

SAFETY GUARANTEED

How a fully integrated isolator and process equipment solution offers high safety, efficient control and cleaning features as well as full compliance in terms of manufacturing regulations.



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The pharmaceutical industry is developing at a faster pace than ever before. New drugs and forms of therapies, persistent market growth, Industry 4.0 and the current Covid-19 pandemic are synonymous to enormous challenges for manufacturing companies.

Due to the high potency of certain active pharmaceutical ingredients (APIs), machine operators have to be protected. At the same time, humans are a high source for product contamination and the key to a successful operation lies in reliably engineered technologies that bring forth equipment capable of offering suitable containment solutions to protect people and products from each other.

In pharmaceutical manufacturing facilities, Isolators are becoming increasingly important as they can achieve the desired level of protection and security.

HIGH CONTAINMENT TRAY DISCHARGE, MILLING, MIXING AND PACK-OFF ISOLATION SYSTEM

For a recent project with the aim to replace parts of an existing thyroid hormone production facility, a new high containment fully integrated isolation system for several interlinked process stages was designed and implemented. The new facility guarantees closed product handling and achieves a very low Occupational Exposure Limit (OEL < 400 ng/m³).

The plant accommodates two distinct process phases starting with the introduction of trays from an adjoining process room

through a transfer door into the conditioning chamber which is equipped with an ergonomic lift system. The conditioning chamber is connected to the rear of the tray offloading and milling chamber.

MILLING AND BLENDING

Equipped with a tray offloading rack and situated at right angles to the conditioning chamber, this chamber collects the product into an integrated discharge hopper able to de-agglomerate the product and connected to feed the cone mill. After the milling, the product is then collected into a suction hopper and automatically transferred to an integrated PTS Batchmixer system where it is homogenised and from which samples from two to 10 grams can be collected.

This mixer is a novel system and offers the advantage of working without rotating tools. The substances are thus mixed or homogenised very gently. With limited circulation speed, particles are not damaged. The system operates under inert conditions and handles hygroscopic, oxygen sensitive or explosive materials. Powders can be transferred automatically from drums, bags or directly from process equipment like a granulator.

It operates on recirculating a single or several products via two circulation lines using a PTS (Powder Transfer System) which is mounted on top of the blender. To ensure a contained closed transfer the PTS Batchmixer is mounted directly above the pack-off isolator chamber discharging the product into a 50 l feeder hopper.

PACK-OFF AND DISCHARGE

The pack-off Isolator consists of two chambers, of which the upper chamber is fitted with an integrated weigh scale mounted on a slide rail system. This allows the scale to be moved to the side when direct bulk discharge into the lower chamber is required. In the upper chamber, the homogenised APIs are filled into bottle containers and stored on a rack before leaving through the

rear wall into the final transfer chamber. The lower chamber permits the direct discharge of APIs into bags using an Ezi-Dock containment valve system. The final transfer chamber serves for the initial empty clean container transfer into the Isolator prior to commencing the batch and for the contained transfer of the filled containers

prior to exiting the chamber through a Rapid Transfer Port continuous liner system providing high containment.

SECOND PROCESS PHASE

The second process phase encompasses reactor charging from bags and previously filled Ezi-Dock bags and the filter dryer discharge, after the product has gone through the pressure filtration, crystallisation, washing and drying processes. To maintain security and high containment, the material is transferred into a filter dryer discharge Isolator before it is milled and transferred to the blending

process. In this second phase, PTS Batchmixer discharge is set to deliver the product in trays again to be reintroduced in the Isolator conditioning chamber for equilibration purposes where humidity is added to the material. Once more the product repasses into the blender for homogenisation and the automated collection of samples as small as from 1g upwards. The product is finally accurately dosed into 1kg containers with a tolerance of +/- 1g.

Reactor charging with PTS allows for oxygen elimination during the charging process

and therefore excludes any explosion risks. PTS is an exceptionally effective and reliable method for transferring and dosing both dry and wet powders. Its unique filtration concept with a flat membrane prevents filter clogging thus avoiding operation failures. The system uses vacuum and pressure to convey materials and can be used in sterile operations as well.

FULLY INTEGRATED CONTROL AND IN-PLACE HYGIENE FEATURES

The plant is controlled by using an integrated PLC system controlling both the isolators and the complete process system. The facility is designed for clean-in-place with integrated fixed and rotating spray nozzles as well as manual hand guns.

Equipment providers to the pharmaceutical manufacturing industry play an important role in supporting manufacturers. Which legal requirements have to be observed and which regulations will be changed in the coming years? How will changing conditions affect the production process and what technologies are required to be immediately and seamlessly integrated into the overall process offering enough flexibility in case of process changes? These are some of the questions to be considered during the preliminary design phase.

Manufacturers should not focus exclusively on individual technologies and machines but rather on complete system integration capabilities and process linkage competences as well as the benefit of receiving advice, in-depth industry knowledge and after-sales services.

