Flexible Containment Solutions Guide

DoverPac® Containment Systems

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.

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.

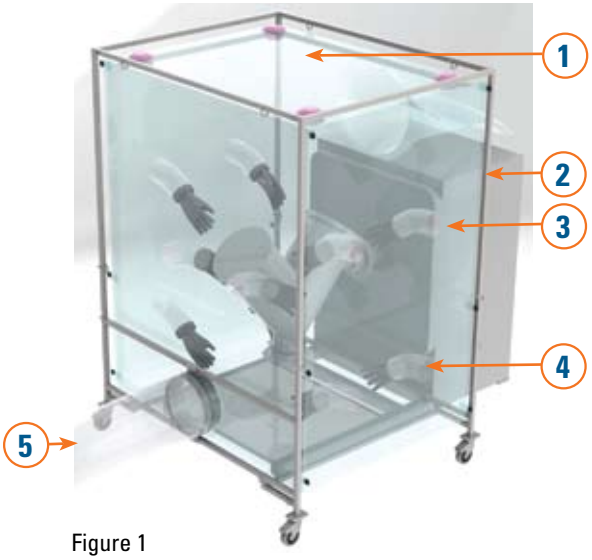

Figure 1

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.

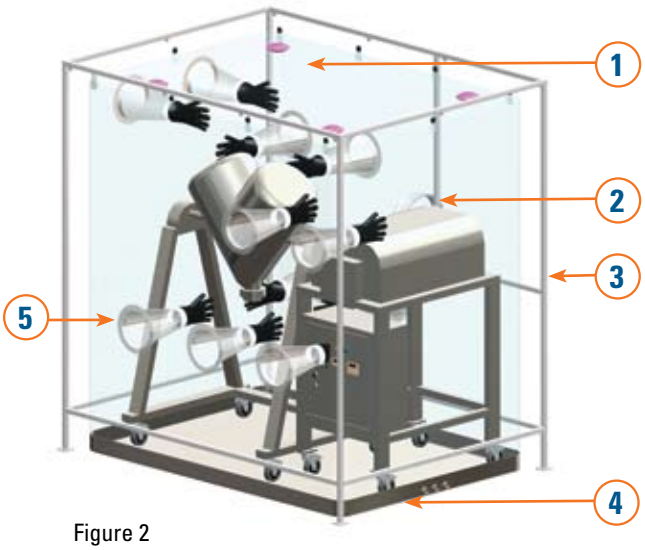

Figure 2

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

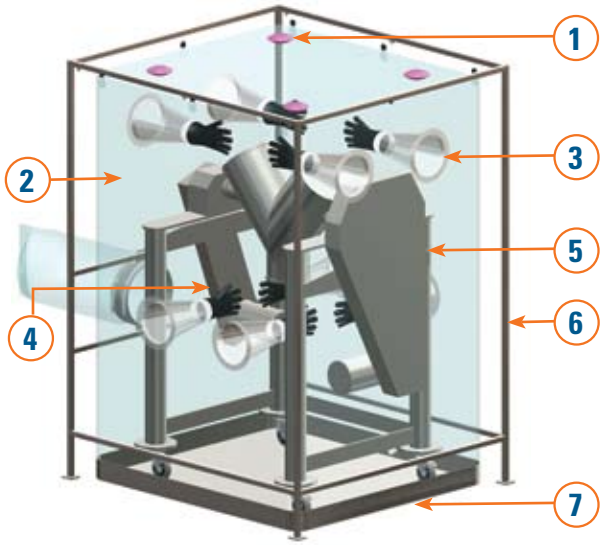

Figure 3

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 asembly 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.

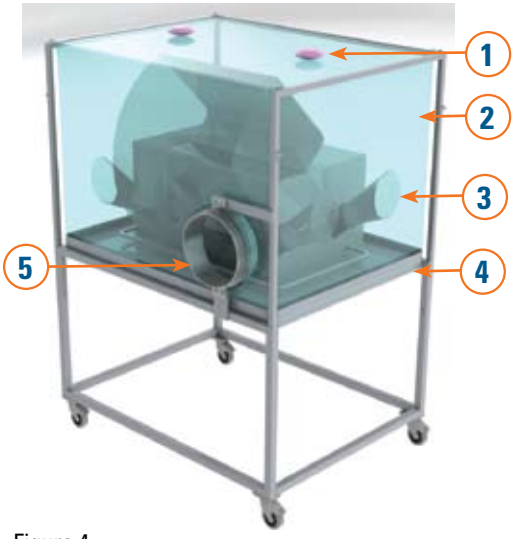

Figure 4

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

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.

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.

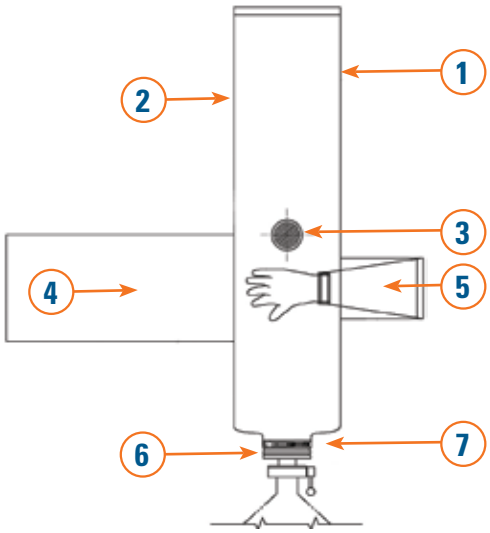

Figure 5a

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

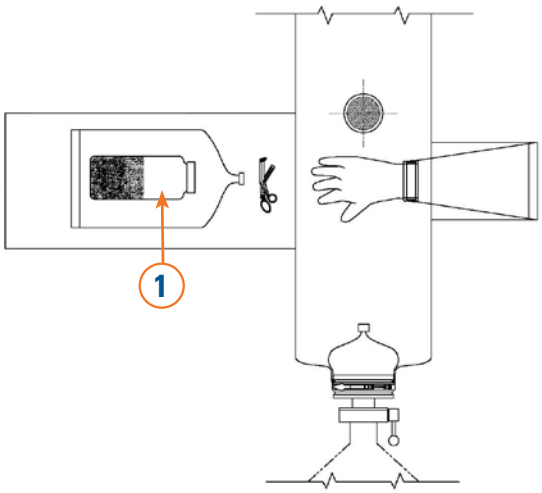

Figure 5b

1	Bin

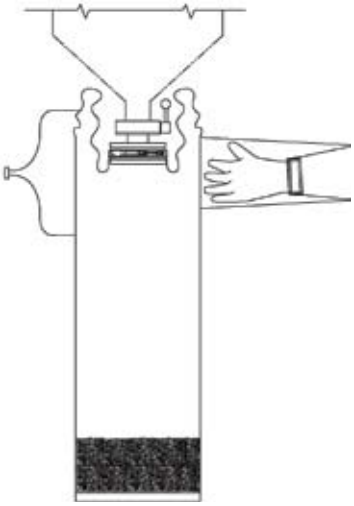

Figure 5c

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?

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.

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