

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

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 | |

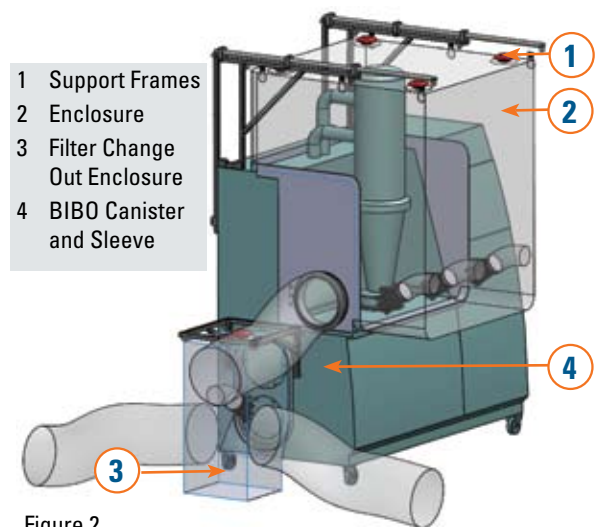


Figure 2

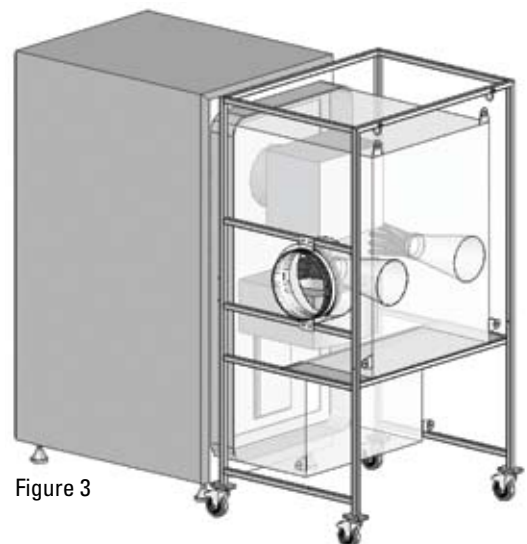


Figure 3

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.

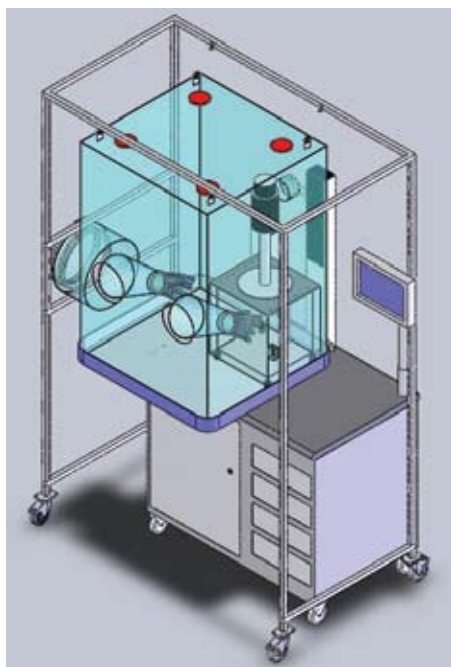


Figure 5

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

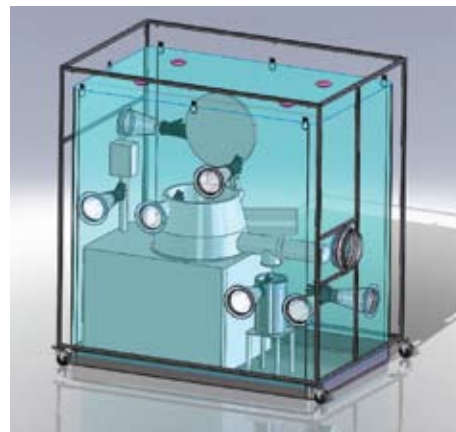


Figure 6



Figure 7

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.

