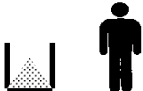
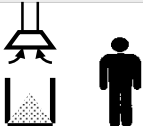
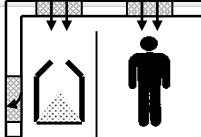
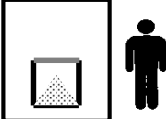
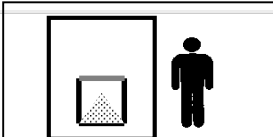


Engineering, health and safety principles high containment in OSD



18-07-2019

Level	OEB1	OEB2	OEB3	OEB4	OEB5
Exposure Limit	1000- 5000 $\mu\text{g}/\text{m}^3$	100-1000 $\mu\text{g}/\text{m}^3$	10-100 $\mu\text{g}/\text{m}^3$	1-10 $\mu\text{g}/\text{m}^3$	$\leq 1 \mu\text{g}/\text{m}^3$
Process Engineering Control	<ul style="list-style-type: none"> No special engineering containment is required. 	<ul style="list-style-type: none"> Open handling should be limited to small quantities. LEV systems 	<ul style="list-style-type: none"> Down-flow booths Contained equipment Wetting 	<ul style="list-style-type: none"> Contained equipment. <i>Wash-In-Place</i> 	<ul style="list-style-type: none"> Totally enclosed equipment under negative pressure Contained transfer ports <i>Wash or Clean-In-Place</i>
Facility Engineering Control	<ul style="list-style-type: none"> Standard design requirements 	<ul style="list-style-type: none"> Negative air pressure room conditions 		<ul style="list-style-type: none"> Once thru HVAC Exhaust air double HEPA filtered Emergency showers Dedicated rooms or segregated areas for unit operation 	<ul style="list-style-type: none"> Once thru HVAC Safe change HEPA in situ Safe change HEPA exhaust Airlocks for materials and personnel
					

High containment has to be designed considering the whole process flow

(processing, cleaning and product transferring) not only based on isolated machines:

- Dust tight docking systems for loading/unloading.
- Isolation of processing areas, minimization of contaminated parts.
- Containment measures on sampling devices (eg. Continuous liner, PP in-line welders, etc.).
- Decontamination systems (vacuum, wetting, flooding, etc.).
- Cleaning in place installations.

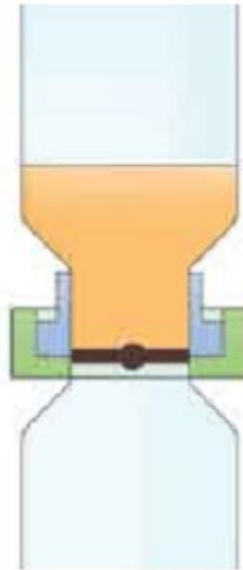
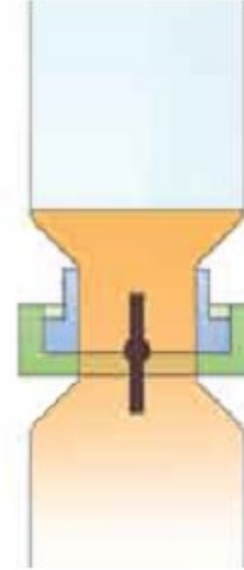
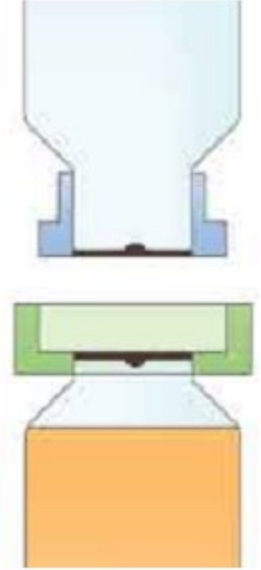
- Technical protection measures (local exhaust ventilation, rooms with negative pressure, containment or enclosure).
- Operating measures (reduction of exposure time, controlled access, training).
- Personal protective equipment (PPE) .

The effectiveness of protection measures should depend as little as possible on employees operation (PPE are considered a protection measure with low effectiveness, as they are highly dependent on employees skill and capacity).



Operational Principle

-  *Passive Body*
-  *Active Body*
-  *Product*
-  *IBC*
-  *Active/Passive Disc*

*Dock**Lock**Open and Close**Unlock and Undock*

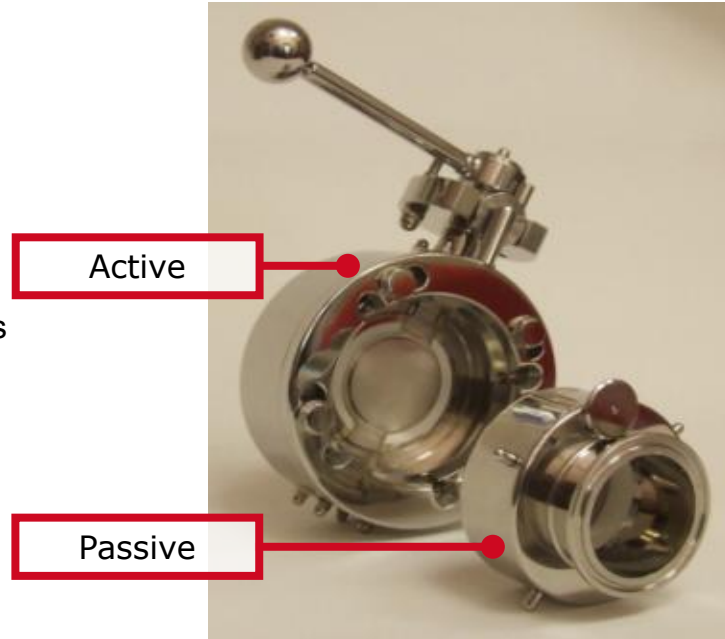
Method of transferring product from process to process in a contained manner.

The benefits of this are:

- Operator protection
- Product protection
- Cross contamination elimination
- Easily handled manually
- Recommended for small sizes
- Recommended for small amount of bins

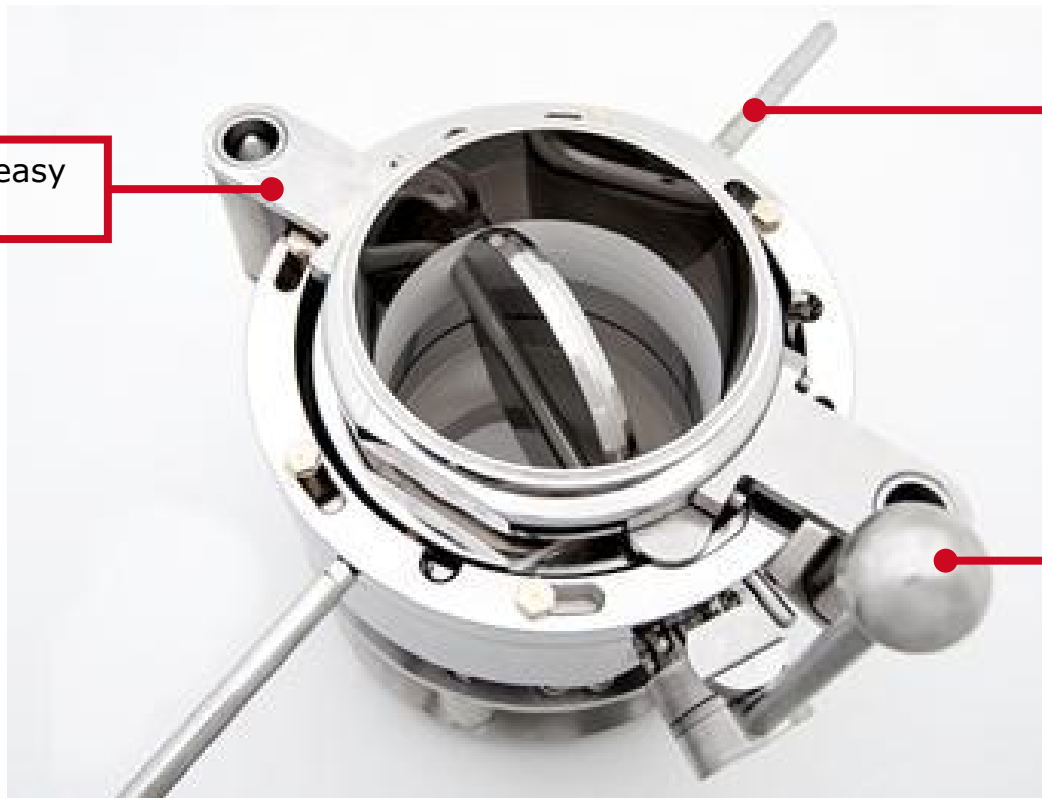
The valve consists of two halves:

- Active
- Passive



SPLIT VALVES

PharmaSafe up to OEB4



Guide/pins for easy docking

Locking lever for Active/Passive part

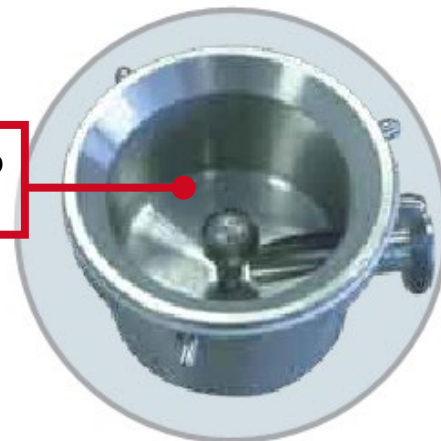
Valve opener on Active part



WIP Passive for docking station



WIP Drain Passive to collect water



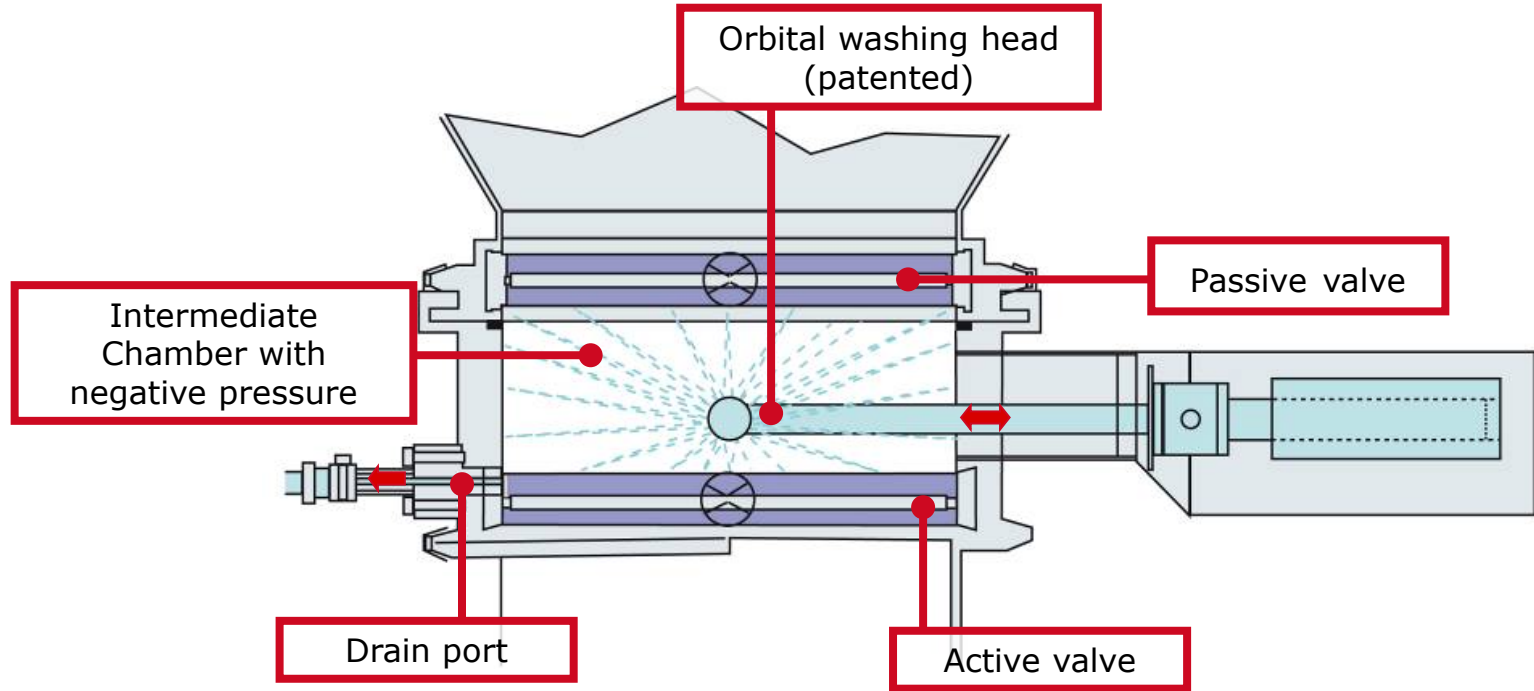


Passive part with
body in POM

As a matter of fact, no system can obtain a high level of O.E.L. without washing the valves. IMA combined experience in powder handling and washing systems has led to the development of **TwinValve**.

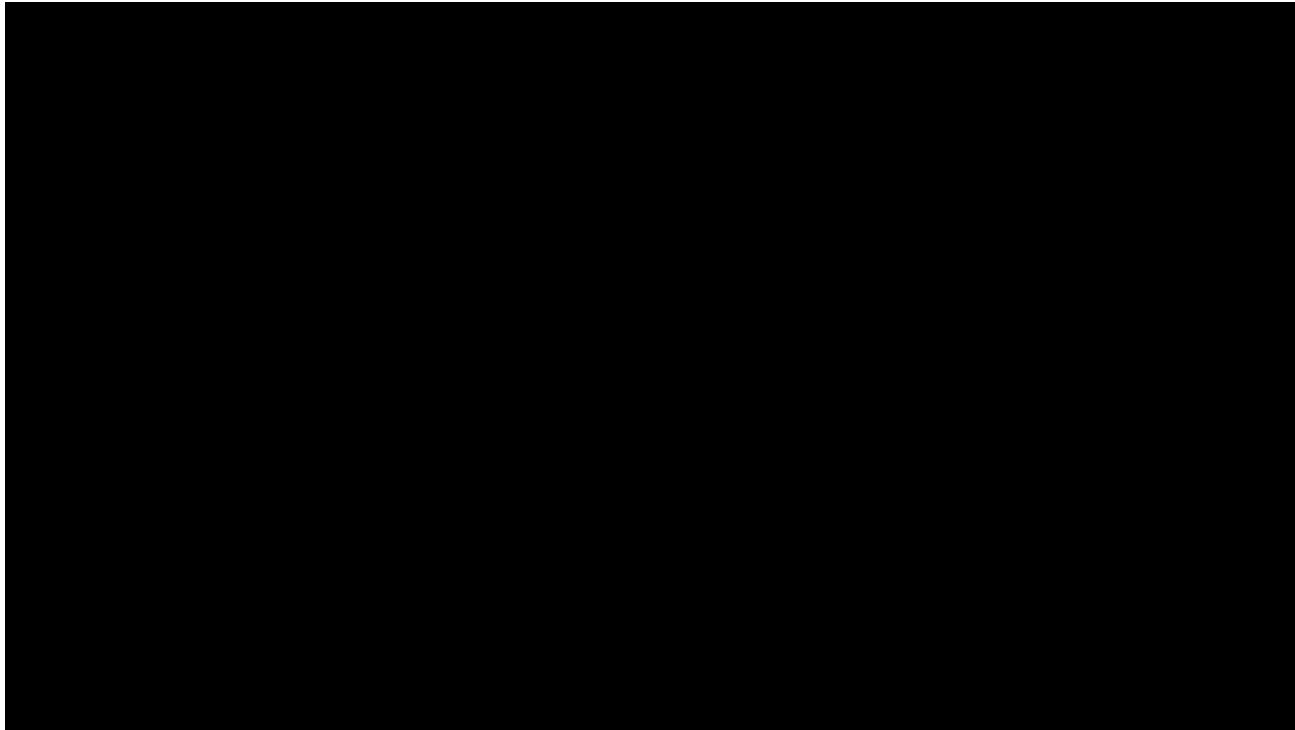
TwinValve is a patented solution based on the combination of two standard sanitary butterfly valves with an orbital rotating spray head.





More space between the valves compared to traditional Split Valves:

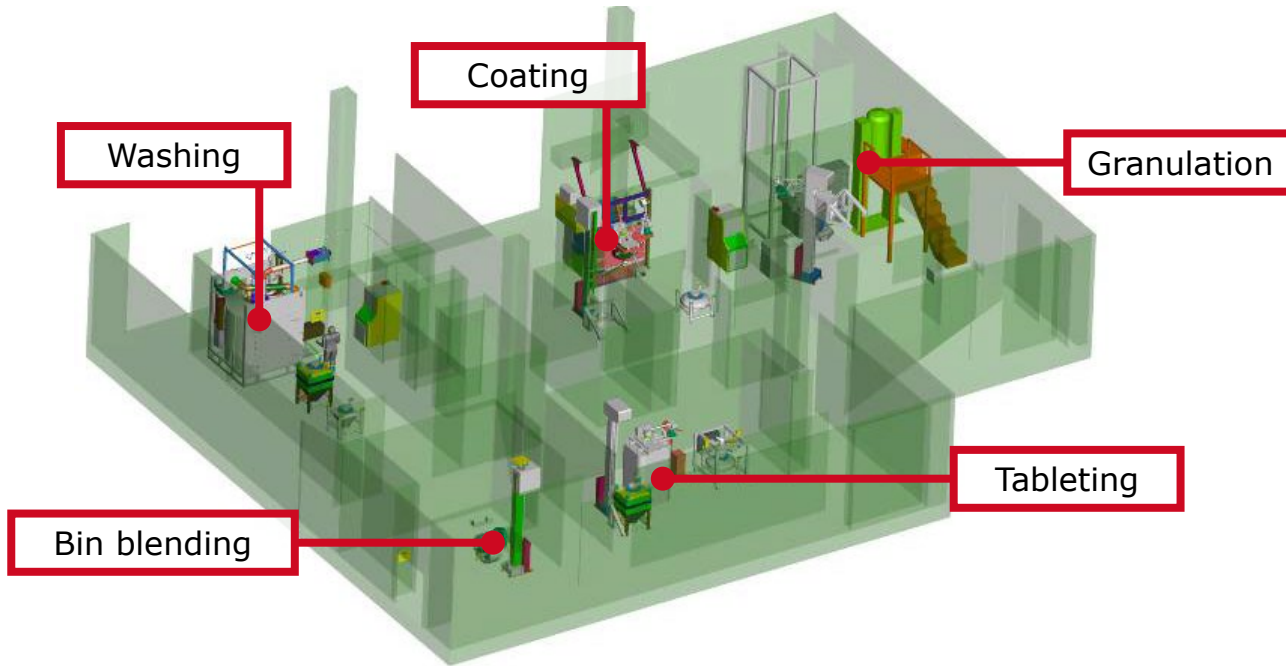
- better and easier cleaning
- no need for extremely precise connection





IMA SOLUTIONS FOR HIGH CONTAINMENT PRODUCTION

IMA Active has recently supplied a complete plant for tablets manufacturing, in total containment.



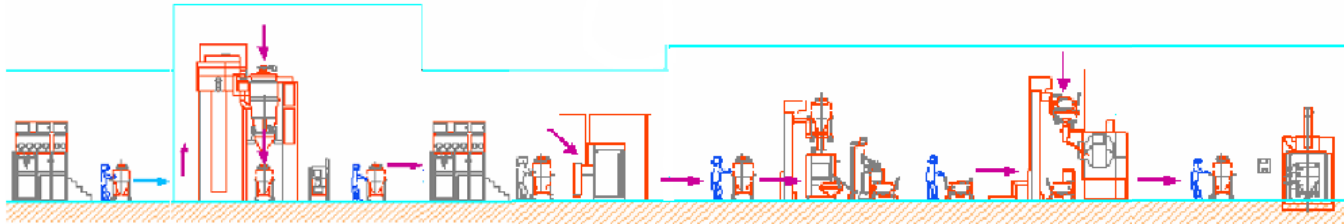
URS

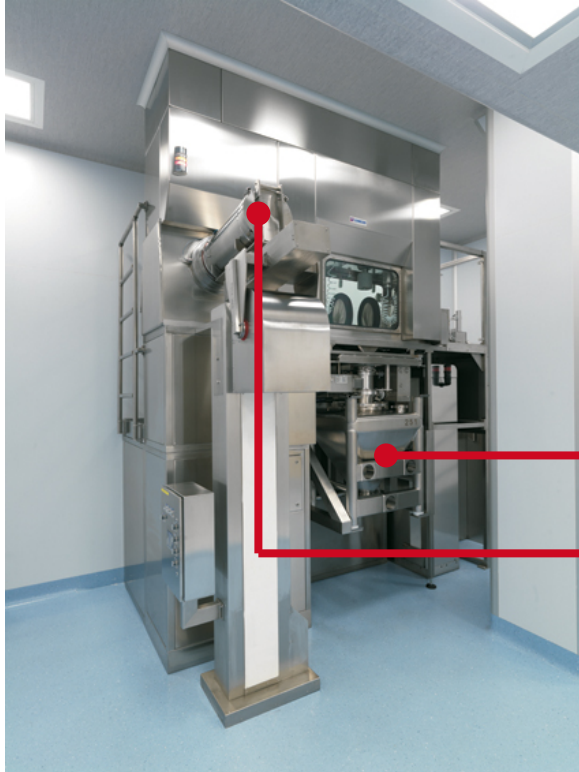
- New **small-scale tablet manufacturing facility**, suitable for development/scale-up, clinical supplies and launch
- **Compliance** with regulatory constraints and technical standards for **OEB 4/5** products
- **OEL** down to **1 µg/m³**
- **Multi-purpose** facility
- Facility realized within existing manufacturing building (**1 level**)
- No pneumatic transfer of powder
- Full Cleaning in Place (**CIP**)
- **Risk based approach** (based on FMEA analysis)
- SCADA system for process control



DESIGN

- Totally **closed** unit operations, separate rooms
- Powder **gravity** charge/discharge with lifting columns
- **Twinvalve** High containment connection
- All equipment fitted with Cleaning in Place (**CIP**) systems

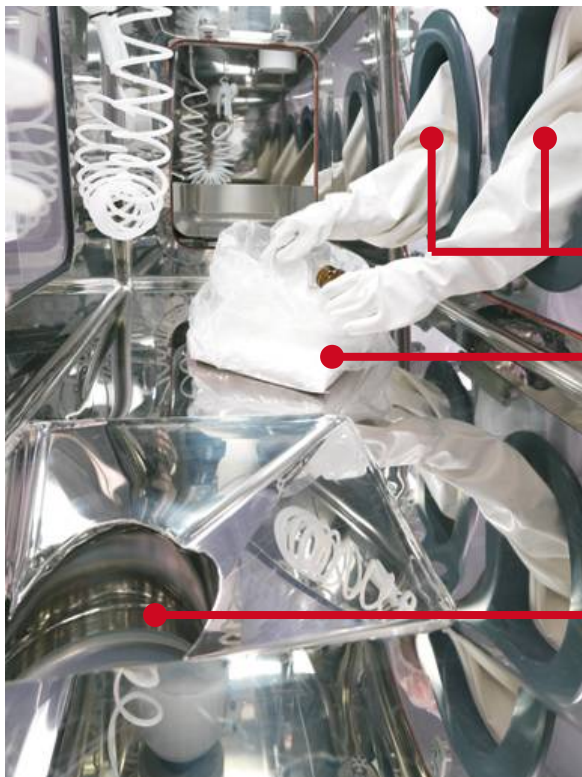




The plastic bag containing the active product is inserted into the PH-Drum which is then emptied inside the isolator by using the glove ports.

PH-Bin

PH-Drum

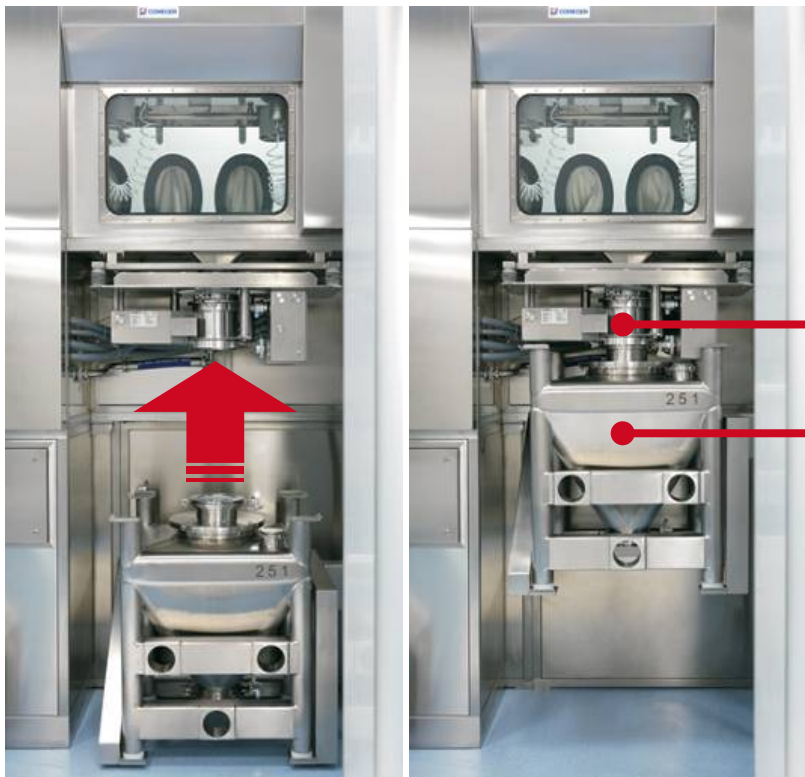


The plastic bag is weighed and opened inside the isolator and the product is then transferred to the PH-Bin.

Glove ports

Plastic bag containing active product

Transfer into the PH-Bin via TwinValve



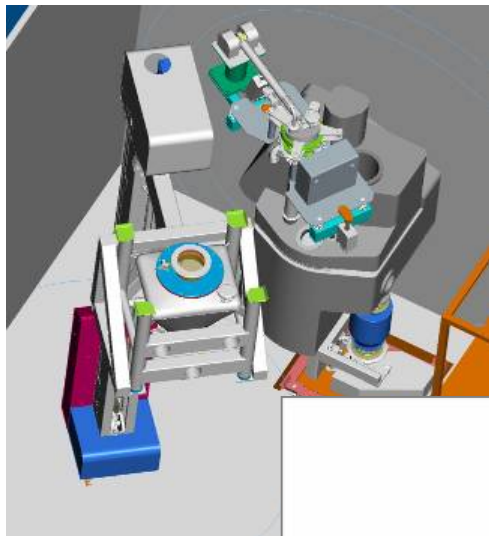
Product transfer to the PH-Bin is carried out by using a high containment valve (TwinValve).

TwinValve

PH-Bin

GRANULATION

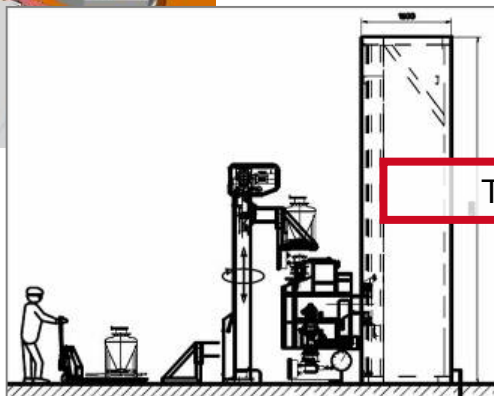
Single-pot technology



TwinValve



TwinValve

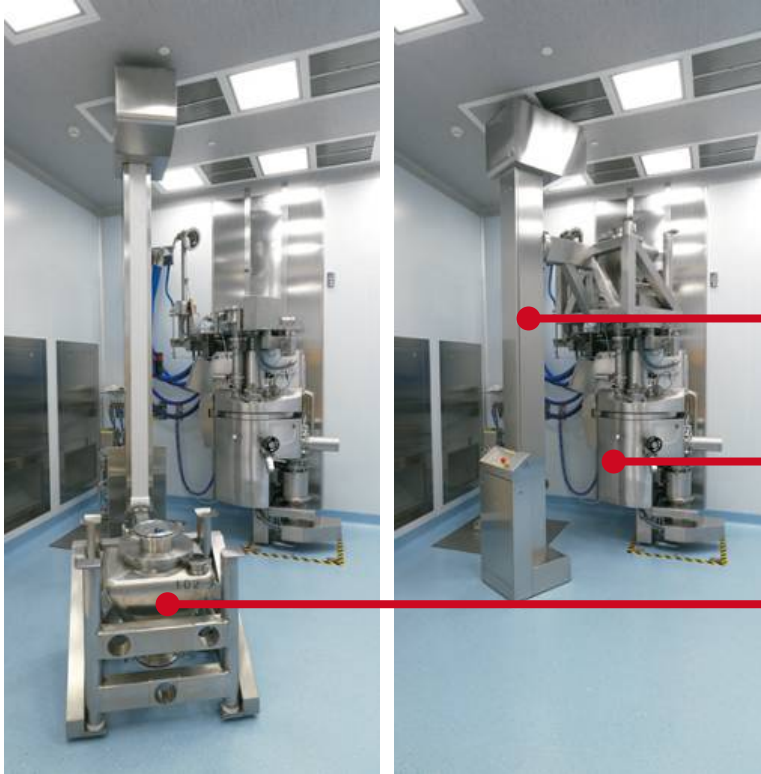


Single-pot processor

- Raw material loading by vacuum or gravity
- Dry mixing
- Wet granulation
- Vacuum drying with Gas Stripping, bowl tilting and MW assisted drying
- Discharge and in-line dry milling

**ALL IN ONE BOWL
TO PROCESS IN
CONTAINMENT**





The PH-Bin is lifted by Hercules lifting column to feed the product into the Roto Cube high shear mixer granulator and vacuum dryer.

Hercules

Roto Cube

PH-Bin

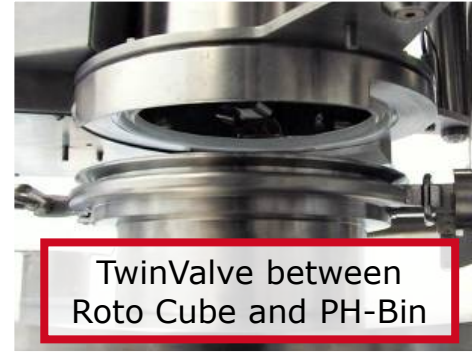


The Roto Cube has a tilting system to shorten the drying times (microwaves) and a lifting system for easy product unloading to the PH-Bin.

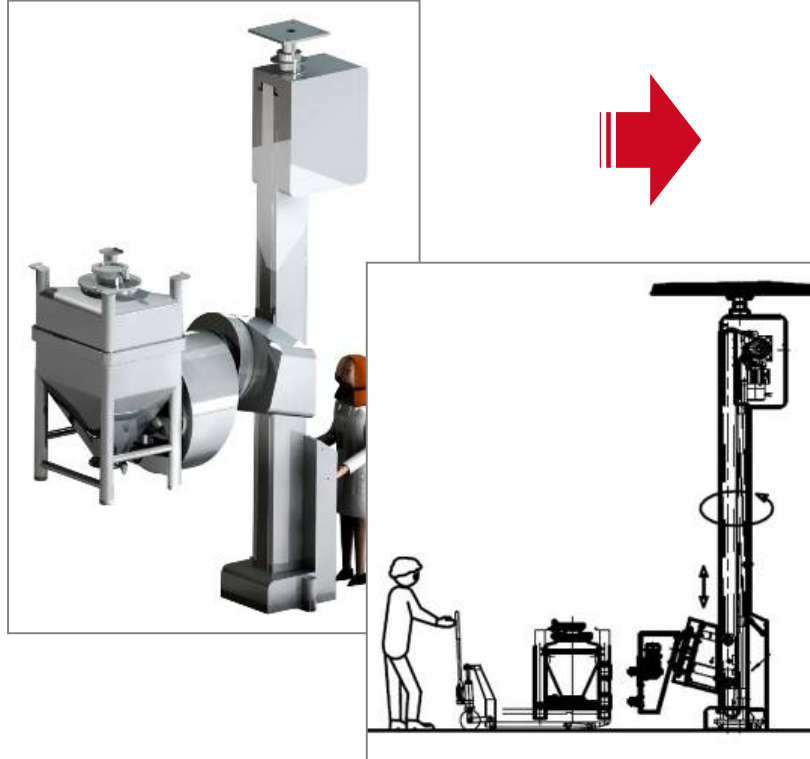
Roto Cube lifted

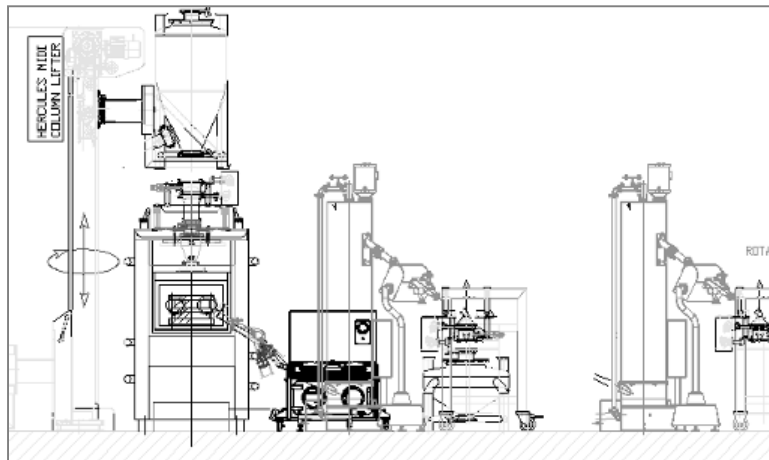


PH-Bin positioned under the Roto Cube



TwinValve between Roto Cube and PH-Bin







The machine is connected to HydroWash washing pump to perform Clean In Place immediately after the production.



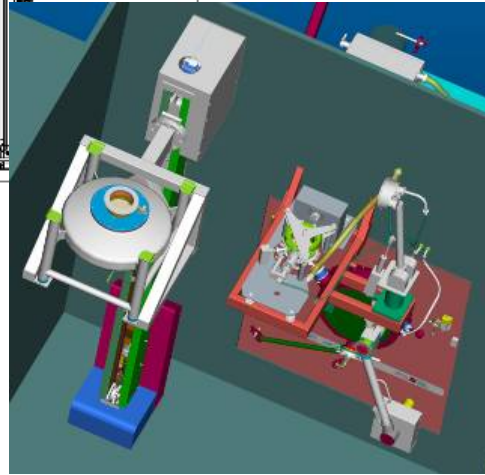
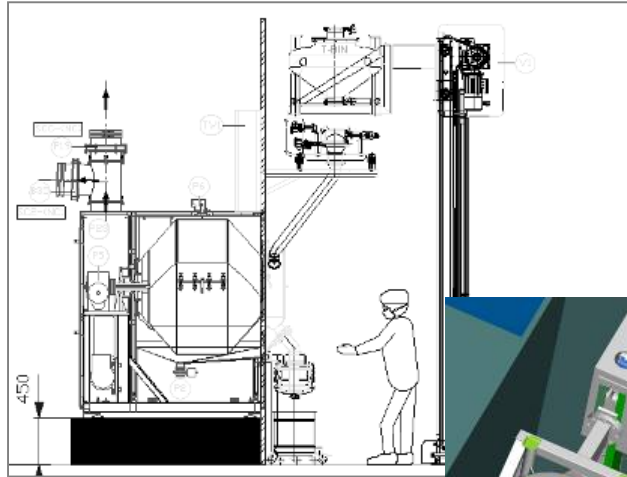
Comprima



IPC unit

The PH-Bin is lifted by Hercules lifting column to feed the product inside the hopper of the Comprima centrifugal die filling tablet press. Transfer is carried out by means of TwinValve.

The Comprima is connected to an isolated IPC unit for tablet check (weight, thickness, hardness) and to a contained deduster with metal check installed at tablet exit.



IMA Perfima Perforated Pan maintains the same shape and mixing baffles positioning of the Pellegrini Pans. This shape has proven over the years to guarantee the best mixing results.

**Patent
pending**





The T-bin is lifted by the Hercules lifting column for tablet loading into the Perfima perforated coating pan, installed through the wall.

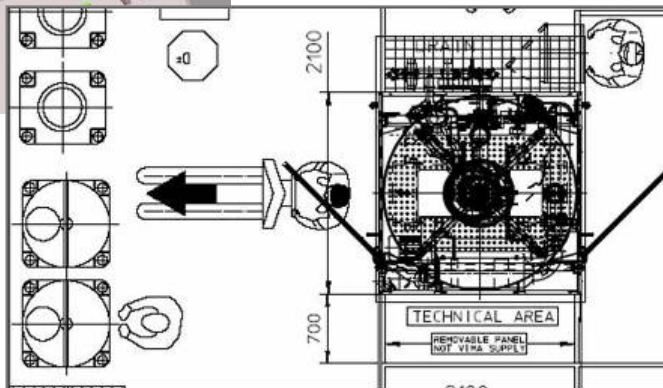
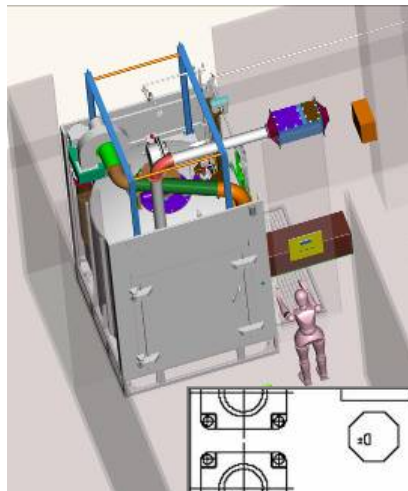


Perfima

Hercules

WASHING

From design to manufacturing



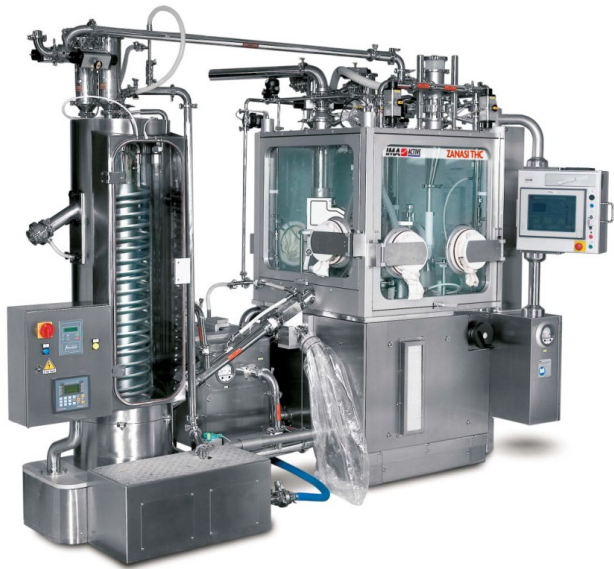


Automatic opening of the upper bin valve

Automatic opening of the lower bin valve



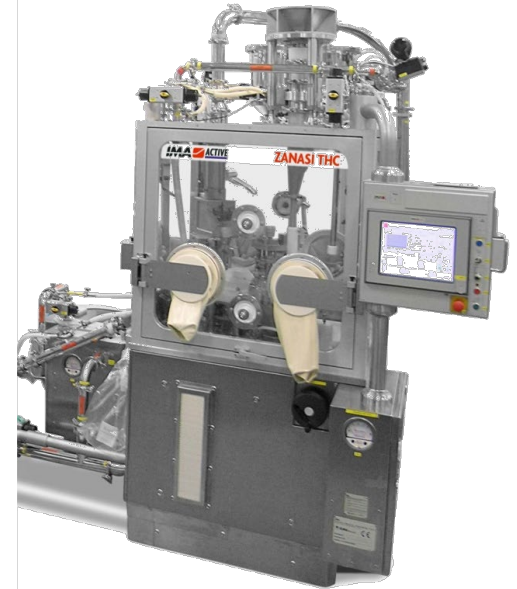
**Different solutions available, according to product category,
customer requirements, machine use.**



Roche-Chugai



Dr. Reddy's



Novartis

25 years of experience in contained production of category III, IV, and V products

- 50 installations for capsule filling
- 69 installations for tableting
- 41 installations for granulation
- 59 installations for dispensing/powder handling
- 42 installations for coating

...and over 250 CIP/WIP Solid Dose running installations

Our customers

Abbott, Akzo Nobel, Astra Zeneca, Biofaktor, BMS, Boehringer Ingelheim, Cardinal Health, Chugai, Cynfa, Doppel, Dr. Reddy's, Farmstandart, Gideon, Grünenthal, GSK, Hemofarm Stada, IDT, IPR, J&J, Lek-Am, Normon, Novartis, Patheon, Pfizer, Roche, Sanofi Aventis, Teva, Warner Chilcott, Wyeth, Zentiva, and many others.

IMA  **ACTIVE**

