PROCESS WORLDWIDE

High Containment

High Containment Processes in the Solid Drugs Production

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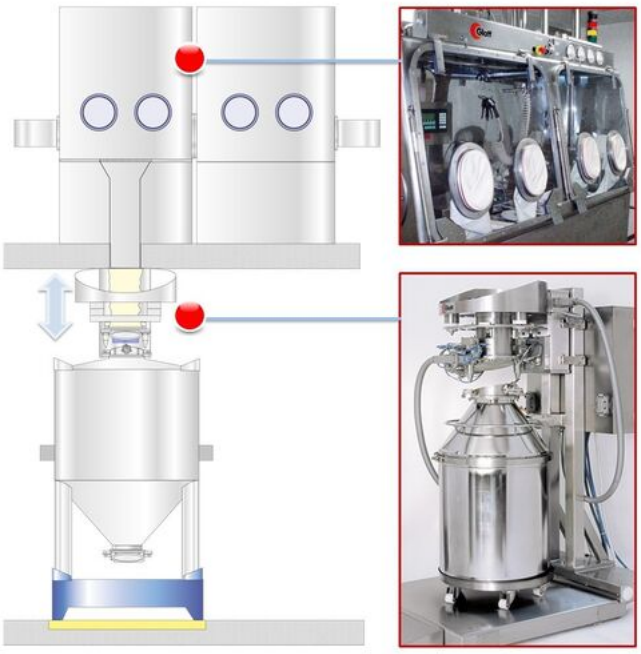
Containment of a solid drugs production is incomplete where the production environment is neglected. Closed process equipment and the production environment need to be considered as an integral solution. There should however be a reasonable balance between protective effects and plant productivity.



Isolator with Glatt containment valve (two-disk valve) system for active ingredient weighing
(Picture: Glatt Ingenieurtechnik)

Apart from personnel and environmental protection, operators of high containment processes put emphasis on product protection. Simultaneously a high productivity of process equipment is required. Problems arise where protection requirements conflict with production capacity and equipment availability. Times for product transfer and cleaning at product change play a decisive role in this conjunction.

The Process Equipment

Project experiences show that the toxic properties of solid drugs are initially often

unknown in multi-product plants. That is why containment components are selected according to the criteria functionality, process safety and extent of automation. Detailed process knowledge is required to develop a safe solution. A more differentiated consideration of the process steps pays off by avoiding oversized protective precautions. Provided that the equipment supplier is involved in the development at an early stage, a modular solution can be achieved that can be used by the plant operator in a flexible manner. Finally, there should be a reasonable balance between protective effects and plant productivity.

Isolators and containment valves have long been used in the high containment area. Equipment suppliers can prove their effectiveness by means of standardised test methods (SMEPAC test). There are alternative technologies for lower containment requirements, for the solid material transfer, for example.

Technical protective precautions can be verified using the multi-stage containment model. Containment stages are not standardised in the solid drugs industry. There are different stage models with individual number of stages and concentrations. Generally, a distinction is made between 5 containment stages or hazard classes.

The Production Environment

Any containment is incomplete where the protective effects end at the supply limit of the process equipment. That is why a system solution also focusses on the design of the production environment. When processing highly active solid materials, material/personnel logistics, conditioning of operating media and room ventilation are relevant, for example.

Material and personnel routs are designed so that regulatory requirements for solid drugs on the protection against contamination and confusion are met. By a vertical product flow, it is possible to transfer solid drugs in an enclosed manner.

There are 5-chamber air-locks with separate entries and exits upstream of the production rooms. Container sizes and measures for surface decontamination determine the air-lock size.

The dimensions of the production rooms depend on the capacity of the production facility and the space required for the protective equipment. When using two-disk containment valves,

sufficient space is required on the charging or discharge port for centring and docking movements of the valve halves.

Areas for the preparation of operating media depend on the consumption rates and required quality parameters. A sufficient supply of water is required for process equipment cleaning to prevent the capacity of cleaning equipment from being restricted. Total loss cleaning is used when processing highly active solid drugs. Lower limits for cleaning residues must be met compared to standard products.

In the high containment area, CIP-capable granulation systems (SC SuperClean Design) are used. Because of their design, metal filters for internal product retention need more cleaning solution than textile filters. The supplier of the granulation equipment knows the consumption from cleaning trials. Results from such trial runs are used in engineering as design aids. In case of lower containment requirements, combinations from WET and WIP cleaning are possible.

Waste water from the cleaning contains solid matters and needs to be collected and decontaminated afterwards. Waste water runs which are only used occasionally may become emission sources for highly active solid materials if they are not dust-tight.

Exhaust air from process equipment contains highly active product dusts and is conveyed via HEPA filter systems. It must be possible to change contaminated filters via a Safe Change filter system and the filters need to be equipped with connections for wetting and cleaning.

The process dedusting equipment often controls the pressure for the containment of the process equipment. Technical areas have to accommodate continuously operating process dedusters with volume flow control and closed dust discharge. Intake air for process dedusting is drawn from the production room via HEPA filters. The correct adjustment of the room pressure, fresh air proportion and the selection of the filter quality, requires a close coordination with the designer of the ventilation and air conditioning systems.

Integral Solution in the Focus

For a complete containment, process equipment and production environment need to be combined to an integral solution. This requires the consideration of technical and regulatory

specifics. Suppliers of process equipment can meet and prove the highest containment requirements. In particular in the high containment area, process competency and project experience are required for an efficient containment solution.

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