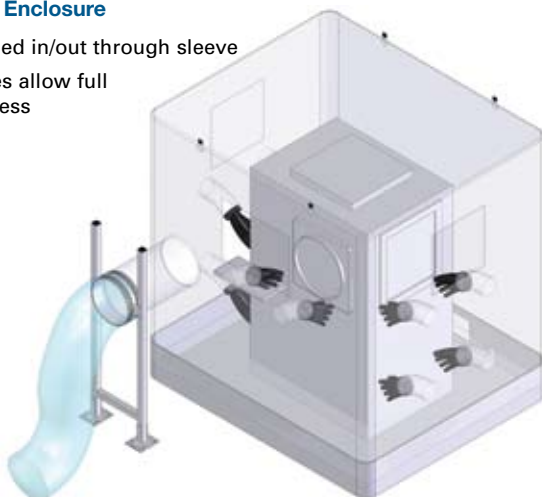


Overdrive Mill enclosure with shroud removed and fully deployed to allow use of glove sleeves for cleaning and maintenance

ILC Dover...pioneers of flexible containment.

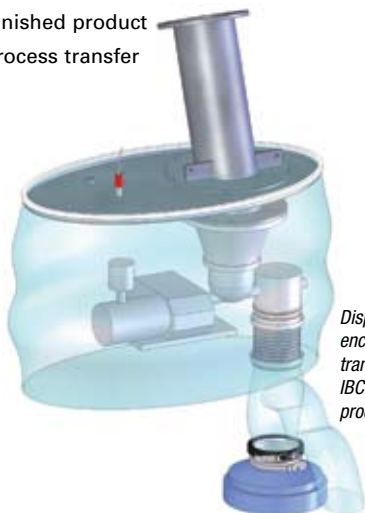
Tablet Coater Enclosure

- Tablets bagged in/out through sleeve
- Glove sleeves allow full operator access



IBC Transfer

- Milled powder or finished product
- Tare weighing in process transfer



*Dispensing device
enclosure with
transfer sleeve to
IBC or downstream
process*



OVERVIEW

The Flexible Document Transfer Enclosure is designed to allow paperwork used in pharmaceutical processing to be handled in a contained way so that powders are not transferred onto the documents and to areas or individuals that are not protected.

The enclosure can be manufactured from a clear ArmorFlex® or polyurethane film that will allow for room light to illuminate the inside of the enclosure for easy viewing and writing on the documents.

HOW DOES THE SYSTEM WORK?

Documents, writing implements, and baggies for enclosing the finished paperwork are preloaded into the enclosure.

A set of glove sleeves (left hand and right hand) are integral to the front of the enclosure at an approximate height of 48". Due to the flexibility of the enclosure, the operators will be able to work at heights approximately +/- 5" from the glove sleeve centerline. This flexibility is provided by the nature of the films employed and the use of bungee cords that allow the enclosure to move with the operator.

On the side opposite of the Glove Sleeves will be a zipper that is used as a pass-through for the documents.

A bag in/bag out (BIBO) canister can also be provided as an optional method for transfer (as shown in the photograph).

Space is also available to store plastic bags that can be used to contain the documents once all work is completed.

A stainless steel frame is used to support the enclosure which includes casters to make the unit portable. The frame will include a rigid plate to use for support during writing.

The top half of the frame can be provided as a table mounted system.

Frames are typically available in 304 or 316L Stainless Steel. Other materials can be provided as required.

The typical document transfer enclosure is sized for dimensions of 24" wide x 24" high x 24" deep. Custom sizes are also available.

FEATURES

- Clear film allows use of existing light from the suite
- Passive system meets ATEX and Ex ratings
- Re-usable for extended campaigns
- Portable
- Small footprint does not take up a lot of floor space



BENEFITS

- No cross contamination transfer to documents and then to other parts of the plant
- Ergonomics are maximized with flexible materials
- Reduced cleaning and cleaning validation
- Low capital and operating cost
- Speed of implementation
- Production and Lab processes supported

WHAT CONTAINMENT LEVEL PROVIDED?

OEB 5 with results in the nanogram range. This is anticipated given third party test results from similar designs and the 100% inflation tests performed on the deliverable enclosures.

WHY USE THIS OVER OTHER TECHNOLOGIES?

The cost of ownership, ergonomic advantages, and speed of delivery benefits of this flexible solution far outweigh those of rigid isolation systems.

OTHER POTENTIAL APPLICATIONS

- Sampling
- Dispensing
- Product Analysis

Drum Transfer System - Contained Drum Dispensing



OVERVIEW

Flexible Containment for offloading drummed materials in a safe and efficient manner is provided by the Drum Transfer System (DTS) platform, at fixed and varying heights.



Figure 1a – Fixed Height Lifter

1. Flexible Enclosure
2. Outer Drum Sleeve
3. DTS Enclosure Frame
4. DTS Base Frame
5. Outlet Canister
6. Lifter



Figure 1b – Variable Height Lifter

The DTS consists of an enclosure attachment frame, a support stand, a drum lifter, an enclosure, an outer drum sleeve, and discharge softgoods that are dependent upon your process equipment.

The basic process steps include:

- Attach the enclosure to the frame.
- Stretch the bottom opening of the Drum Sleeve over the drum and attach the sleeve to the ring on the back of the frame.
- Pull the drum slightly into the enclosure and open the inner drum liner using the integral gloves on the enclosure.
- Scoop/pour powder into the process equipment to be utilized.
- Put trash in the empty drum and move the drum back out of the ring with the translating arm of the lifter.
- Twist and crimp the Drum Transfer Sleeve for disposal of the drum.
- Attach a new sleeve to a new drum and attach the sleeve over the stub remaining from the previous drum. Pull the stub into the enclosure to allow a clear pass through for the drum and repeat the process steps above.

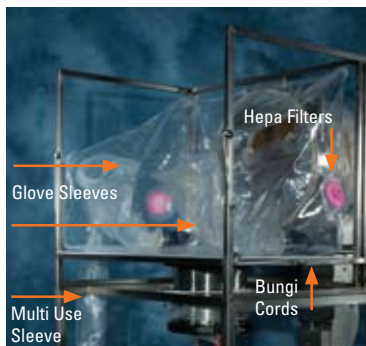
Drum Transfer System - Contained Drum Dispensing

HOW DOES THE SYSTEM WORK?

The Enclosure Frame sits on a series of bases offering a modular approach to processing drums in a contained fashion. This provides the benefit of processing into various mills, DoverPacs® and other vessels.

The entire assembly is mobile and can be wheeled over the piece of process equipment to be charged. The castors used here are conductive. Two wheels are locking while the other two pivot for steering.

The enclosure functions as a flexible isolator. It is attached to the frame at the drum inlet ring and the outlet canister. Bungee cords are used to attach the enclosure to the frame and allow the enclosure to move with the operator to take advantage of the system's built in flexibility.



The drum lifting unit is provided as part of the system. The lifter is pneumatic powered to lift and tilt the drum into position. The unit is a stainless steel construction and meets cGMP requirements. The maximum lift capacity of the standard unit is 100 Kg though larger lifts can be provided.

The drum's inner liner can then be accessed from the enclosure after the outer drum liner is removed as depicted here.

The outlet canister supplied with the frame is typically our 5 liner, multiple o-ring groove system. For transfer direct to a process vessel a Transfer Sleeve is used. If filling with a DoverPac® is required, the canister supports interface to this containment technology.

Figure 2

WHAT CONTAINMENT LEVEL PROVIDED?

OEB 5 with results in the nanogram range. This is based on proven applications, third party testing to the "SMEPAC" protocols, and the 100% inflation tests performed on the deliverable enclosures.

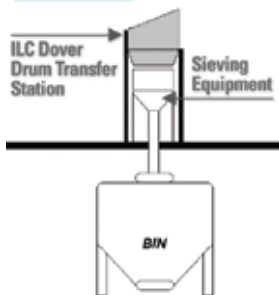
WHY USE THIS OVER OTHER TECHNOLOGIES?

The cost of ownership, ergonomic advantages, and speed of delivery benefits of this flexible solution far outweigh those of rigid isolation systems.

APPLICATIONS

Given the modularity features designed into the Drum Transfer System, contained transfer of drummed powders for the following applications is possible:

MILLING



In the application pictured in Figure 3, powder is processed from a drum, through a mill (a Quadro Sifter in this example), into a stainless steel Intermediate Bulk Container (IBC).

An interface to the mill is provided at the outlet of the Enclosure frame using a transfer sleeve. A similar sleeve is used to go from the outlet of the mill to the inlet of the IBC.

Figure 3

Drum Transfer System - Contained Drum Dispensing



Figure 4



Figure 5

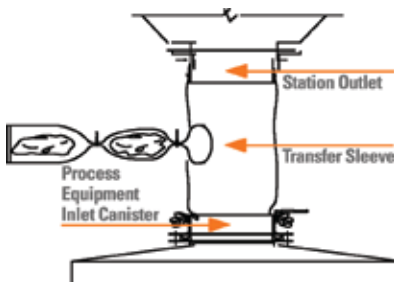


Figure 6

In Figure 4, the milled powder is processed into a DoverPac® for future charging into a vessel. The example pictured uses a Quadro overdrive mill. This same approach has been accomplished with the Quadro under drive mill as well as other mills.

In this application, a transfer sleeve would be attached to the discharge canister of the DTS frame and to the inlet canister on the mill.

SUBDIVIDING

Using the DTS, a scale can be placed either inside the enclosure or just underneath it between the support tray and the enclosure. In this approach, the discharge canister was moved to the side to allow room for the scale.

On a larger size system, like the BNL repackaging effort discussed in the next paragraph, the DTS was placed around a floor scale so that a tare weight was measured. In this instance a Sartorius scale was used but others can be accommodated. In this type of application it is important to confirm the interface sizes.

REPACKAGING

We have worked recently with a repackaging company, BNL Labs, for an application with one of our customers in Ireland. In this application, drums and bags of intermediate materials were transferred directly into DoverPacs®. These were for 185L, 400L and 700L sizes.

The customer would have rejected any lot of repackaged materials if any powder were seen on the outside of the restraint. In order to be successful, BNL adopted our Drum Transfer Station.

CHARGING TO VESSELS

The Transfer Sleeve between the bottom of the DTS and the inlet of the next piece of equipment is depicted in Figure 6. This uses our standard technology of multiple groove o-rings and bag out techniques.

The Transfer Sleeve between the enclosure outlet and the process equipment inlet will be sized using our standard 12" hardware. In this case, we will be able to use our unique crimp system for contained separation.

After processing, the Transfer Sleeve will be twisted and crimped closed using the red, 14" crimps. The hand tool applies two crimps at once. The cutter is then used to cut between the two crimps and the cap is slid onto the closed crimp body.

In addition, the DoverLoc™, a molded clamp that secures the liner at the bottom interface point of the canister, supports the twisting/crimp operation and minimizes cleaning.

Drum Transfer System - Contained Drum Dispensing

Feature	Benefit
Flexible enclosure follows operator's movements	Ergonomic performance is better than rigid system Fits a wider range of operator sizes without ergonomic issues of rigid designs
Lightweight, portable design	Can move to process area when needed, freeing room in process suite when not in use unlike a rigid, fixed system Better utilization of facilities
Disposable	Significant operational cost savings in cleaning time and validation
Third Party proven containment	Engineered process control Protection of operator No product loss of expensive APIs
Reduced capital cost over rigid systems	Significant savings of capital budget leaving money for other priorities
Maximized use of contained processing commonality	Operator training minimized across multiple processes
Time to manufacturing readiness is shorter than capital intensive systems	Improved speed to market
cGMP system	No cross contamination
Modular frame design	Allows attachment to a process specific frame Improved interface to multiple pieces of process equipment and DoverPac® sizes
Proven in customer applications	This is a validated system

OVERVIEW

Milling is a common operation throughout the Pharmaceutical Manufacturing Process. Sizing of powders is a dusty operation and with more potent powders being processed the need for containing this operation becomes even more critical from safety and cross contamination avoidance purposes.

In addition to contained powder throughput, it is imperative that access to the interior of the mill be made available without breaking containment in case the screen blinds, for changing to a different mesh, impeller change, or cleaning.



Figure 1

1. Underdrive Mill
2. DoverPac®
3. Charging Canister with Transition Adapter
4. Screen Access Enclosure Hardware
5. Outlet Canister

HOW DOES THE SYSTEM WORK?

The configuration shown in Figure 1 consists of the basic mill with modifications to support the attachment hardware needed for the standard DoverPac® charging and offloading systems. In addition, a flexible enclosure interface is provided between the base of the charging canister and the mill's inlet housing.

Safety is maintained as provided in the base mill design. Safety Grids are included in the inlet and outlet canisters. In addition, the interlocks are relocated to the Charging Canister and Screen Access Enclosure Ring.

In the event that a screen blinds during operation, the mill is turned off and the screen is accessed using the enclosure shown in Figures 2, 3, and 4. This is accomplished by:

- Applying the Lifting Shroud to the canister
- Removing the protective shroud from around the enclosure (used when the enclosure is in the stowed position only, not shown in this document)
- Inserting hands in the integral glove sleeves in the enclosure and opening the tri-clamp
- Hoisting the canister and using the glove sleeves again to remove the impeller and screen

The enclosure is manufactured from clear ArmorFlex® film that will allow room light to illuminate inside the enclosure for easy viewing. It is also equipped with a bag in/bag out sleeve which is used for housing the tool needed to loosen the bolt that secures the impeller and bagging out the screen as required.

The opening at the top of the enclosure includes an encapsulated o-ring that is clamped onto the bottom groove of the canister. The bottom of the enclosure has a similar arrangement that is clamped to the interface ring shown in Figure 3.

Mill Containment System



Figure 2. Shroud used to hoist canister.



Figure 3. Grooved interface ring

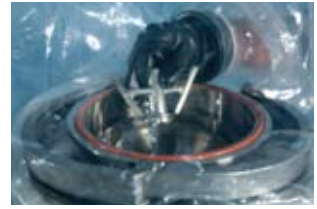


Figure 4. Integral glove sleeve for manipulating screen.

FEATURES

- Validated containment technology
- Clear film
- Passive system
- Flexible materials
- Disposable components
- Retrofit to existing mills
- Adaptable to other mills and size reduction designs

BENEFITS

- Nanogram containment levels achieved
- Supports visibility for maintenance
- Does not affect ATEX and Ex ratings
- Ergonomics maximized
- Reduced cleaning and cleaning validation
- Low capital and operating cost
- Speed of implementation

WHAT CONTAINMENT LEVEL PROVIDED?

OEB 5 with results in the nanogram range. This is based on proven applications, third party testing to the "SMEPAC" protocols on similar designs, and the 100% inflation tests performed on the deliverable systems.

WHY USE THIS OVER OTHER TECHNOLOGIES?

The cost of ownership, ergonomic advantages, and speed of delivery benefits of this flexible solution far outweigh those of rigid isolation systems.

OTHER POTENTIAL APPLICATIONS

- Continuous liner hardware on outlet of mill for contained filling in drums
- Transfer Sleeve on outlet of mill for direct transfer to IBCs or other vessels
- Transfer Sleeve on inlet of mill with drummed materials being introduced using the DoverPac® Drum Transfer System (Flexible Containment Solution Guide # FCSG 003)

Drum Sampling Enclosure System



OVERVIEW

Sampling of active pharmaceutical ingredients, sensitizers, and other highly hazardous compounds for quality assurance purposes is a process that is performed on a routine basis. The ability to perform this work in a warehouse or other parts of the facility, on a task operation basis, and without having to make significant capital expenditures are key in meeting this operational need.

The Drum Sampling Enclosure (DSE) system, a proven containment solution, supports accessing drummed materials - with the drum fully contained. Some processes advocate the safety of removing the drum lid before placing the drum inside the containment device. Experience proves the risk exists, even with a dual inner liner, that cross contamination and operator exposure can occur when the lid can not be removed within a robust flexible enclosure.

HOW DOES IT WORK?

The DSE System consists of a Flexible Enclosure and Support Stand. Sampling to an integral flexible sleeve, bottles or a thief are all proven capabilities.

The enclosure includes one pair of integral glove sleeves, a storage sleeve and sampling sleeve. Loops for supporting the enclosure by the stand are added to provide the attachment mechanism for the bungee cords. The combination of HEPA filters and bungee cords support the flexibility of the ergonomic design.

Operationally, the following basic steps are employed:

1. Sampling tools are preloaded into the 14"/350mm diameter sleeve and the open bottom of the enclosure is stretched over the drum and then taped to the drum wall.
2. The integral grommets on the top of the enclosure are connected to the support frame to provide the operator with space to work using the supplied bungee cords.
3. The drum lid is removed and placed along side of the drum but remains inside the containment area. The inner drum liners are then opened.
4. The sample is taken via the 4"/100mm sleeve using the process desired scooping directly into the sleeve or a sample bottle that is placed in the sleeve or using a standard sample thief and depositing that sample in the sleeve or a sample bottle. The samples can then be removed from the enclosure through the 4"/100 mm diameter sleeve by using the ILC Dover developed Crimping process.
5. The inner drum liner is resealed and the drum lid is put back into place without breaking containment.



FEATURES

- Clear film allows use of existing light from the process area
- Static dissipative film
- Re-usable for repeated sampling
- Tamper Proof sampling
- Portable
- Small footprint does not take up a lot of floor space
- Enclosure is attached to drum wall allowing lid to be contained
- Stretch on enclosure interfaces with common size drums but can also be customized
- One person operation

BENEFITS

- Can be used in any part of the facility
- No cross contamination transfer to other parts of the plant
- Ergonomics and secure operations are maximized with the integrity of ArmorFlex® materials
- Low capital, depreciation and operating costs maximizes true cost of ownership
- Immediate implementation supports Production and Lab processes in any part of the plant
- Reduced cleaning and cleaning validation
- Drums can be moved freely without breaking containment

WHAT CONTAINMENT LEVEL PROVIDED?

OEB 5 with results in the nanogram range. Even lower to non-detectable levels would be expected if the system were to be used in conjunction with an existing down flow booth. This is anticipated given actual customer feedback and third party IH test results from similar designs as well as the 100% inflation tests performed on the deliverable enclosures.

WHY USE THIS OVER OTHER TECHNOLOGIES?

The cost of ownership, ergonomic advantages, ease of use, integrity of the ArmorFlex material and speed of delivery benefits of this proven flexible solution far outweigh those of rigid isolation systems.

OTHER POTENTIAL APPLICATIONS

This technology is applicable for multiple process steps and includes, but is not limited to:

- cGMP access to buffer prep powders
- Liquid sampling
- Dispensing

Drum Sampling Enclosure FAQ's



At ILC Dover we are always “creating what’s next” by listening carefully to our customers. In some cases, we are continually improving our offerings using this same voice of the customer commitment.

The Drum Sampling Enclosure (DSE) is just such an example. ILC first started supplying drum sampling enclosures internationally in 2002. Based on our patented flexible containment transfer technology, we have evolved those original designs to the DSE system that we offer today.

High performance features:

- ▶ Clear film allows use of existing light from the process area
- ▶ Static dissipative film
- ▶ Reusable for repeated sampling
- ▶ Portable
- ▶ Small footprint utilizes small amount of floor space
- ▶ Enclosure is attached to drum wall allowing lid to be contained
- ▶ Stretch on enclosure interfaces with common size drums but can also be customized
- ▶ One person operation
- ▶ Crimp separation for containment and sample security

Benefits:

- ▶ Drum lid can be opened after drum is contained
- ▶ Can be used in any part of the facility
- ▶ No cross contamination transfer to other parts of the plant
- ▶ Ergonomics are maximized with flexible materials
- ▶ Low capital, depreciation and operating costs offers best cost of ownership
- ▶ Speed of implementation. It supports Production and Lab processes in any part of the plant
- ▶ Reduced cleaning and cleaning validation
- ▶ Drums can be moved freely without breaking containment
- ▶ Crimping with DoverPac® system confirmed as the best possible containment
- ▶ Tamper proof sampling achieved

Drum Sampling Enclosure FAQ's



Q:	A:
<i>How is the flexible liner removed from the drum after use? Seems like containment would be lost once the tape is removed.</i>	The containment level stated was for operation and leaving the enclosure on (original customer's operation). To remove the enclosure, the Twist/Tie/Tape/Cut (TTTC) method would need to be employed due to the film used for the body of the enclosure and the material thickness. While the TTTC method can be slightly variable in how tight the bundle is, the amount of powder that becomes airborne inside the enclosure will be very minimal. If the sampling is done with care, the enclosure and the TTTC area should have very little powder and so the containment level should still be excellent with expectations in the nanogram range.
<i>Have you thought about a DoverLoc type of clamp to give you a positive seal without taping?</i>	We looked at a flexible strap originally but were concerned that the enclosure might slip out from that type of attachment.
<i>Does it work equally well with plastic and steel drums (you show a fiberpacks in the brochure).</i>	This works as well with plastic or SS drums.
<i>Specifically, what level of containment are you reaching (there is mention to nanogram ranges; what are they, <50 ng/m3, better, worse?). Do you have test data that would be available for review?</i>	We have not tested this specific design in ILC's SMEPAC test facility. Our intent is qualification by similarity to other enclosures that we have tested (like the Drum Transfer Station) where our results ranged from non detects to under 500 nanograms. We do perform an inflation dwell test on this design as we do with all of our high containment systems.
<i>Does the size of the drum matter (i.e. 30 gallon, 50 gallon, etc.)?</i>	We currently have three standard sizes that cover a range of drums (15" to 17.5" (381mm – 445mm) diameter – Model FE8615S; 17" to 19.5" (432mm – 495mm) diameter – Model FE8615M; 19" to 21.5" (483mm – 546mm) diameter – Model FE8615L). Custom sizes can also be accommodated.
<i>How is the drum lid supported inside of the liner? Seems like it would get in the way.</i>	The lid is set up vertically on the side. Since this is not a long term application, we felt the trade off of leaving it set inside was more cost effective than supporting it with a stand. The good news is that you can remove the lid inside the enclosure rather than risking a potential exposure by removing the lid first.
<i>Is the stand support adjustable regarding height?</i>	The stand is three lengths of square SS stock that are connected by push pins. Sections can be removed for gross height adjustment.
<i>Which film are you using for this system?</i>	The body is AF113, a clear PE film that has been formulated to meet FDA and the new EU regulations but not tested to date. The sleeves are AF110.
<i>For removal and disposal, I assume the HEPA filter allows the liner to collapse; where is the filter, how is it mounted to the liner, what size, etc.?</i>	The HEPA filter is attached via a screw attachment to a fitting that is welded to the enclosure on the top panel. This is one of our standard 85L/m (3 cfm) HEPA filters.
<i>What size crimps does the sampling sleeve use (red, yellow or blue)?</i>	Yellow

OVERVIEW

The original DoverPac® SF was launched to be used in conjunction with Split Butterfly valves (Figure 1). This system replaces rigid bottles.

HOW DOES THE SYSTEM WORK?

The basic DoverPac® SF is used either unrestrained (Figure 2), with an integral restraint (Figure 3) or with a reusable restraint.

The system can be filled and emptied through a standard 4" (100mm) DN100 or DN150 integral sanitary flange. The design is set up so that the SF can be used with any Split Butterfly Valve. Filling and emptying the liner is accomplished by attaching the passive half of the valve to the liner which then docks with the active half of the valve. Other sizes have been accommodated as well.

The sanitary flange is injection molded and then thermally welded to the liner. This is done with a blended lap weld which keeps all of the load in shear and eliminates any possibility of powder hangup or bioburden build up in an otherwise raised lip at the seal area.

The unrestrained design uses a separate lifting bar when it is supported for vessel charging. This is significantly more robust than an encapsulated plate.

The restrained version is provided when a concern over back pressure exists. This design uses an integrated restraint that has been proven to withstand pressure excursions of 0.499 bar with a 2X safety factor. A window is included in the restraint so the operator can see that all powder has been discharged into the vessel.

A variety of configurations are available including

- Sizes from 1L, 5L, 10L, 15L, 25L, 30L, 50L, and 100L.
- An integral tube for addition of liquids creating slurry within the liner or for rinsing out the liner to recover any remaining powder (Figure 4)

The DoverPac® SF has also been adapted for cGMP and higher containment applications. For cGMP, a dual tied/S-folded neck is incorporated. (Figure 5). For containment needs past that of split butterfly valves, a model that attaches to our patented multi O-ring system can be used. (Figure 6).



Figure 1



Figure 2



Figure 3

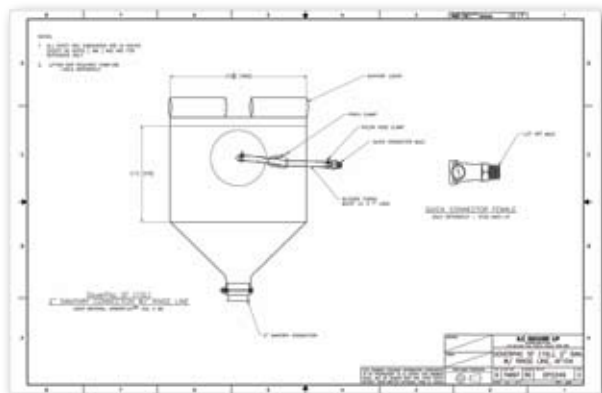


Figure 4

WHAT ARE THE APPLICATIONS?

This system has been proven to be of value in:

- Dispensing from Isolators
- Reactor Charging
- Tank charging for mixing creams
- Creating a slurry for later charging into a tank

WHAT ARE THE FEATURES/BENEFITS?

Features

- Flexible
- Clear
- Sanitary Flange
- Range of Sizes
- ArmorFlex Family of Films

Benefits

- Can be manipulated to overcome bridging, also achieves over 99.5% product discharge
- Operators can see product without breaking containment
- Interfaces with any Split Butterfly Valve
- Supports Lab scale through Bulk production
- Assures ruggedness, static dissipation and material of contact compliance

WHAT CONTAINMENT LEVEL IS PROVIDED?

The containment level achieved is that of the Split Butterfly Valve selected.

If a configuration is selected that interfaces with a DoverPac® multiple o-ring canister as in Figure 6 above at the right, containment to the OEB5 levels in the nanogram range can be achieved.

WHY USE THIS OVER OTHER TECHNOLOGIES?

- Reduced cost of ownership
- Eliminates cleaning and cleaning validation
- Eliminates waste treatment of cleaning solutions
- Best product recovery
- Visual access to drug product being manufactured
- Liner can be manipulated to overcome bridging



Figure 5

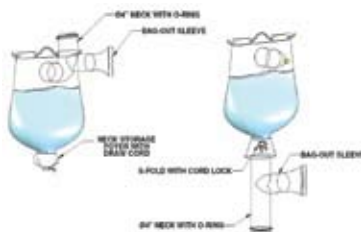


Figure 6

DoverPac® SF (BioPharmaceutical) From Lab Scale Through Production Processes



OVERVIEW

The DoverPac® SF (BioPharmaceutical) consists of a series of standard and customized applications based on the DoverPac® SF (Split Flange) technology (FCSG 007). This expansion of single-use manufacturing is designed to meet the needs of speed of implementation, ease of facility design, reduced validation, cost savings over cleaning and cleaning verification, and reduced capital costs to the operation.

HOW DOES IT WORK?

The DoverPac® SF can be attached to a variety of process vessels with by an integral sanitary flange (either sealed or clamped to the liner) or via our patented multi o-ring technology.

Materials of Contact

The ArmorFlex® Film is utilized to provide structural integrity, as well as meet the rigorous demands for materials of contact. Using existing and specific reference, monographs, key needs, such as no animal derived components, extractable/leachable limits, and food contact compliance, to name a few, are addressed.

The Sanitary Flange Interface

The sanitary flange is injection molded and then thermally welded to the liner. This is done with a blended lap weld which keeps all of the load in shear and eliminates any possibility of powder hang-up or bioburden build up in an otherwise raised lip at the seal area.

The unrestrained design uses a separate lifting bar when it is supported for vessel charging. This is significantly more robust in larger volumes and supported weights than an encapsulated plate. In fact, customer testing has shown the 100L version to hold 165 pounds/75 kgs. Reusable restraints are also available for added support.

The DoverPac® SF is also available with an optional S-fold on the neck as shown in Figure 2. This functions as an integral “clamp” to shut off powder flow when making the connection to the vessel.

Multi O-ring Canister Attachment

The interface to the vessel can also be supplied in our patented multiple o-ring technology. This configuration is shown in Figure 3. Attachment of the first liner to the first groove in the canister is made. The powder transfer operation is completed and the neck attached to the vessel is then removed using our crimp separation method. The subsequent liner is then attached to the next groove above the stub and the stub is then bagged out.

Standard solutions are also available for DN 100 and 150 flange interfaces. A variety of configurations are available including 1L, 5L, 10L, 15L, 25L, 30L, 50L, and 100L.



Figure 1 shows the basic design with a 4 inch/100mm sanitary flange.



Figure 2

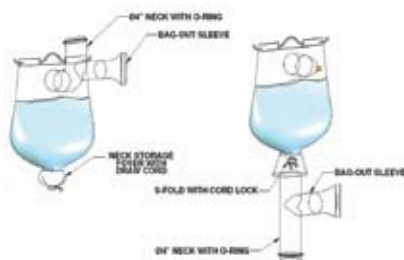


Figure 3

WHAT ARE THE APPLICATIONS?

Use of powder transfer devices within existing buffer prep processes whether new or existing operations, is gaining momentum as well. Figure 4 illustrates just such an example during the Factory Acceptance Test (FAT) stage of the project at METO where dispensing to weight operations were being trialed. Now that this has been successfully completed, process installation efforts are underway.

DoverPac® SF (BioPharmaceutical) From Lab Scale Through Production Processes

Since this was a dispense to weight operation within a tightly controlled tolerance, the need to separate the support frame and scale from the drum inverter was needed. Figures 5 and 6 show the application of a flexible sleeve with molded sanitary flanges as a method for achieving this need.

FEATURES

- Flexible
- Clear
- Sanitary, DN and multi o-ring flange interfaces
- Range of Sizes
- ArmorFlex® Family of Films
- Gravity feed
- No capital
- Reduced cleaning and disposal

BENEFITS

- Can be manipulated to overcome bridging, also achieves over 99.5% product discharge
- Operators can see product without exposing product
- Interfaces with any vessel interface
- Supports clinical through production scale up
- Assures ruggedness, static dissipation and material of contact compliance
- No expensive mechanical systems, eliminates validation of mechanical components, simple to use
- Best overall cost of ownership, small footprint
- Supports Green Initiatives

WHAT CONTAINMENT LEVEL PROVIDED?

Often applied for cGMP containment, however, if a configuration is selected that interfaces with a DoverPac® multiple o-ring canister as in Figure 3, containment in the nanogram range can be achieved.

WHY USE THIS OVER OTHER TECHNOLOGIES?

- Reduced cost of ownership
- Eliminates cleaning and cleaning validation
- Eliminates waste treatment of cleaning solutions
- Best product recovery
- Visual access to drug product being manufactured
- Liner can be manipulated to overcome bridging



Figure 4



Figure 5



Figure 6

DoverPac® Tray Dryer Enclosure Technology



OVERVIEW

Tray Dryers are a common method of drying wetcakes and granulated drug products. This is especially true in the early product development phase. The issue of containment for this type of process equipment is unique in that open scooping of powder onto multiple trays that get slotted into the dryer one at a time prohibits a mass, single transfer as with charging a vessel through a nozzle.

There are many styles of Tray Dryers that drive the Engineering Control here to a custom design. However, containment is accomplished with a standard set of interface and design techniques.

The various styles of dryers, interfaces, door types, volumes, ergonomics, and life cycle costs must all be taken into account in order to meet the need of containing the dryer. Included here is whether the dryer is portable or a fixed installation.

HOW DOES THE SYSTEM WORK?

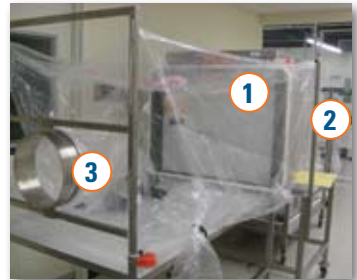
The final design may vary from operation to operation but a typical installation includes adding a flange to the face of the dryer to the outside of the door. An enclosure made from the rugged ArmorFlex® family of films is then attached to the flange and a supporting frame assembly. The door is within an enclosed environment when loading and unloading the trays with the drug product.

The trays, drug product and associated process tools can either be preloaded into the enclosure or bagged into the isolated area via bag in/bag out (BIBO) canisters or larger drum ring attachment canisters. The steps outlined below represent a typical example of this type of process:

1. Attach the enclosure to the support frame using the bungee cords supplied. Also attach the enclosure to the BIBO canister.
2. Preload trays into the enclosure (or bag in after the enclosure is attached).
3. Attach the enclosure to the flange on the dryer using the tape and V-Groove trim method developed by ILC and open the dryer door.
4. Load the bags of wet cake material into the enclosure through a bag-in sleeve.
5. Scoop material from the bags onto the dryer trays, load the trays into the dryer and close the dryer door for processing.
6. After the drying process is complete, open the door, remove the trays within the enclosure and scoop the powder into plastic bags which in turn will be placed into a bag-out sleeve. Alternatively, the powder can be scooped directly into a DoverPac®, Continuous Liner, or Transfer Sleeve.
7. Crimp, cut a remove the contained materials for further processing.

After processing is completed, spray mist the inside of the enclosure as part of the overall wash down. The flexible enclosure will then be removed from the dryer while wearing personal protective equipment (PPE) as part of the wash down process.

Frames are typically supplied in 304 Stainless Steel with a 2b mill finish. Other materials can be provided as required.



Portable Tray Dryer

- 1 Enclosure
- 2 Frame
- 3 BIBO Canister
- 4 Portable Tray Dryer
- 5 V groove trim attachment to flange
- 6 Flange

DoverPac® Tray Dryer Enclosure Technology

WHAT ARE THE APPLICATIONS?

Portable and permanently installed Tray Dryers have been fitted with this type of flexible containment technology.

Features

- Clear film allows use of existing light from the process area
- Bungee cords and HEPA filters allow the enclosure to move with the operator
- Static dissipative film supports ATEX and Ex operations
- Re-usable for repeated processing of same drug product
- Portable or permanent installations supported
- Customized to specific process and equipment without change to drug product drying process

Benefits

- Ergonomics maximized for visibility, operator height and reach
- No cross contamination transfer to other parts of the plant
- Low capital, depreciation and operating costs maximizes true cost of ownership
- Speed of implementation supports Lab and Production processes in any part of the plant
- Reduced cleaning and cleaning validation
- Product can be transferred between operations without breaking containment
- No change in validation



WHAT CONTAINMENT LEVEL IS PROVIDED?

OEB 5 with results in the nanogram range. This is anticipated given actual customer feedback and third party IH test results from similar designs as well as the 100% inflation dwell tests performed on the deliverable enclosures.

WHY USE THIS OVER OTHER TECHNOLOGIES?

The cost of ownership, ergonomic advantages, and speed of delivery benefits of this flexible solution far outweigh those of rigid isolation systems.

Mill Containment System - Bohle BTS 100

OVERVIEW

Particle size reduction is commonly required in pharmaceutical manufacturing. Taking into account today's need to mill highly hazardous compounds in conjunction with the need to minimize capital cost spending, the application of flexible containment to an existing Bohle BTS – 100 sieve design demonstrates the use of this containment strategy.

The Bohle Turbo Sieve (BTS) is a small volume, size reduction piece of equipment that is used in the drug product development stages. Typically provided without containment, options for the end user in the past were limited to installing a rigid isolator or using personal protective equipment (PPE).

Today, as demonstrated in a successful installation at an international pharmaceutical manufacturer, outfitting the system with flexible containment has proven to be successful from operational and business perspectives. Best of all, this has been accomplished on an existing, non contained design without the need for expensive retrofits past the addition of attachment flanges.

This example of how ILC Dover is applying the use of highly engineered materials and state of the art design techniques is described in detail below.

HOW DOES THE SYSTEM WORK?

Containment of the BTS 100 is provided by a rectangular flexible enclosure with an angled front surrounding the entire mill head including the inlet hopper, outlet nozzle and interlock switch. Integral glove sleeves are positioned to provide a means of charging and collection of product, as well as servicing and cleaning the machine.

A single entry/removal point provides a means for moving product and supplies in and out of the enclosure. This entry/removal point will support use of a bag-in/bag-out (BIBO) sleeve or interface with ancillary containment devices such as an in-process flexible isolator. (Figures 1 and 2)

The enclosure also incorporates HEPA filters into the design to balance the pressure in the enclosure and allow it to move freely as the operators perform various operations.

The system is movable via the incorporation of conductive, locking castors. This allows safe movement between the processing suites and storage areas. The system is lightweight and can easily be moved by personnel from the 5th percentile female to the 95th percentile male without the need for material handling equipment.

Installation of the enclosure is accomplished by means of an attachment plate and flange that are secured to the mill drive tube behind the interlock switch. This assembly is attached to the perimeter of the drive shaft tube without modification of the sieve. An external enclosure support frame is constructed to support the enclosure as well as the bag-in canister and product staging table. (Figure 3)

The enclosure is manufactured from clear ArmorFlex® film that allows room light to illuminate inside the enclosure for easy viewing. This rugged film provides a safe working environment while enabling the enhancements developed through numerous installations using this flexible containment technology.



Figure 1

- 1 - Enclosure
- 2 - HEPA Filters
- 3 - Integral Glove Sleeves
- 4 - BIBO Canister
- 5 - Conductive, locking castors

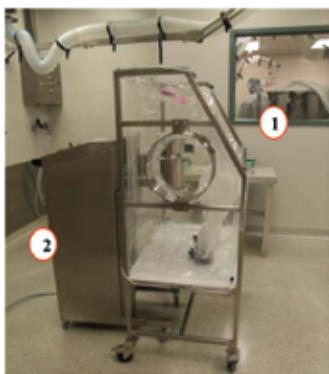


Figure 2

- 1 - Angled front of enclosure
- 2 - Bungee Cords

Mill Containment System - Bohle BTS 100

FEATURES

- Process and Technical areas separated
- Clear film
- Flexible materials
- Retrofit to existing mills
- Adaptable to other particle size reduction equipment
- Validated containment technology
- Passive system
- Disposable components

BENEFITS

- Process is contained without contamination of motor, drive shaft, and controls
- Nanogram containment levels achieved
- Supports visibility for maintenance
- Does not affect ATEX and Ex ratings
- Ergonomics maximized
- Reduced cleaning and cleaning validation
- Low capital and operating cost
- Speed of implementation

WHAT CONTAINMENT LEVEL PROVIDED?

OEB 5 with results in the nanogram range. This is based on customer test data, other proven applications, third party testing to the "SMEPAC" protocols on similar designs, and the 100% inflation tests performed on the deliverable systems.

WHY USE THIS OVER OTHER TECHNOLOGIES?

The cost of ownership, ergonomic advantages, and speed of delivery benefits of this flexible solution far outweigh those of rigid isolation systems.

OTHER POTENTIAL APPLICATIONS

Successful installations have been provided for similar size reduction equipment including Quadro and FitzMill systems as well as microfibers.

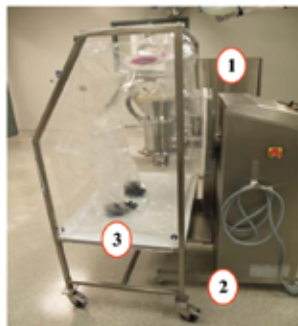


Figure 3
1 - Attachment Flange Assembly
2 - Enclosure Support Frame
3 - Support Table

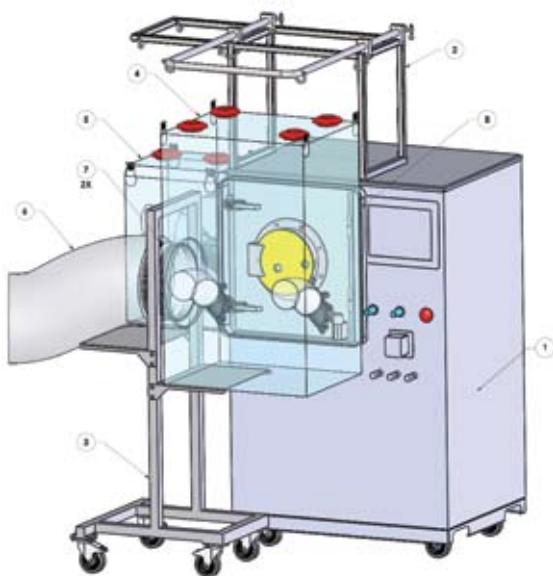
Tablet Coater Containment System - O'Hara LCM Tablet Coater

OVERVIEW

Recently delivered for lab scale operations at an International Pharma manufacturer, the installation described in this Containment Guide takes the idea of retrofits to another level. Here, a new piece of equipment was needed but cost savings were realized by modifying an existing design. Flanges added to the unit by the original equipment manufacturer (OEM) allow this end user to process contained when needed and to use existing procedures when containment is not required.

Containment for the O'Hara LCM Tablet Coater is provided by two individual rectangular enclosures. One enclosure surrounds the pan access door and the second the exhaust plenum access door.

The enclosure is manufactured from clear ArmorFlex® film that allows room light to illuminate inside the enclosure for easy viewing. This rugged film provides a safe working environment while enabling the enhancements developed through numerous installations using this flexible containment technology.



- | | |
|--------------------------------------|---|
| 1 Coater | 5 Filter Change Out Enclosure with HEPA Filters |
| 2 Enclosure Support Frame | 6 BIBO Sleeve |
| 3 BIBO Canister Support Frame | 7 BIBO Canister |
| 4 Coater Enclosure with HEPA Filters | |

HOW DOES IT WORK?

The pan access enclosure is used for product charging and removal as well as sampling, cleaning and spray gun maintenance. It has one pair of glove sleeves. A single entry/removal point provides a means for moving product and supplies in and out of the enclosure. This entry/removal point supports the use of a bag-in/bag-out sleeve or interface with ancillary containment devices such as an in-process isolator.

The enclosure is mounted in such a way that it can be collapsed inward toward the front of the coater. This simplifies loading and unloading product through the circular door on the coater. The enclosure is fully extended to provide clearance when opening the larger pan access door for cleaning operations.

The exhaust plenum enclosure is mainly used for cleaning operations. It has a pair of glove sleeves and a cleaning wand sleeve. It can also be equipped with a storage/waste sleeve if desired. Both enclosures also include HEPA filters to balance the pressure in the enclosure and allow it to move freely as the operators perform various operations.

Attachment flanges running outward from the cabinet around each of the access doors provide a means of attachment for the enclosures. This allows for containment to be applied to the process area of the equipment with the technical area segregated from any contamination. A bag-in canister is mounted on a mobile stand with integral product staging table. An external enclosure support frame supports the enclosures without need of ceiling attachment.

The enclosure also includes a spray-wand cleaning sleeve to allow misting of the interior of the enclosure during cleaning. Spray mist of the inside of the flexible enclosure and surfaces of the equipment within the contained area eliminates airborne contaminants prior to removing the containment. Cleaning of the surface of the equipment is done following normal practices.

Tablet Coater Containment System - O'Hara LCM Tablet Coater

WHAT ARE THE FEATURES AND BENEFITS OF THIS TECHNOLOGY?

Features

- Retrofit to existing equipment design
- Process and Technical areas separated
- Validated containment technology
- Clear film
- Passive system
- Flexible materials
- Disposable components
- Adaptable to other process equipment

Benefits

- Provides the lowest overall cost of process ownership through low capital and operating cost including reduced cleaning and cleaning validation
- Fastest turnaround of a processing suite for subsequent manufacturing campaigns
- Process is contained without contamination of motor, drive shaft, and controls
- Nanogram containment levels achieved
- Supports visibility for maintenance
- Does not affect ATEX and Ex ratings
- Ergonomics maximized
- Speed of implementation

WHAT CONTAINMENT LEVEL IS PROVIDED?

OEB 5 with results in the nanogram range. This is based on customer test data, other proven applications, third party testing to the "SMEPAC" protocols on similar designs, and the 100% inflation tests performed on the deliverable systems.

WHAT ARE THE APPLICATIONS?

This containment technology can be applied to any Oral Solid Dosage (OSD) type of processing equipment. Applications to myriad Tablet Presses, Coaters, Dedusters, Blenders, Granulators, Mills, Roller Compactors, Spheronizers, Extruders, Fluid Bed Dryers, and weighing/subdivision processes have been demonstrated successfully.

WHY USE THIS OVER OTHER TECHNOLOGIES?

The cost of ownership, ergonomic advantages, and speed of delivery benefits of this flexible solution far outweigh those of rigid isolation systems.

Tools such as Lean Manufacturing come into play more and more. For example, the time to clean and validate the cleaning are major bottlenecks for processing efficiencies in the plant. Being able to minimize this part of the process results in getting products to market faster and at an overall reduction in operating costs when considering labor, utilities, and waste disposal costs. It also supports getting multiple products to market faster within an existing facility without risking product safety.



Contained Offloading of Aurora Filters - Processing from Nutsche Filters



OVERVIEW

Nutsche Filters are a mainstay in processing in the Pharmaceutical and Chemical industries. They typically function by keeping the slurry contents fluidized until most of the mother liquor is filtered through. When filtration is complete, the cake can be washed by reslurrying the cake. After washing, the mother liquor can be refiltered and the cake can then be discharged.

AURORA FILTERS, a Division of ALL-WELD Company Limited, designs and fabricates a line of Nutsche filters for the pilot scale production of active pharmaceutical ingredients. These designs typically combine a glove box with a single plate vacuum Nutsche under an inert gas blanket to ensure operator safety and product integrity.

- Each filter has seven process connections - Slurry Inlet, Nitrogen Inlet, CIP Wash Inlet, Vent, Nitrogen Inlet for Drying, Final Vacuum Outlet, and Filtrate Vacuum Outlet.
- Each filter has a large viewing window on the Upper Chamber as well as a small sight glass on the Lower Chamber.
- A Heating/Cooling Jacket designed for 50 to 75psi and registered to ASME Code surrounds the cake collection area. This jacket is for use with heat transfer fluids only, such as cooling brine, hot water, Dowtherm, Silthane, Glycol, or similar liquids.
- The remainder of the filters are not considered a registered pressure vessel. The Upper Chamber is designed for atmospheric conditions only and the Lower Chamber is designed for atmospheric to full vacuum conditions.
- The CIP Spray ball assembly is designed such that the entire spray ball assembly can be extracted from the nozzle without disassembly within the filter. The spray ball components are either Teflon or equivalent to the wetted material of choice.

However, the outlet of the filter is not typically contained. This Flexible Containment Solutions Guide outlines several methods of achieving a contained discharge from the Aurora Filter.

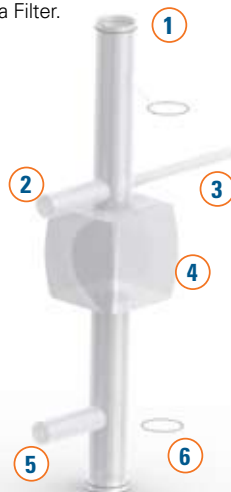
HOW DOES THE CONTAINED OFFLOADING SYSTEM WORK?

There are a variety of methods that can be used to achieve contained offloading of an Aurora Filter. The designs of the filters are varied so the applications below represent a few of the installed solutions. Some customization may be needed depending on the specific filter.

Offloading to DoverPac®

The key components in The DoverPac® system include:

- Transition adapter between the vessel and the DoverPac® canister
- Multiple o-ring canister (typically separate from the Transition Adapter but these can be combined into one piece of hardware)
- DoverPac® which is a combination of inner liner and outer Type C restraint
- The new FlexLoc clamp (an improvement over the original DoverLoc clamp that replaced the original cir-clip)
- The Crimp Separation System (the replacement for the original twist, tie, tape and cut system for repeatable separation of the liner from the vessel without breaking containment)



- | | |
|--------------------------|-------------------------------|
| 1 Fill neck with o-rings | 4 Body |
| 2 Bag Out Sleeve | 5 Bag Out Sleeve |
| 3 Sample Sleeve | 6 Discharge neck with o-rings |

DoverPac Liner (shown without Restraint)

Contained Offloading of Aurora Filters - Processing from Nutsche Filters

The basic operational steps are performed for offloading the filter:

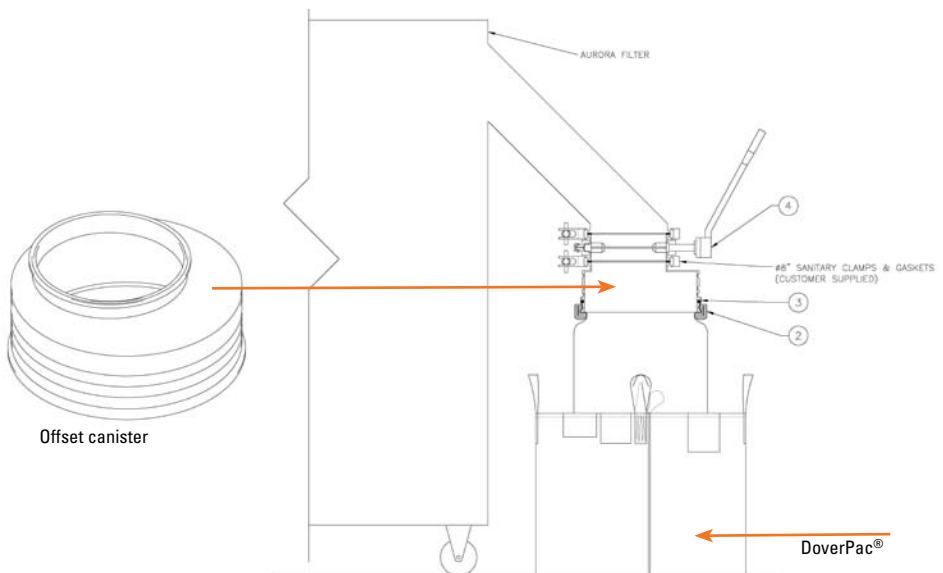
- 1 Attach the fill neck of the DoverPac® to the ILC Dover supplied multiple o-ring canister and shuffle up some of the neck to create a clean zone for crimp separation
- 2 Bag out the stub from the previous liner
- 3 Open the valve on the vessel and use the sample sleeve to take a sample if required by the process
- 4 Finish filling
- 5 Pull down the clean zone, twist the neck, and apply the crimps.
- 6 Cut between the two crimps and close the caps on the crimps. Note that this leaves the stub that will be bagged out with the next DoverPac®
- 7 Repeat steps 1 – 6.

The same process is used to charge the next vessel except there is no sampling sleeve at that point.

In the application below, an offset canister with the capability to offload to three 110L DoverPacs® was installed on the sanitary flange of the 8" (200mm) Cora Valve on the discharge chute of the vessel. Once the filtration process is complete, the valve is opened and the Operator scoops powder through the chute and into the DoverPac® using the glove ports that are supplied as part of the Aurora Filter.

The DoverPac process outlined above is then followed.

After processing, a Clean In Place (CIP) tundish is attached to the sanitary flange on the canister by bagging it in with the CIP sleeve.



Contained Offloading of Aurora Filters - Processing from Nutsche Filters



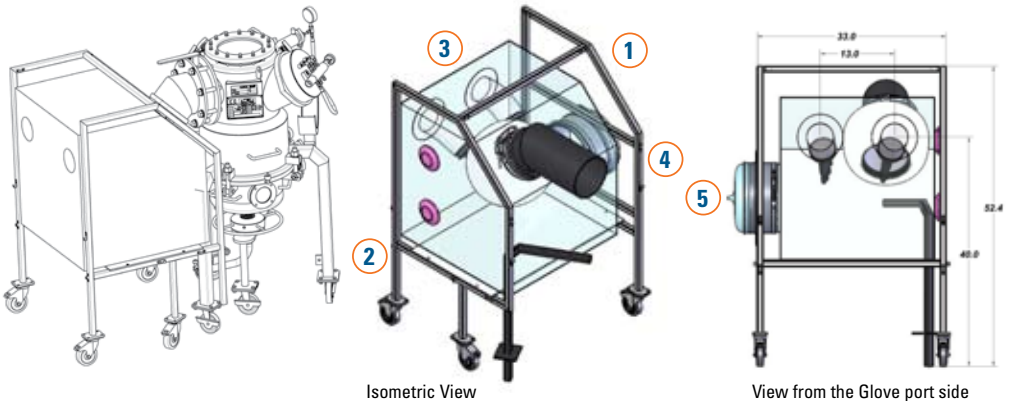
Flexible Enclosure Offloading

Flexible Enclosures are a proven alternative to rigid gloveboxes. These can be provided in either a passive system or with a Ventilation System included.

The enclosure is manufactured from clear ArmorFlex® film that will allow room light to illuminate inside the enclosure for easy viewing. It is also equipped with a bag in/bag out sleeve which is used for introducing product and tools to and from the enclosure without breaking containment.

In this application, a standard 8" multiple o-ring canister is attached to the outlet of the filter. The enclosure is then attached to the same canister to provide a contained connection during the transfer of powder.

A 14" Continuous Liner is connected to the canister inside of the enclosure. This is a factory packed, 35' long liner. Once the Continuous liner is filled, it is crimped and the bagged out using the BIBO Sleeve on the side of the Enclosure.



- | | |
|----------------------|-------------------------------|
| 1 Mobile Frame | 4 Attachment to Filter Outlet |
| 2 Flexible Enclosure | 5 BIBO Canister |
| 3 Glove ports | |

Contained Offloading of Aurora Filters - Processing from Nutsche Filters



The basic process steps include:

- 1 pull a length of the Continuous Liner down from the pack
- 2 open the valve on the filter outlet to allow powder transfer to the liner
- 3 when filled, twist and crimp the liner
- 4 place the filled section of the liner into the bag out sleeve and then twist and crimp the BIBO Sleeve. This is then moved to the next step of the process.

FEATURES

- Validated containment technology
- Clear film on enclosures
- Passive and ventilated systems available
- Flexible materials
- Disposable components
- Retrofits to existing filters

BENEFITS

- nanogram containment levels achieved
- visibility during operation
- Containment to a broad range of requirements
- Ergonomics maximized
- Reduced cleaning and cleaning validation
- Low capital and operating cost
- Speed of implementation

WHAT CONTAINMENT LEVEL PROVIDED?

OEB 5 with results in the nanogram range. This is based on proven applications, third party testing to the "SMEPAC" protocols on similar designs, and the 100% inflation tests performed on the deliverable systems.

WHY USE THIS OVER OTHER TECHNOLOGIES?

The cost of ownership, ergonomic advantages, and speed of delivery benefits of this flexible solution far outweigh those of rigid isolation systems.

OTHER POTENTIAL APPLICATIONS

AURORA FILTERS are designed primarily for the applied research, development and pilot scale operations within the pharmaceutical and chemical industry. Containment for offloading in addition to the applications outlined above can be applied via:

- Continuous liner system on outlet for contained filling in drums
- Transfer Sleeve on the outlet for direct transfer to IBCs or other vessels

Mill Containment System - Jet Mills

OVERVIEW

The process for this application consists of the controlled feeding of a mill through a feeder. The powder is introduced into the feeder using a Drum Transfer System. After the particle reduction is complete, the powder is passed through a Cyclone housing and collected in a continuous liner system.

The Jet Mill, or Micronizer as this style of mill is also called, used in this application is a Jet Pulverizer 8" Micron Master. In this process, air drives the particles which are reduced in size when they impact upon each other. Smaller particles flow up the transfer tube to the Cyclone housing while the larger particles continue to be impacted on each other until they are reduced to the desired size (see Figure 1 at right).

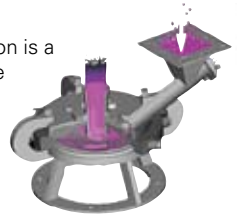


Figure 1

The Feeder in this application is the K-TRON Model number K-PH-MV-KT20 feeder. This is a 20L, twin screw, volumetric feeder with a separate control system.

This equipment was on site prior to this effort. Some modifications were required by the customer which included, but were not limited to, modification of the piping going to the Cyclone and mounting the equipment on the ILC supplied cart.

HOW DOES IT WORK?

This system (Figure 2 at right) provides a contained method of transferring the complete or partial contents of drums to a variety of processes including milling. The design will accommodate the charging of several different types of mills with various sizes and shapes though the Jet Pulverizer 8" Micron Master was used in this application.

In the case of partial transfers, the system provides a contained method of resealing the drum for return to stock. The system consists of a flexible enclosure mounted on a mobile stainless steel frame (see Figures 3 and 4 on next page).

Product drums are over-sleeved with disposable drum attachment sleeves. The sleeves are stretched over the drum and taped to the drum. The opposite end of the sleeve is attached to the 23" diameter stainless steel bag-in ring using a band clamp and integrated O-rings. This provides a connection interface to attach the sleeve and introduces the drum into the enclosure.

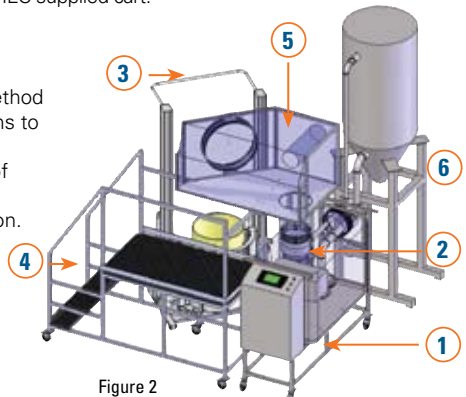


Figure 2

- 1 Mill Containment Cart
- 2 Feeder Inlet Canister
- 3 Drum Lifter
- 4 Drum Transfer System Frame and Platform
- 5 Drum Transfer System Enclosure
- 6 23" Diameter Continuous liner (not shown)

The enclosure containing the Mill and Feeder is mounted on a tray integral to the cart provided by ILC Dover. All air and electrical lines are passed through the tray. The milled product feed pipe to the Cyclone passes through a single interface ring which includes a groove for enclosure attachment. This ring is mounted to the cart. The feed hopper is fitted with a grooved canister to also allow enclosure attachment for the Drum Transfer Station and the Mill.

The mill enclosure includes three butyl gloves. A right and left pair are on the front of the enclosure. The third is a bidirectional glove on the opposite side on the enclosure. HEPA filters and bungee cords allow for the enclosure to move with the operator which is an ergonomic benefit that is not achieved with a rigid system.

Mill Containment System - Jet Mills

The milled powder is collected from the bottom of the cyclone via a 23" diameter, 50 foot continuous liner in this application. This interface is fitted with a valve to prevent inflation of the liner. DoverPacs® could be used instead if contained powder transfer to the next step in the process were required.

WHAT ARE THE APPLICATIONS?

In addition to the Jet Pulverizer system, containment has been proven on other Micronizers. Fielded applications include, but are not limited to, the Microtech Midas Mikronizer – 200.

Enclosures that separate the process and technical areas as well as systems that encapsulate the entire Jet Mill have been supplied.

WHAT ARE THE FEATURES/BENEFITS?

Features

- Process and technical areas separated
- Clear film
- Flexible materials
- Retrofit to existing equipment
- Validated containment technology

Benefits

- Process is contained without contamination of motors and controls
- Visibility optimized and use of room lighting achieved
- Ergonomics maximized
- Capital equipment costs minimized
- Reduced cleaning and cleaning validation

WHAT CONTAINMENT LEVEL PROVIDED?

The Occupational Exposure Level for this application was set to be less than 1 µg/m³. The flexible containment technology utilized in this application has been proven to be capable of being below this level in third party and customer testing. Test results on a variety of powders have shown that containment in the 250 to 500 nanogram range is achievable.

WHY USE THIS OVER OTHER TECHNOLOGIES?

The cost of ownership, ergonomic advantages, and speed of delivery benefits of this flexible solution far outweigh those of rigid isolation systems.



Figure 3



Figure 4

Granulator Containment Technology

OVERVIEW

In the pharmaceutical industry, granulation is used to create bonds between multiple particles as part of the oral solid dosage manufacturing process. Two types of granulation technologies are employed, Wet Granulation and Dry Granulation.

The containment systems described in this guide center around wet granulation which involves the massing of a mix of dry primary powder particles using a granulating fluid. The powders can range in properties and potency and are subjected to a variety of additional steps including sieving, drying and milling.

Used for lab scale and production operations at multiple International Pharma manufacturers, our contained Granulator applications take the idea of retrofits to another level. Here, a broad range of existing and new equipment are supported as a tool to eliminate the risk of contained powder processing.

HOW DOES IT WORK?

Two methods of containment have been applied. One uses flanges that are added to the piece of process equipment that then have a flexible enclosure attached to the flange in operation. The second is to totally encapsulate the granulator with a pan mounted flexible enclosure.

Equipment Mounted Enclosures Separate the Process and Technical Areas

The use of stainless steel flanges added to the granulator enables the containment of the process area. The enclosure is attached to the flange and includes glove sleeves, bungee cords, and HEPA filters. These features support access to the equipment while maximizing ergonomics and support operators from the 5th percentile female to the 95th percentile male.

Pan Mounted Enclosures Encapsulate the Entire Granulator

Pan mounted enclosures allow the entire piece of process equipment to be contained. This is beneficial for equipment that can not be modified to use the flange mounted approach.

Again, the enclosure is supported by bungee cords, attached to the pan, and includes glove sleeves for access to the equipment. The enclosure "moves" with the operator, as is the case with all of our flexible enclosure systems, to maximize ergonomics as noted above.



Flange Mount Style



Pan Mount Style

Granulator Containment Technology

WHAT ARE THE APPLICATIONS?

The enclosures are manufactured from clear ArmorFlex® 113 film that allow room light to illuminate inside the enclosure for easy viewing. This rugged film provides a safe working environment while enabling the enhancements developed through numerous installations. Transfer Sleeves are made from another version of ArmorFlex® film. This is the same monolayer film used in our DoverPacs® and as such brings regulatory pedigree for materials of contact.

The use of flexible containment allows the end user to process contained when needed or to follow existing, open processing procedures when containment is not required.

FluidAir PharmX Model PX-1

In this design, containment is achieved by encapsulating the entire granulator inside a pan mounted flexible enclosure (see figures 1). In this case the pan is 33" (838 mm) x 60" (1524 mm). Space beside the granulator is maintained inside the enclosure for staging of product and materials to support the overall process.

Three ambidextrous gloves are incorporated into the flexible enclosure to support ease of operations when loading and unloading the granulator and operating the controls. A bag-in bag-out (BIBO) interface allows materials to be passed in and out of the enclosure without breaking containment. The entire unit is supported on a frame that includes conductive casters which make the system portable.

Glatt GPGC2 Fluid Bed Granulator

In the application shown in figure 2, flanges were added to an existing design that allows the attachment of the flexible enclosures. The two enclosures allow for access to the bowl of the granulator and the filters. A telescoping frame supports the enclosure when charging and offloading the equipment. This frame can be collapsed on itself to allow the enclosure to be folded out of the way when not being operated.

Collette High Sheer Granulator – 10L and 20L

Figures 3 and 4 depict this containment system which also uses the flange mount feature to achieve containment while separating the process and technical areas. A roll away frame supports the enclosure. This frame also includes a platform that functions as a table to support the bags of material.



Figure 1

1 Enclosure	4 Support frame
2 Pan	5 Glove Sleeves
3 BIBO canister	

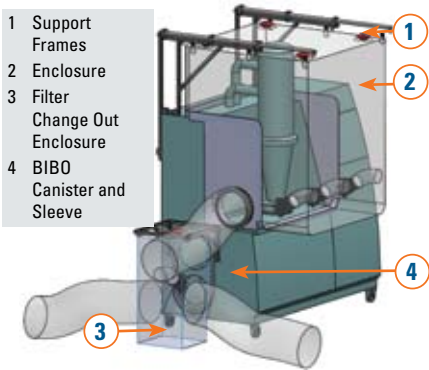


Figure 2

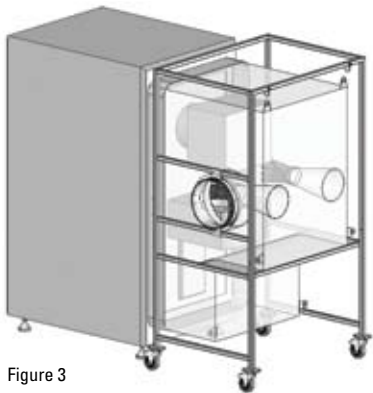


Figure 3

Granulator Containment Technology

This style of granulator includes a separating cover as part of the top-driven mixer and chopper with a removable bowl. The enclosure and flange are elongated on the lower front face of the equipment to support the movement of the process area without breaking containment.

ProCepT Mi Pro 1900

Containment of the Mi-Pro Mixer/Granulator, figure 5, is achieved by a flexible enclosure surrounding the process chamber and staging area forward of the control system connection column. A single pair of glove sleeves is provided to charge and collect product from the process vessel. A single entry/removal point using replaceable bag-in sleeves provides a means for moving product and supplies in and out of the enclosure. The enclosure also includes integral HEPA filters to balance the pressure in the enclosure and allow it to move freely as the operators perform various operations.

The enclosure is attached to a stainless steel base pan with vertical attachment flanges. A small attachment canister with liquid tight connectors provides a method of introducing utilities into the contained area. An external frame supports the enclosure and the bag-in canister.

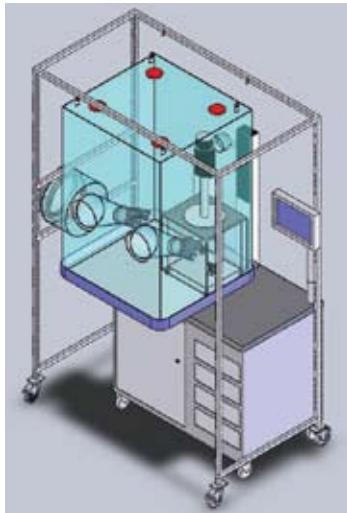


Figure 5

RapidMix 100 Granulator

This granulator is a fixed installation as opposed to a mobile design. As seen in figures 6 and 7, the granulator is placed on a floor pan that is 85" (2159 mm) by 54" (1372 mm).

The overall height of the enclosure is 88.5" (2248 mm) to allow clearance for the opening of the lid of the granulator. Seven glove sleeves are located to support opening of the lid, access to the controls, discharge of the materials, and bag in/bag out of raw materials and the processed powder. The frame is used to support the enclosure during operations and can be wheeled out of the way for storage when not in use.



Figure 4

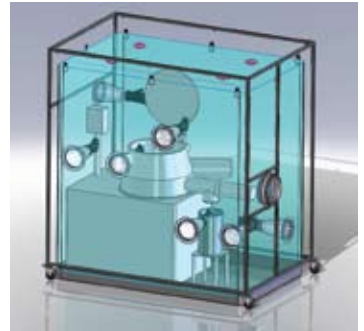


Figure 6



Figure 7

Granulator Containment Technology

WHAT ARE THE FEATURES AND BENEFITS OF THIS TECHNOLOGY?

Features

- Retrofit to existing equipment design
- Process and Technical areas separated
- Validated containment technology
- Clear film
- Passive system
- Flexible materials
- Disposable components
- Adaptable to other equipment

Benefits

- Provides the lowest overall cost of process ownership through low capital and operating cost including reduced cleaning and cleaning validation
- Fastest turnaround of a processing suite for subsequent manufacturing campaigns
- Process is contained without contamination of motor, drive shaft, and controls with flange mount design
- Nanogram containment levels achieved
- Supports visibility for maintenance
- Does not affect ATEX and Ex ratings
- Ergonomics maximized
- Speed of implementation

WHAT CONTAINMENT LEVEL PROVIDED?

OEB 5 with results in the nanogram range. This is based on customer test data, other proven applications, third party testing to the “SMEPAC” protocols on similar designs, and the 100% inflation tests performed on the deliverable systems.

OEB 1	OEB 2	OEB 3	OEB 4	OEB 5
10,000 to 1000	1,000 to 100	100 to 50 50 to 10	10 to 1	1 to 0.1 0.1 to 0.01

Occupational Exposure Levels above are in µg/m3.

WHY USE THIS OVER OTHER TECHNOLOGIES?

The cost of ownership, ergonomic advantages, and speed of delivery benefits of this flexible solution far outweigh those of rigid isolation systems.

Tools such as Lean Manufacturing come into play more and more. For example, the time to clean and validate the cleaning are major bottlenecks for processing efficiencies in the plant. Being able to minimize this part of the process results in getting products to market faster and at an overall reduction in operating costs when considering labor, utilities, and waste disposal costs. It also supports getting multiple products to market faster within an existing facility without risking product safety.

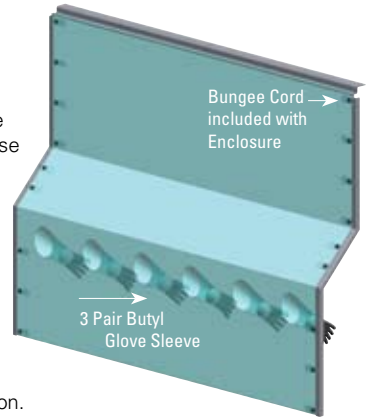
Process Area Barrier Curtains

OVERVIEW

Process Area Barrier Curtains are a useful tool in improving the containment levels in existing installations as a method to reduce operational exposure risk and to restrict access. Examples of these types of applications include, but are not limited to, down flow booth curtains and room access barriers.

Down flow booths, for example, work by pulling air across a drum or piece of processing equipment which typically provide a containment level of 100 µg/m³ on an 8 hour time weighted average (TWA). While this draws the powder into a set of filters, the airflow is disrupted when an operator is working at this type of station. When that occurs, eddy currents of air and entrapped powder start to swirl which disrupts containment. The barriers described in this guide are a tool in improving this type of application.

Similarly, restricting access to another part of a processing suite has been a demonstrated need as well. Here, a barrier can be added to a doorway, for example, to restrict the flow of personnel between the suites.



HOW DOES IT WORK?

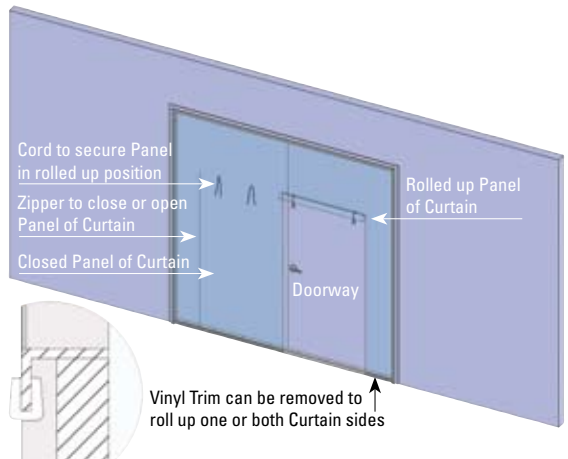
By isolating the operator's breathing zone from the point of exposure with this form of secondary containment the operator is protected from the product and vice versa.

The curtains are manufactured from clear ArmorFlex® 113 film that will allow room light to illuminate inside the barrier and not restrict visibility. This rugged film provides a safe working environment while enabling the enhancements developed through numerous installations using this flexible containment technology.

Typically, the ArmorFlex® 113 is patterned to interface with the opening to be contained. This can be a flat sheet or a three dimensional design. The barrier is attached using flanges and U-Groove channel as a locking mechanism or by grommets.

Glove sleeves are incorporated into the panel as needed by the specific process. These can include right handed, left handed, or ambidextrous gloves.

There are myriad flow booths installed and as such no one curtain design fits everyone's needs. As such, customization is provided to make sure the process and ergonomics are covered correctly.



Process Area Barrier Curtains

WHAT ARE THE APPLICATIONS?

This type of containment can be an extension of down flow, cross flow, and laboratory fume hoods. In addition, doorway restrictions have also been designed to prevent access from one part of a suite to another.

The use of flexible containment allows the end user to process contained when needed or to follow existing, open processing procedures when containment is not required. In both cases, cost savings are realized by modifying an existing design or using an existing piece of equipment with no modifications.

WHAT ARE THE FEATURES/BENEFITS?

<i>Features</i>	<i>Benefits</i>
Retrofit to existing equipment designs	Provides the lowest overall cost of process ownership through low capital and operating cost including reduced cleaning and cleaning validation
Clear film	Supports visibility for maintenance
Passive system	Does not affect ATEX and Ex ratings
Flexible materials	Ergonomics maximized
Disposable components	Speed of implementation

WHAT CONTAINMENT LEVEL PROVIDED?

These types of barriers are designed to enhance the capabilities of the booths and facilities installed and rely on the airflow from the primary source of containment.

WHY USE THIS OVER OTHER TECHNOLOGIES?

The cost of ownership, ergonomic advantages, and speed of delivery benefits of this flexible solution far outweigh those of rigid isolation systems.

Tools such as Lean Manufacturing come into play more and more. For example, the time to clean and validate the cleaning are major bottlenecks for processing efficiencies in the plant. Being able to minimize this part of the process results in getting products to market faster and at an overall reduction in operating costs when considering labor, utilities, and waste disposal costs. It also supports getting multiple products to market faster within an existing facility without risking product safety.

OVERVIEW

Two methods of containing blenders have been demonstrated. Included here are the use of flexible enclosures and separate, disposable powder transfer systems.

The systems described in this containment guide center around bin blending and V-Blender applications in Oral Solids Dosage (OSD) manufacturing using Transfer Sleeves, DoverPacs® and Continuous Liners. Blending involves the controlled mixing of dry primary powder particles and excipients. The powders can range in properties and potency and, if not contained, can present cleaning and exposure issues.

Dry mixing of granular and other processing constituents includes a significantly high number of blending steps. This includes potent and highly hazardous compounds, excipients, and materials such as lubricants as processing aids.

As demonstrated by the Risk-MaPP principles, both current good manufacturing practices (cGMP) and Industrial Hygiene (IH) needs can be met by containing the process at the source. By employing flexible containment and using the logic diagrams from the Risk-MaPP process, cleaning is minimized and the operator is protected with this Engineering Control. As such, processes in multi product facilities can be safely performed without the risk of cross contamination.

Used for lab scale and production operations at multiple International Pharma manufacturers, our contained Blending applications take the idea of retrofits to another level. Here, existing and new equipment are supported as a tool to eliminate the risks posed by uncontrolled powder processing. At no time are the blenders' angle of repose affected so as to change the blending performance.

Note that the powder containment applications described below are based on proven designs supported for customers based on the process equipment that they specified. ILC Dover does not have any specific ties to these equipment suppliers and does not recommend one type of blender over another. Rather, this guide depicts a sampling of flexible containment applications to a variety of styles of equipment as standard and customized containment solutions.

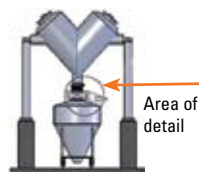


Figure 1a

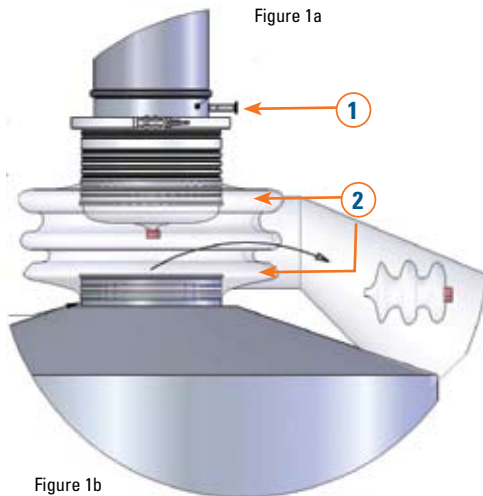


Figure 1b

- 1 Vac/Purge Port
- 2 DoverLoc®

Contained Blending - Transfer Sleeve, DoverPac®, Continuous Liner Technology

HOW DOES IT WORK AND WHAT ARE THE APPLICATIONS?

Three methods of flexible containment using powder transfer systems have been applied to blenders. These include charging and offloading with transfer sleeves, charging and offloading with DoverPacs® and offloading with a continuous liner system.

This rugged film provides a safe working environment while enabling the enhancements developed through numerous installations using this flexible containment technology.

The Transfer Sleeves, Continuous Liners and DoverPacs® are made from ArmorFlex® film. This rugged monolayer film brings regulatory pedigree for materials of contact as well as proven use from multiple process applications.

The use of flexible containment allows the end user to process contained when needed or follow existing, open processing procedures when containment is not required. In both cases, cost savings are realized by modifying an existing design or using an existing piece of equipment with no modifications.

Charging and offloading with transfer sleeves

A transfer sleeve is essentially a flexible chute that attaches to the blender and the piece of process equipment being used to fill or offload the blender. Contained attachment is achieved through the use of a multiple groove canister on the blender and on the IBC, for example. The sleeve is then clamped onto the blender and IBC to support powder flow.

In the case of a bin blender, the bin can be attached to the tablet press or to an interface in the floor of the suite where powder transfer to a piece of equipment on a lower floor is part of the process.

Gemco V-Blender to IBC

In the example shown in figures 1a and 1b, a 30 cubic foot Gemco blender is being emptied to a rigid IBC. The application posed a challenge in lining up for docking with the IBC and in clearances while the blender rotates.

The system includes a 5 groove multiple o-ring canister attached to the V-Blender, a 2 groove canister clamped to the IBC, the Transfer sleeve, the DoverLoc®, and the crimp components. The transfer sleeve is also made with an ArmorFlex® film.

Charging and offloading with DoverPacs®

DoverPacs® are a proven method for contained transfer from vessel to vessel. This system consists of a liner that is attached to a multiple o-ring groove canister. By incorporating a fill and discharge neck the same liner can be filled at one process point and discharged into another.

DoverPacs® utilize the crimping system and ArmorFlex® family of films developed by ILC. Various standard and custom designs are available to fit any process need from lab scale to full production.

Conta Bin Blender Charging and Discharging

While DoverPacs® can be used for charging and discharging any type of blender, the wall mounted Bin blender shown is an example of an application with this flexible containment technology. In this design, the process is supported by the installation of a single, 8" (200 mm) multiple o-ring groove canister on the bin which allows for contained powder transfer through one port for charging, figure 2a, and offloading, figure 2b, the bin. This minimizes the capital expense versus a rigid isolator even further and allows for existing bins to be used without modification.

Following this step the filled 20L DoverPac® is used to charge a capsule filler.

Offloading with a continuous liner system

Utilizing a similar multiple o-ring groove canister, ArmorFlex® film, and crimping technique as above, this system allows contained offloading into drums. Liners are factory packed with standard bundles of 150' (45 m), 100' (30 m), and 50' (15 m). Custom lengths are also provided.

Gemco V-Blender to Continuous Liners

Figure 3 is an example of offloading a 30 cubic foot V-blender with a Continuous Liner system to drums. In this case the rotational clearance did not allow the Continuous Liner canister to be installed directly on the blender as in other applications.

To account for the clearance, a three groove canister was mounted on the blender and the standard canister was mounted on the Transfer Stand shown. In addition, the stand allows the Operator to reach the valve on the outlet of the blender and the transfer sleeve since this interface is 92" (2337 mm) above the floor in this installation.

A transfer sleeve is then used as the contained chute to direct the powder from the blender to the Continuous Liner. The Continuous Liner is pulled into a drum that sits on the existing scale in the floor between the blender supports. This allows for the drum to be weighed as part of the process.

Input from the operation of this system included "this saved us significant cleaning time as we no longer need to hose down the entire suite". This is a key in the Risk-MaPP logic for supporting operations in a multi process facility by eliminating cross contamination concerns.



Figure 2a



Figure 2b

- 1 Bin
- 2 DoverPac®

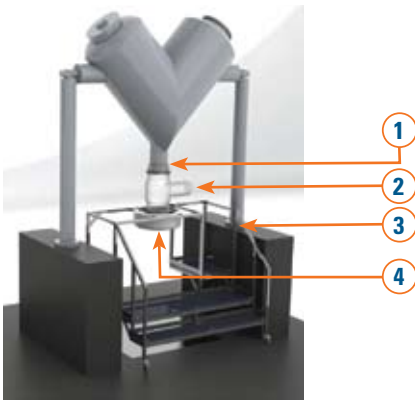


Figure 3

- | | |
|----------------------------|---------------------------|
| 1 Blender Mounted Canister | 3 Transfer Stand |
| 2 Transfer Sleeve | 4 Continuous Liner System |

Contained Blending - Transfer Sleeve, DoverPac®, Continuous Liner Technology

WHAT ARE THE FEATURES AND BENEFITS OF THIS TECHNOLOGY?

Features

- Retrofit to existing equipment design
- Process and Technical areas separated
- Validated containment technology
- Passive system
- Flexible materials
- Disposable components
- Adaptable to other process equipment
- No blender shape modifications

Benefits

- Complies with the Risk-MaPP initiative
- Provides the lowest overall cost of process ownership through low capital and operating cost including reduced cleaning and cleaning validation
- Fastest turnaround of a processing suite for subsequent manufacturing campaigns
- Process is contained without contamination of motor, drive shaft, and controls
- Nanogram containment levels achieved
- Does not affect ATEX and Ex ratings
- Ergonomics maximized
- Speed of implementation
- No affect on blend uniformity

WHAT CONTAINMENT LEVEL PROVIDED?

OEB 5 with results in the nanogram range. This is based on customer test data, other proven applications, third party testing to the “SMEPAC” protocols on similar designs, and the 100% inflation tests performed on the deliverable systems.

OEB 1	OEB 2	OEB 3	OEB 4	OEB 5
10,000 to 1000	1,000 to 100	100 to 50 50 to 10	10 to 1	1 to 0.1 0.1 to 0.01

Occupational Exposure Levels above are in µg/m3.

WHY USE THIS OVER OTHER TECHNOLOGIES?

One of the driving forces of this technology is that it reduces the risk of cross contamination in multi process facilities and it provides safety to the operators in both multi process and dedicated facilities. By using this disposable Engineered Control, highly hazardous powders are contained at the source which significantly reduces cross contamination risks and cleaning of process suites and rigid containment devices.

The cost of ownership, ergonomic advantages, and speed of delivery benefits of this flexible solution also far outweigh those of rigid isolation systems.

Tools such as Lean Manufacturing come into play more and more. For example, the time to clean and validate the cleaning are major bottlenecks for processing efficiencies in the plant. Being able to minimize this part of the process results in getting products to market faster and at an overall reduction in operating costs when considering labor, utilities, and waste disposal costs. It also supports getting multiple products to market faster within an existing facility without risking product safety.

Contained Blending - Flexible Enclosure Technology

OVERVIEW

Two methods of containing blenders have been demonstrated. Included here are the use of flexible enclosures and separate, disposable powder transfer systems.

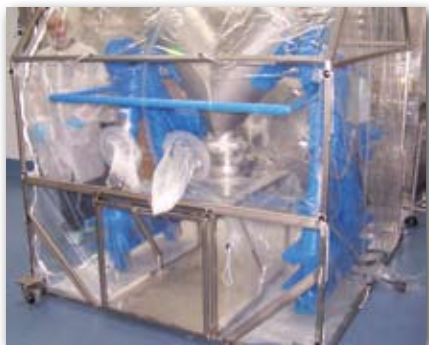
The systems described in this containment guide center around bin blending and V-Blender applications in Oral Solids Dosage (OSD) manufacturing using Flexible Enclosures. Blending involves the controlled mixing of dry primary powder particles and excipients. The powders can range in properties and potency and, if not contained, can present cleaning and exposure issues.

Dry mixing of granular and other processing constituents includes a significantly high number of blending steps. This includes potent and highly hazardous compounds, excipients, and materials such as lubricants as processing aids.

As demonstrated by the Risk-MaPP principles, both current good manufacturing practices (cGMP) and Industrial Hygiene (IH) needs can be met by containing the process at the source. By employing flexible containment and using the logic diagrams from the Risk-MaPP process, cleaning is minimized and the operator is protected with this Engineering Control. As such, processes in multi product facilities can be safely performed without the risk of cross contamination.

Used for lab scale and production operations at multiple International Pharma manufacturers, our contained Blending applications take the idea of retrofits to another level. Here, existing and new equipment are supported as a tool to eliminate the risks posed by uncontrolled powder processing. At no time are the blenders' angle of repose affected so as to change the blending performance.

Note that the powder containment applications described below are based on proven designs supported for customers based on the process equipment that they specified. ILC Dover does not have any specific ties to these equipment suppliers and does not recommend one type of blender over another. Rather, this guide depicts a sampling of flexible containment applications to a variety of styles of equipment as standard and customized containment solutions.



Contained Blending - Flexible Enclosure Technology

HOW DOES IT WORK AND WHAT ARE THE APPLICATIONS?

Three methods of flexible containment using enclosures have been applied to blenders. These include containing the entire blender in an enclosure, using an enclosure and flanges attached to the blender to separate the process and technical areas, and charging and offloading a blender with an enclosure attached to the valve on the blender.

The enclosures are manufactured from clear ArmorFlex® 113 film that allows room light to illuminate inside the enclosure for easy viewing. This rugged film provides a safe working environment while enabling the enhancements developed through numerous installations using this flexible containment technology.

The Bag-in/Bag-out (BIBO) Sleeves and DoverPacs® are often used to transfer powders into and out of the enclosure. The Sleeves and DoverPacs® are made from another version of ArmorFlex® film and as such brings regulatory pedigree for materials of contact.

The use of flexible containment allows the end user to process contained when needed or follow existing, open processing procedures when containment is not required. In both cases, cost savings are realized by modifying an existing design or using an existing piece of equipment with no modifications.

Separating the Process and Technical Areas of the Blender

In this method, flanges are added to the piece of process equipment, usually by the original equipment manufacturer (OEM). A Flexible Enclosure is then attached to the flange.

The use of stainless steel flanges added to the blender enables the containment of the process area. This then keeps the controls, motors and other components of the technical section of the equipment away from the powder being processed to avoid contamination. The enclosure is attached to the flange and includes glove sleeves, bungee cords, and HEPA filters. These features support access to the equipment while maximizing ergonomics for operators from the 5th percentile female to the 95th percentile male.

Globe Pharma Blend Master V-Blender

In the application shown in figure 1, flanges were added to an existing design that allows the attachment of the flexible enclosures. The frame is included to support the enclosure. This frame is on casters so it can be moved out of the processing suite and stored when not being operated. The overall enclosure is 58" (1473 mm) x 44" (1118 mm) x 70" (1778 mm) tall.

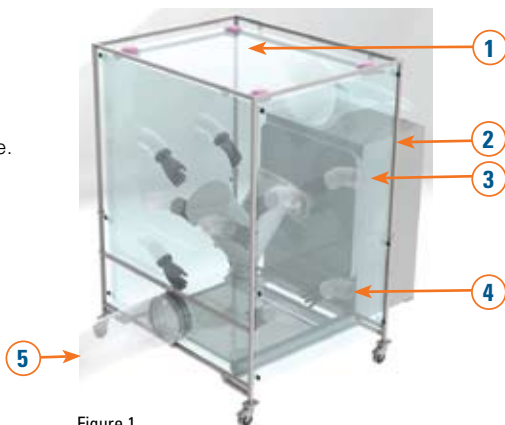


Figure 1

1 Enclosure	4 Glove Sleeves
2 Support Frame	5 BIBO Canister and Sleeve
3 Attachment Flange	

Containing the Entire Blender

Pan mounted enclosures contain the entire piece of process equipment. This is beneficial for equipment that can not be modified to use the flange mounted technology described above.

The enclosure is supported by bungee cords, attached to the pan, and includes glove sleeves for access to the equipment. The enclosure “moves” with the operator, as is the case with all of our flexible enclosure systems, to maximize ergonomics as noted above.

Chitra V- Blender

In this design, the containment is achieved by encapsulating the entire blender inside a flexible enclosure. The enclosure is of the pan mounted style, see figure 2, where the pan is situated on the floor of the process suite. In this case the pan is 53.5” (1359 mm) x 74.5” (1892 mm). The enclosure height is 75.5” (1918 mm).

Multiple sets of gloves are incorporated into the flexible enclosure to support ease of operations when loading and unloading the blender and operating the controls. A Bag-in Bag-out (BIBO) interface is included to allow materials to be passed in and out of the enclosure without breaking containment. The entire unit is supported on a frame.

PK Blendmaster

A similar design contains the PK Blendmaster in Figure 3. The pan is 56” (1422 mm) x 61” (1549 mm) and the overall height is 81” (2057 mm). Operational features such as integral glove sleeves located at key process points, a BIBO canister, HEPA filters, and bungee cords are incorporated into the design.

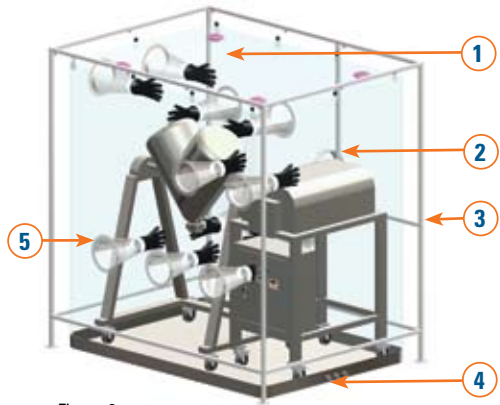


Figure 2

1 Enclosure	4 Pan
2 BIBO Canister	5 Glove Sleeves
3 Support Frame	

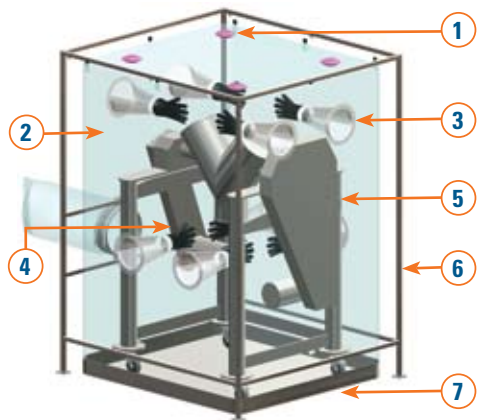


Figure 3

1 HEPA Filters	6 Enclosure Support Frame
2 ArmorFlex® Enclosure	7 Base Tray and Enclosure Mounting Flange
3 Glove Sleeves	
4 Bag-in Canister	
5 PK Blender Existing	

PK Blendmaster Yoke Blender

The Yoke Blender provides a tumble blending operation for free flowing materials in small volumes. As such, it can be cart mounted using a pan mount design, figure 4. The pan is mounted on a frame assembly with conductive casters. Overall dimensions of this portable system are 54" (1372 mm) x 42" (1067 mm) x 73.3" (1861 mm) tall.

Standard features carried over to this design include a BIBO canister for introducing raw materials into the enclosure and passing blended product out for processing to the next step, HEPA filters and bungee cord attachment to support a range of operator heights, and integral glove sleeves at optimal processing locations.

Flexible Enclosure loading and offloading

By attaching a multiple groove canister directly to the valve on the blender, small volumes of powders can be charged and removed from a blender using a Flexible Enclosure. Typically used in Lab Scale and Clinical Development trials, this process supports processing in early stages where the acceptable daily exposure (ADE) and Occupational Exposure Level (OEL) are often not known yet.

Double Cone Blender Mounted Flexible Enclosure System

Here a small volume of powder is charged into the blender from a bottle. In order to contain this transfer a flexible enclosure is attached to the blender. In this design a 6" (150 mm) multiple groove o-ring canister is attached to the valve on the double cone blender. A custom enclosure was developed based on this process that included a bag in/waste sleeve, an ambidextrous glove sleeve, a HEPA filter, and an encapsulated o-ring for securing the enclosure to the canister.

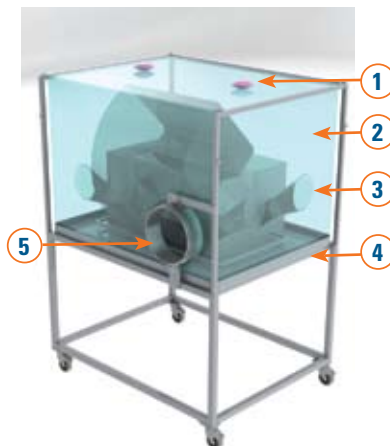


Figure 4

- 1 HEPA Filters
- 2 ArmorFlex® Enclosure
- 3 Glove Sleeves
- 4 Frame Mounted Pan
- 5 BIBO Canister (sleeve not shown)

Figures 5a and b illustrate the charging process. These steps include attaching the enclosure to the canister, bagging the powder into the sleeve on the enclosure, bagging out the stub from the previous enclosure, pouring the powder from the jar into the blender, placing the waste product back in the sleeve, and crimping off the sleeve. The enclosure is then folded and placed inside a fabric support shroud while still attached to the blender. This protects the enclosure during the tumbling operation and saves the enclosure for use when offloading the blended product.

Offloading the blender, figure 5c, includes removing the support shroud, unfolding the enclosure, opening the valve to discharge the product, and crimping off the enclosure so that the contained powder can be taken to the next processing step.

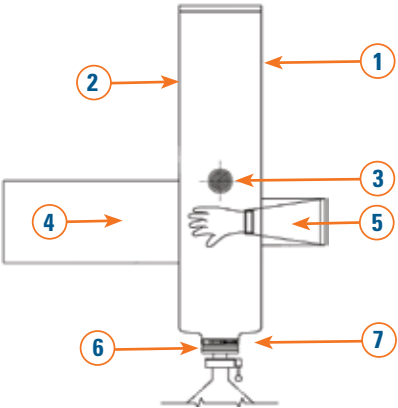


Figure 5a

- | | |
|---------------------|--------------------|
| 1 Collection Area | 5 Glove Sleeve |
| 2 Blender Enclosure | 6 Blender Canister |
| 3 HEPA Filter | 7 Band Clamp |
| 4 Bag-in Sleeve | |

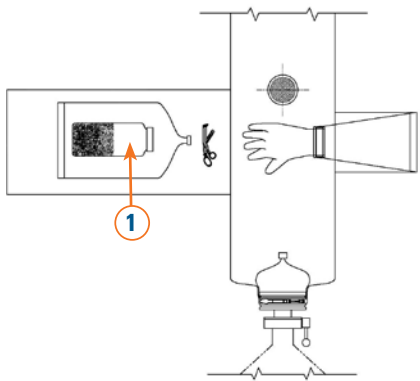


Figure 5b

- 1 Bin

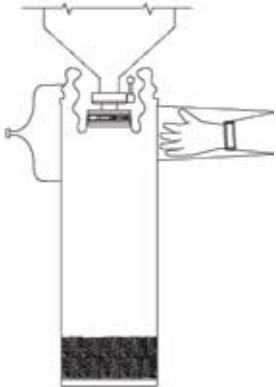


Figure 5c

Contained Blending - Flexible Enclosure Technology

WHAT ARE THE FEATURES AND BENEFITS OF THIS TECHNOLOGY?

Features

Retrofit to existing equipment design
Process and Technical areas can be separated
Validated containment technology
Clear film
Passive system
Flexible materials
Disposable components
Adaptable to other process equipment
No blender shape modifications

Benefits

Complies with the Risk-MaPP initiative
Provides the lowest overall cost of process ownership through low capital and operating cost including reduced cleaning and cleaning validation
Fastest turnaround of a processing suite for subsequent manufacturing campaigns
Process is contained without contamination of motor, drive shaft, and controls using flange attachment design
Nanogram containment levels achieved
Supports visibility for maintenance
Does not affect ATEX and Ex ratings
Ergonomics maximized
Speed of implementation
No affect on blend uniformity

WHAT CONTAINMENT LEVEL PROVIDED?

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**Designed for your process,
Delivered on time,
Supported by the ILC Dover Team!**

**Combining flexible technology with
manufacturing expertise to deliver
economic disposable solutions to
the biopharm industry**

- ▶ Robust construction using ArmorFlex® to assure integrity even when dropped
- ▶ Custom designs to meet your specific process needs including turnkey systems for weighing powders
- ▶ Inventory programs to assure you will always have the right product available at the right time

Powder transfer containers for media and buffer prep

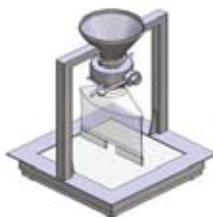
- ▶ **ILC Dover** – global experts in powder transfer systems which meet cGMP requirements and control cross contamination
- ▶ **ArmorFlex®** – a unique anti-static film meeting global product contact requirements including stringent USP Class VI and other regulatory directives
- ▶ **Compliance** – Certificates of Conformance to comply with your Quality program

**Ask how our options can
be combined to solve your
specific process needs.**

Gamma Irradiation of 25 – 50 KGy
High containment using patented
technology



*100 L DoverPac® SF prior to and following
sanitary flange interface*



Complete Range of DoverPac® Products

DoverPac® SF sizes	Vessel Connection options
5 Liter	1.5" Sanitary Flange
10 Liter	2" Sanitary Flange
20 Liter	3" Sanitary Flange
30 Liter	4" Sanitary Flange
50 Liter	DN 100 Sanitary Flange
100 Liter	DN 150 Sanitary Flange
	6" Sanitary Flange
	8" Sanitary Flange

Sentinel Clear™



Panoramic Hood

*clear vision
for the future*



Sentinel XL™ Blower

Sentinel Clear™

with ArmorFlex® Material
NIOSH Approved TC-21C-0848
and TC-23C-2537

Benefits of the Panoramic Hood

- » Clear hood provides 320° panoramic field of view.
- » APF of 1000 provided.
- » The 8 scfm (230 lpm) of air supplied is above the NIOSH minimum of 6 scfm (170 lpm)
- » Air distribution plenum improves comfort.
- » Adhesive tab system keeps hood in place even while bending. Patent pending.
- » Unique Skirt/exhaust system fully inflates suit to deliver improved protection and comfort.
- » Safety glasses and hard hats are readily accommodated.
- » Elimination of neckdam improves comfort.
- » No suspension system increases comfort and eliminates sizing concerns.

Sentinel XL™
 **POWERED AIR PURIFYING
RESPIRATOR**

www.doverpac.com customer_service@ilcdover.com Ph 302.335.3911, X506 or 800.631.9567
ONE MOONWALKER RD., FREDERICA, DELAWARE USA 19946-2080



Blower with HP Filters and Quick-Loc™ Belt



OV/AG/HE Filters



Adhesive tab system keeps hood in place even while bending

▶▶ Sentinel XL™ Blower

- ▶▶ Integrated blower and battery pack reduces bulk and eliminates “battery falling off” and snagging issues
- ▶▶ Quick-Loc™ belt greatly simplifies adjustment and cleaning
- ▶▶ Operation with two P100 filters (vs. 3) provides excellent protection while reducing operating costs
- ▶▶ NIOSH-approved OV/CD/CL/HF/SD/HE filter operation available.
- ▶▶ Low voltage alarm – flashing LED and continuous beep alert wearer



ILC Dover has been “*creating what's next*” for over 60 years.

To “*create what's next*” ILC Dover listens to its customers. Our skilled engineering staff, building on years of experience with NASA, military, and commercial customers, translates those needs into high performance products. We look forward to hearing from you so we can continue to “*create what's next*”.

Sentinel Clear™ Hood FAQ's



Sentinel XL™
 POWERED AIR PURIFYING
 RESPIRATOR

Q:	A:
<i>What user operations are appropriate for the Sentinel Clear™ hood?</i>	The Sentinel Clear™ hood supports the broad range of pharmaceutical processing operations. The hood is designed for comfortable, non-encumbering use over long operating periods. When combined with the Sentinel XL™ PAPR blower and NIOSH-approved cartridges, it provides protection from airborne particulates, aerosols, and organic and acid gas vapors.
<i>What is the difference between Sentinel Clear™ Hood and HP head tops?</i>	The Clear Hood covers the head and neck and includes bibs that get tucked into coveralls. The HP hood covers the head and face only.
<i>What are the major advantages to the Sentinel Clear™ hood?</i>	First and foremost is the field of view, the Sentinel Clear™ offers a 320 degree field of vision. Attention to ergonomic detail has also resulted in a system that does not require a headband, thus no uncomfortable mechanism riding on your head and no neck dam which eliminates any chocking feeling.
<i>Are the Sentinel XL™ Clear Hood and HP systems NIOSH approved?</i>	Yes, both have NIOSH approvals.
<i>What are the assigned protection factors for these designs?</i>	The Clear Hood system has been rated with an assigned protection factor (APF) of 1000 and the HP system is rated with an APF of 25.
<i>How many sizes of hoods are there?</i>	The hood is designed and NIOSH approved as a one size system.
<i>Can I wear standard personal protective gear in the hood?</i>	Yes, the head top supports the use of equipment such as hard hats, hearing muffs, and safety glasses as needed.
<i>What types of filters are available?</i>	The system has NIOSH approvals for the option of using two High Efficiency Particulate (HE) or three OV/CD/CL/HC/HF/SD/HE filters.
<i>What airflow does the PAPR provide?</i>	The powered air purifying respirator (PAPR) delivers 8 scfm (230 LPM) of filtered air. This is 33% more than the minimum flow required by NIOSH.
<i>What is the advantage of all this added air flow?</i>	Aside from increased protection for the worker, the added flow provides additional prevention of lens fogging as well as cooling to the head and torso as the air passes from the internal duct in the hood, across the breathing zone and down into the Tyvek suit.
<i>What keeps the hood from rising up when it is inflated?</i>	The outer bib includes four adhesive tabs. These tabs adhere to the Operator's Tyvek suit creating a shear mode resistance to any lifting load. Additionally, a portion of the air from the blower is exhausted to the room which balances the comfort and protection features of the system.

Sentinel Clear™ Hood FAQ's



Sentinel XL™
POWERED AIR PURIFYING
RESPIRATOR

Q:

A:

What type of batteries are used with the Sentinel XL™ system?

Nickel metal hydride (NiMH) rechargeables which do not exhibit “memory effects” like NiCad batteries.

How long does the charge last?

8 hours.

Will I get the same flow as the battery charge runs down during use?

Yes, the PAPR is equipped with an integrated circuit board that is designed to maintain a steady flow during operation.

Does the PAPR incorporate a low voltage alarm?

Yes, both an audible and visible alarm are included.

How much does the PAPR weigh?

The integrated blower and battery weigh 2.75 pounds.

How is the PAPR worn?

The PAPR is supported on the Quick-Loc™ comfort belt. The integrated system sits comfortably on the Operator's hips and does not present any snag hazards.

What is the advantage of an integrated blower/battery system?

An integrated battery is ergonomically more suitable to the wearer with the weight distributed over the Quick-Loc™ comfort belt versus having the blower riding on the back and the separate battery riding on the hip, thus two points where one has to carry weight. An integrated system also does not require a separate cable to attach the blower and battery, which can be a snag hazard.

How rugged is the system?

The entire system has been designed and tested to support vigorous use in a plant environment. One example is the Breathing Tube. The Breathing Tube is a reinforced design that resists crushing when an operator needs to be working on their back.

How do I decon my system after use?

Your typical cleaning SOPs would be used, however, there is an approved list of cleaning materials that should be followed.

What documentation is available?

System Level User Instruction Manuals, Filter User Instructions, Battery Charging Instructions, Recommended Cleaning Solution list, Donning Posters, and a Training presentation.

Weigh and Dispense System



A NEW era in dispensing technology

OVERVIEW

This modular design is developed to allow weighing or subdividing materials in a highly contained way while maintaining weighing accuracy. The system can be used for weighing and then directly charging into a process vessel or other equipment.

BENEFITS

- Modular design to meet specific process demands using proven containment and weighing technology
- Improved ergonomics over hard wall isolators by utilizing the comfort of the flexible wall system
- Low capital cost to purchase and install
- Accurate weighing system designed for the application and process typically to ± 5 grams depending on scale capacity (higher accuracy available with custom design and scale selection)
- Proven containment using the static or dynamic Flexible Isolator System to less than $1.0 \mu\text{g}/\text{m}^3$

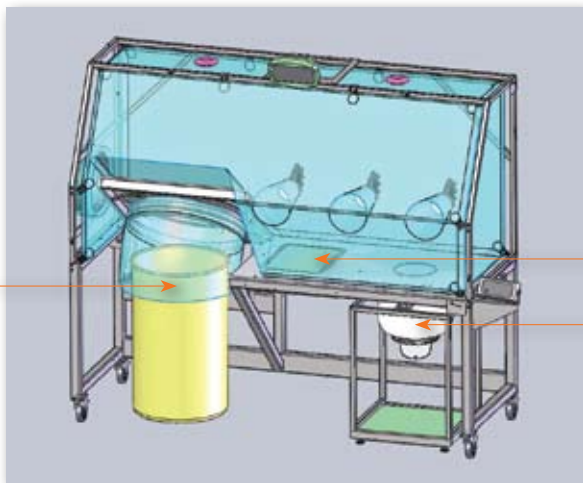
WEIGHING CAPABILITY

- Versatile design to use balance, load cell system or floor scale systems
- Accurate weighing along with tare removal of packaging for net weight accuracy
- Weighing accuracy is determined by the scale capability and the weights being handled

DRUM DISPENSING

- The system is primarily designed to dispense from drums
- Easily attach drums using the ILC Dover drum attachment ring technology
- Standard design for drum diameters up to 23"
- Drums can be completely or partially discharged and then removed from the system maintaining containment for subsequent discharging
- ILC Dover Crimping System completes the safe and secure process

The unique drum attachment method provides high containment and ease for the operator to dock a drum



The scale can be located outside of the containment area so cleaning is not required

The System can discharge to a continuous liner system, DoverPac, or other packaging. This frame can include load cells or use a floor scale to assure accurate net weights.

Weigh and Dispense System

STATIC FLEXIBLE ISOLATOR

- This passive system is proven for high containment
- Using our robust ArmorFlex® 113 flexible film, the integrity of the system is secure
- Testing results consistently report an OEL below 1.0 µg/m³ TWA
- Systems have been provided up to 200" long with no limit on size capacity



DYNAMIC FLEXIBLE ISOLATOR

- Designed with a fan and HEPA filter system to provide an additional level of containment protection while reducing the risk of any breach
- Pressure control is maintained and monitored by PLC System
- Breach control to sense and indicate a pressure drop while changing the operating parameters to maintain a negative pressure



PROCESS EXAMPLES

- Dispense to DoverPac's for charging
- Dispense to Continuous Liner
- Subdivide drums of potent materials
- Sampling from drums
- Weigh and dispense directly to the process

DESIGN OPTIONS

- N₂ inerting of the system
- Low humidity control
- Alternate transfer options including RTP units and transfer valves
- Wash-in-place cleaning
- Adjustable height base
- Collapsible frame for storage

ARMORFLEX®

- The ArmorFlex® family of films has been developed for the specific needs of the pharmaceutical industry including FDA approval for product contact
- The flexible isolator is manufactured from ArmorFlex® 113 film and is typically 8 mil thick. This robust material will resist against damage from typical use and is more functional than a hard wall type design
- ArmorFlex® is developed to be resistant to most solvents, environmentally friendly for incineration with no chlorides, and has a 5-year shelf life

The Premier Closure System In Pharmaceutical Processing

New CrimpLoc™ System From ILC Dover

ILC Dover pioneered flexible containment for the pharmaceutical industry and continues to innovate processes for better performance. We invented the original crimping system and now we have created the CrimpLoc™ System. This NEW system is the next generation to provide high containment and a secure closure when using the DoverPac®, Continuous Liner, and other ArmorFlex® film solutions.

- ▶ Less hand force and more ergonomic
- ▶ One Tool for all Crimp Sizes
- ▶ Uses the same Crimps as the existing ILC Dover Crimp System
- ▶ Light weight

Key factors to consider for closure of in process pharmaceutical packaging

- ▶ Containment
- ▶ Quality
- ▶ Ergonomics / Safety
- ▶ No plastic shards from separation cut
- ▶ Validation
- ▶ Operator Ease of Use



Innovation Timeline of Film Closures



The CrimpLoc™ System is a complete kit to provide the secure closure for ArmorFlex® film packages. Current users can upgrade to the CrimpLoc and realize the benefits of the new design. New kits are available including the CrimpLoc™ tool, Cutting Tool, and Crimps.

One CrimpLoc™ tool is needed for the range of ArmorFlex® closures offered by ILC Dover:

ArmorFlex® size	Crimp Designation
23" Diameter	Blue
14" Diameter	Red
4" Diameter	Yellow



CrimpLoc™ Kit



Crimp Removal Tool - The latest innovation for safe removal of the crimp. The crimp remains in one piece so no risk of contamination upon opening.



ArmorFlex® Family of Films Meeting Your Current And Future Process Requirements

ArmorFlex® 114 - The latest addition to the ArmorFlex® Family

- » Complies with FDA 21 CFR
- » Fully compliant to 2002/72/EC and amendments
- » Meets test parameters of EP 3.1.3
- » Passes USP <661> Physicochemical Tests for Plastics
- » Passes USP <88> Class VI (7 day implant)
- » Passes <87> biological reactivity, in vitro
- » No animal derived components
- » 5-year shelf life
- » Permanent antistat replaces migrating additives
- » Passes Chilworth incendivity tests
- » Tested for solvent resistance
- » DMF filed with FDA

ArmorFlex® 104 - Continuing to be the most used ArmorFlex® film

This space age film continues to be used for meeting process and regulatory needs throughout the pharmaceutical industry. With over 150,000 containment solutions completed from ArmorFlex® 104, this high tech film is a proven standard. DoverPacs, continuous liners, and other containment solutions will be available using ArmorFlex® 104 for years to come.

- » At ILC Dover we are always “creating what’s next” by listening carefully to our customers. In response to customer input and emerging regulations, we’ve developed a robust new film to support our DoverPac® Containment Systems. This revolutionary film, ArmorFlex® 114, delivers permanent static dissipative properties while meeting FDA and 2002/72/EC requirements for food contact and EP 3.1.3 test conditions.

ArmorFlex® Family



ArmorFlex® 114 Solvent Resistance Solvent Contact Recommendations

Chemical	Resistance
Acetone	Excellent
Acetonitrile	Excellent
Anisole	Good
Butyl Acetate	Good
Cyclohexane	Excellent
Cyclohexane – Ethyl Acetate (50/50)	Excellent
Dichloromethane	Excellent
Diethylether	Excellent
Dimethylacetamide	Excellent
Dimethylformamide	Excellent
Ethanol	Excellent
Ethyl Acetate	Excellent
HCL (37.4%)	Very Good
n-Heptane	Very Good
HMDS	Excellent
Isopropanol	Excellent
KOH (50%)	Very Good
Methanol	Excellent
2-Methoxyethanol	Excellent
Methylethyketone	Excellent
n-Methylpiperazine	Excellent
n-Methypyrrolidone	Excellent
Methyl-tert-butylether	Excellent
Mineral Oil	Excellent
Reagent (3A) Alcohol	Excellent
NaOH (50%)	Excellent
Tetrahydrofuran	Very Good
Toluene	Fair
Water, Distilled	Excellent

Criteria

% Change in Physical Properties	Resistance
0 - 10	Excellent
10 - 20	Very Good
20 - 30	Good
> 30	Fair



Crimp Separation



Continuous Liner System



DoverPac®



ILC Ireland facility

ILC Ireland operating since 2007

ILC Ireland located in County Cork has been providing standard products from this facility for 4 years. Established to support the pharmaceutical industry in Ireland, the facility warehouses all standard products offered by ILC Dover. DoverPac's, continuous liners, crimps, etc. are readily available for immediate delivery with the convenience of all customs clearance completed. ILC Ireland is committed to providing superior service with quick responses for process needs locally in Ireland.



Process Train Containment in CMO Operations



Flexible Containment Technologies are critical to Pharmatek's CMO Operations

OVERVIEW

Pharmatek Laboratories, Inc. is a premier pharmaceutical chemistry development organization supporting the pharmaceutical and biotechnology industries.

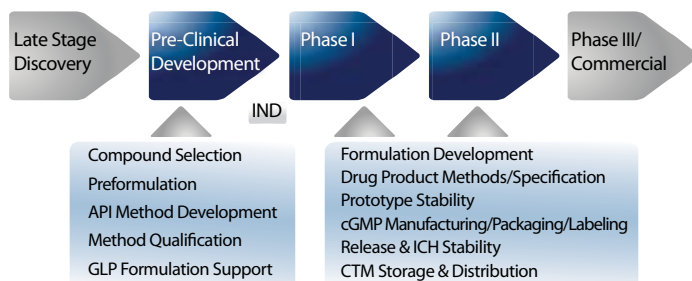
Pharmatek offers development and manufacturing services for highly-potent and cytotoxic (HP/C) compounds including:

- Analytical methods development
- Preformulation testing
- Formulation development
- GMP manufacturing of phase I/II clinical supplies
- Stability storage and testing services (all ICH storage conditions)
- Technical transfer for commercialization
- Clinical distribution and fulfillment

Handling HP/C compounds requires highly specialized facilities and controls. As part of Pharmatek's overall corporate safety program, they have chosen after careful consideration to integrate ILC Dover Flexible Containment Solutions into their HP/C facilities. Wet Granulation, Dry Granulation, Oven Drying, Fluid Bed Drying, Milling, Blending, Encapsulation, Tableting and De-dusting are all examples of manufacturing processes in which Pharmatek has integrated the ILC Dover containment technology.

Pharmatek's focus on pharmaceutical chemistry development, combined with their state-of-the-art HP/C facilities, ensures their customer's molecules move efficiently from discovery to clinical trials.

Pharmatek focuses on preclinical and early-phase development & manufacturing of small molecules and peptides



HOW DO FLEXIBLE ENCLOSURES WORK?

Flexible Containment Enclosures are designed using two basic methods – flange mount and total encapsulation.

The flange mount approach is used for the tray dryer where the flange is added to the face of the dryer outside of the door. An enclosure made from the rugged ArmorFlex® family of films is then attached to the flange and a supporting frame assembly. The door is within an enclosed environment when loading and unloading the trays with the drug product.



Flange Mount Flexible Containment Selected for Tray Dryer

Process Train Containment in CMO Operations

The trays, drug product and associated process tools can either be preloaded into the enclosure or bagged into the isolated area via bag in/bag out (BIBO) canisters or larger drum ring attachment canisters.

For the wet granulation process, Pharmatek selected the total encapsulation method by working with ILC Dover engineers.

Solid pan mounted enclosures allow the entire piece of process equipment to be contained. The enclosure is supported by an elastic suspension system, attached to the pan, and includes glove sleeves for access to the equipment and integrated HEPA filters. Based on the suspension system, the operator is able to get in close proximity to the process, as if containment wasn't even present.



Solid Pan Mount Total Encapsulation
Selected for Granulator

WHAT ARE THE APPLICATIONS?

Flexible Containment enclosures have applicability across Pharmatek's entire high potency process train.

WHAT ARE THE KEY BENEFITS OF THIS TECHNOLOGY?

- **Prevents cross contamination** – the enclosures are single-use and are dedicated to a specific compound to prevent cross contamination, which is of extreme importance to their customers.
- **Supports lean manufacturing** – with over 100 product runs per year, Flexible Containment supports easy product changeover and helps Pharmatek meet stringent EH&S requirements and project timelines.
- **Superior operator protection** – proven nanogram level containment (reference table below)

Additional advantages

- **Durability** – manufactured using puncture resistant ArmorFlex® films, the enclosures hold up during the most demanding operations.
- **Improved ergonomics** – the flexibility of the enclosures in terms of configuration (glove sleeves, ports, and passthru configured for the equipment), the film clarity, and the elastic suspension attachments simplify the process for their operators.
- **Custom designed** – with ILC Dover's engineering expertise, Pharmatek custom designs enclosures for each process train unit.

WHAT CONTAINMENT LEVEL IS PROVIDED?

ILC Dover Enclosure System	Test Material	OBZ-TWA* (µg/m3)	Comment (No. of operators)
Granulator	Lactose	0.0026-0.0027	Operation (2)
Granulator	Lactose	0.0027-0.0331	Cleaning (2)
Drying Oven	Lactose	0.0026-0.0028	Operation (2)
Drying Oven	Lactose	0.0026-0.0037	Cleaning (3)

*Operator Breathing Zone - 8 Hour Time Weighted Average

Based on surrogate monitoring testing conducted by Kasai Consulting, Pharmatek's facilities in San Diego achieved the nanogram containment values shown at left.

WHY FLEXIBLE?

Flexible Enclosures prevent cross contamination and help assure operator safety in Pharmatek's development and manufacturing operations.



ILC DOVER
creating what's next»

PHARMATEK
PHARMACEUTICAL CHEMISTRY DEVELOPMENT

State-of-the-Art Powder Transfer for Biotech

Applications Typically for Media Prep and Buffer Prep

OVERVIEW

ILC Dover has developed a new powder transfer process to solve issues related to contamination and reduce the fill time of each powder bag. The EZ BioPac™ is proven to reduce contamination that typically occurs during filling a powder transfer bag or, more importantly, when it is discharged at the reactor or mix tank.

BENEFITS

- Open fill design provides an easy target for manual filling without spillage
- Significantly less time required per dispense cycle
- Minimizes cleaning with fold over neck
- Additional parts eliminated
- Eliminates the need for additional tools and fixtures. It is self standing and self supporting
- Custom designs to meet specific process requirements
- ArmorFlex® 114 film is the standard material for the product contact area. This unique antistatic film meets FDA, USP, and EU regulatory compliance standards

FEATURES

- 1 liter thru 100 liter capacity
- 1.5" thru 6" sanitary ferrule reactor charge connections
- Rinse ports, vent filters and other process features available
- Smaller sizes have a handle for manual lifting, and larger sizes have lifting loops



Complete Range of DoverPac® Products

EZ BioPac™ flange sizes	Vessel Connection options
5 Liter	1.5" Sanitary Flange
10 Liter	2" Sanitary Flange
20 Liter	3" Sanitary Flange
30 Liter	4" Sanitary Flange
50 Liter	DN 100 Sanitary Flange
100 Liter	DN 150 Sanitary Flange
	6" Sanitary Flange
	8" Sanitary Flange

OVERVIEW

In an effort to provide a better solution for containment to the standard PTS / DCS system, FlexiVac™ was developed along with our partners CSV Life Sciences in Italy and Micro-Macinazione S.A. The resulting innovative solution improves the ergonomics of the system while containment levels have been verified to $<1.0 \mu\text{g}/\text{m}^3$ on a TWA.

BENEFITS

- Operator motion is less restricted with a flexible isolator compared to using a hard box style.
- The “Flexi” system can be provided stand alone to work with an existing powder pump. The filter design and the wand support are designed to work with typical installations.
- Integrated FlexiVac™ with powder pump is a turnkey system available in non-rated electrics or Ex-Proof.
-
- Can be operated with nitrogen inerting or the stand-alone static filters which allow for air flow, thus balancing the pressure in the flexible enclosure.

FEATURES

Operator is aided visually in the wanding process, as the flexible wall allows for clear sight into the drum.

Integral Bag-Out sleeves are included which can be used for samples or for the spent liners after a transfer is complete.

A choice of Allen-Bradley or Siemens control platforms are available.



SYSTEM FUNCTIONAL DESCRIPTION

FlexiVac™ features an ArmorFlex® 113 flexible isolator that can be attached within minutes. This safe isolator system is designed to minimize cleaning requirements while providing high containment. The flexible isolator is robust for use on many drums and then disposed. The improved ergonomics and head space above the drum allows operators, while dispensing, to easily take a spent drum liner with its residual level of powder and stow it until the next drum is attached. The residual powder is easily emptied into the next drum (maintaining high containment) eliminating batch shrinkage.

A stretch fit ArmorFlex® sleeve is used to dock the standard drum o'ring canister with the product drum. This is a fast and effective process to make a contained connection. After the powder is vacuumed from the drum, a high containment separation process using the CrimpLoc™ is performed. The drum and the FlexiVac™ remain contained and are ready to attach the next drum. This process has been used with isolators in many applications and proven effective. Designed for operator ergonomics, the drum connection has a pivoting position to allow the drum to be easily moved into position, connected, and then removed when empty.

The FlexiVac™ system is available with or without a powder pump for compatibility with existing PTS units or other vacuum systems. The fully integrated FlexiVac uses dilute phase conveying technology for the best powder transfer possible.

ARMORFLEX® FILMS

ArmorFlex® 113 film's superior visual clarity makes this the clear film of choice for flexible enclosures and flexible isolators.

- Polyethylene base film provides excellent solvent resistance
- Permanent antistat provides better than 1×10^{11} Ohms per square surface resistivity
- No incineration off-gassing concerns
- ArmorFlex® is designed for high strength and has a 500% elongation before failure, assuring safety from tearing during typical use.

ArmorFlex® films contain no animal derived components and have a 5-year shelf life.

ArmorFlex® 114 film delivers permanent static dissipative properties while meeting FDA and 2002/72/EC requirements for food contact and EP 3.1.3 test conditions.

- Complies with FDA 21 CFR
- Passes USP <661> Physicochemical Tests for Plastics
- Passes USP <88> Class VI (7 day implant)
- Passes <87> biological reactivity, in vitro
- Passes Chilworth incendency test to assure the static dissipative qualities of the flexible isolator
- Tested for solvent resistance
- DMF filed with FDA

CONTAINED DRUM TRANSFER OPTIONS



DTS-Drum Transfer System



VTS-Contained Drum Transfer



DSE-Drum Sampling Enclosure

Ventilated Enclosure System

FLEXIBLE CONTAINMENT TECHNOLOGIES



Ventilated Enclosure System

- ▶ User friendly control system
- ▶ Stable running conditions
- ▶ Automatic breach condition protection with audible and visual alarms
- ▶ Provide EC GMP Grade A internal conditions
- ▶ Enclosures available in static dissipative Polyurethane, PVC or ArmorFlex® 113 Polyethylene film
- ▶ System can be offered to provide negative or positive pressure operation
- ▶ Capable of 30 air changes per hour (minimum)
- ▶ Incorporates Bag In/Bag Out multiple O-Ring canister capability
- ▶ Incorporates a visual pressure indicator
- ▶ Incorporates Exhaust Filter pressure drop monitoring
- ▶ Transportable by one person
- ▶ Available in ATEX and Non ATEX rated versions



The Ventilated Enclosure System combines the benefits of Flexible Containment with a unique, light weight ventilation unit. This system provides all the advantages of a negative or positive pressure isolator providing reduced costs for cleaning and validation with the disposable enclosure that is utilized.

Typical pharmaceutical process operations with this system include, but are not be limited to, dispensing, sampling, milling, mixing, and processing potent compounds. Containers, solvents, and raw material containers can be opened, used, sealed, and cleaned, within the enclosure.

Ventilated Enclosure System

TECHNICAL SPECIFICATIONS

Operates on standard European power of 220/240V, 50 Hz and United States Power of 110V, 60 Hz

Automatically operates and maintains an enclosure negative pressure of -15 Pa (nominal)

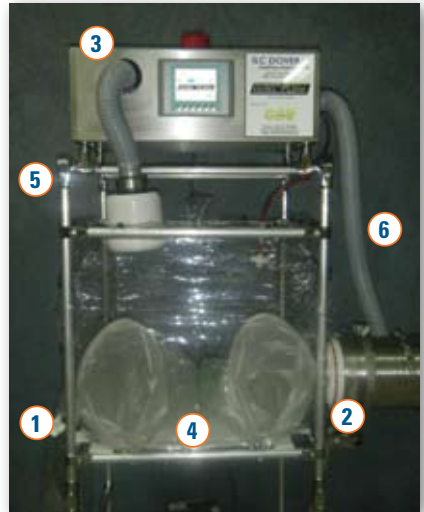
Audible and visual alarms are set at -25 Pa and -3 Pa to notify operator in case of pressure change outside of the safe operating range or in case of excessive exhaust filter pressure drop

Complies with the following Regulatory Requirements:

- ▶ GAMP 5
- ▶ 21CFR Part 11
- ▶ Machinery Directive 2006/42/EC replacing 98/37/EC
- ▶ IEC 60529
- ▶ CE Marking available



Inlet Filter and BIBO Canister Location



1. Frame Assembly
2. Bag In/Bag Out (BIBO) canister
3. Fan and Controls Assembly
4. Flexible Enclosure
5. Inlet Filter
6. Outlet Filter (behind BIBO canister)

Active in the design and development of products for both government and industry since 1947, ILC Dover consistently provides solutions to a dynamic and diverse customer base.



ILC Dover has been “*creating what’s next*” for over 60 years.

To “*create what’s next*” ILC Dover listens to its customers. Our skilled engineering staff, building on years of experience with NASA, military, and commercial customers, translates those needs into high performance products. We look forward to hearing from you so we can continue to “*create what’s next*”.



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