

Customer: CMO (Contract Manufacturing Organisation)

Location: United Kingdom

Project: Retrofit of an API facility for multipurpose high containment operations

Background

The need arose when feedback from a customer programme of toxicity testing resulted in a reduced Occupational Exposure Limit (OEL) for an API manufactured at the plant from 20µg/m³ to 0.5µg/m³. As a result of the API being reclassified as a PB-ECL category 5 product, manufacturing was immediately halted to assess the impact of change. The conclusion to this assessment was that the containment in the current facility needed to be re-engineered as the design was no longer considered suitable for the protection of staff. The impact of cleaning requirements and cross-contamination risk management were also factored into the solutions.

Requirements

The new design requirements mandated the removal of open handling around the facility for which the powder transfer and handling equipment were seen as the key part of the control strategy. The CMO decided that an upgrade, focused on re-engineering, was the most appropriate strategy for change. This approach meant that the new powder handling methods had to fit around and complement the existing process equipment layout and chemistry. It was also important to the CMO that the chosen supplier was responsive and efficient in delivering the solutions on time and on budget. In addition quality was paramount, the technology used had to meet the containment performance target of 0.5µg/m³. It also had to be easy to use and competitively priced.

Ultimately, the plant had to be closed for the minimum time so as not to disrupt the commercial supply chain, meaning that the timeline for this project was tight. During the planning process, several contractors and technologies were considered for the powder handling elements of the project. As a result, the ChargePoint valve was selected. The supplier ChargePoint Technology was able to work closely with the

CMO to provide the solutions to meet specific requirements of the process application. The building of long-term partnerships with the



suppliers was seen by the customer as key to the project's success.

Solution

The underlying requirement from the CMO was to provide a contained method of powder handling and processing. The entry level 'ChargePoint' split valve provides a containment performance of <10µg/m³. To meet the process performance targets an

Extraction Ring system was added to reduce further the risk of airborne exposure, providing an enhanced level of containment performance of <1µg/m³.



The introduction of the ChargePoint system has enabled the removal of open handling at a number of powder transfer points. For reactor charging and dryer vessel off-loading 100mm pressure rated valves were installed, coupled to 25 litre polypropylene ChargeBottle containers. For a seed charging application, 50mm valves, coupled to 1 litre containers were introduced to dispense seed crystals from an isolator and subsequently charge these into a reactor vessel. A key requirement of the reactor charging process was that the valves must be pressure rated to provide a containment seal at 4 bar g. The standard ChargePoint valve is capable of performing at up to 6 bar g.

To meet manual handling requirements, the customer selected polypropylene ChargeBottle containers and POM (polyoxymethylene copolymer) material for the Passive half of the valve. As a result, the operators are handling the minimum weight while docking the valve and transferring containers from process to process. In addition to this, mobile pneumatic ChargeBottle hoists are in use for automated docking and handling of the containers at less accessible points of product transfer.

Contained cleaning

As a multiproduct facility, cleaning is of utmost importance to reduce the risk of cross contamination and operator exposure. The two considerations for cleaning in relation to product



transfers were to clean the valves in place and also clean the contaminated ChargeBottle containers outside of the process.

The ChargePoint WIP Lance device was employed to achieve contained washing of the Active half of the valves coupled to the reactor vessels. This device features sprayballs that penetrate through the open valve and into the process vessel itself providing localised cleaning of the product contact surfaces of the Active valve, the connection to the vessel and into the vessel itself.

Outside of the process, the same lance system was integrated into a remote ChargeBottle Wash Station that allows the container and coupled Passive valve to be opened and cleaned in a contained and safe manner with a pneumatically automated WIP Lance.

The use of a rigid ChargeBottle was imposed by process

requirements for material compatibility and toughness. This choice also has a benefit in terms of cost-effective re-use. However when transferring difficult or poorly flowing materials, this choice could present issues with regards to maximising the yield from each transfer. In this instance, these potential problems were prevented with the introduction of a Vibratory Clamp to the circumference of the ChargeBottle. This pneumatically powered device takes the form of a simple removable clamp that can be utilised on multiple containers.

Contained sampling

One of the more challenging aspects of the project involved containing the removal of samples from a vertical basket centrifuge. ChargePoint engineered a solution that involved much collaboration between CMO and the various contractors. The system installed for this application involved the use of a retractable sample thief housed inside a flexible

bag coupled to the Passive valve. When the valve is docked and opened, the sample thief is placed into the process to take the sample. The thief is then retracted and the valve closed and undocked. The whole operation is completed under contained conditions. The sample is then taken to a safe area to be retrieved from the bag/Passive arrangement. A series of safety interlocks and sensors on the valve ensure that this operation procedure is completed correctly and ultimately safely.

Result

Once the build was completed, surrogate trials and (ongoing) performance monitoring confirmed adequate containment under operational conditions. Overall the project was deemed a huge success as it was completed on time and on budget.

The CMO has benefited greatly from the plant upgrade. The facility can now handle category 5 products and MHRA approval has been given for the multipurpose manufacture of highly active ingredients. This places the customer in good stead for future manufacturing, as the demand for capable multipurpose facilities and potency of pharma ingredients increase.

Table 1: The CMO's process requirement and the solutions provided

Requirement	Solution
High containment	Entry level ChargePoint valve – containment performance <10µg/m ³ . Extraction Ring system used to enhance containment performance to <1µg/m ³ .
Removal of open handling	Reactor charging and dryer vessel offloading – 100mm pressure rated ChargePoint split valves coupled with rigid 25 litre ChargeBottle containers.
Seed charging	Two 50mm ChargePoint valves coupled to a 1litre container were installed to dispense seed crystals from an isolator then charge to a reactor vessel.
Easy manual handling of equipment	Mobile pneumatic ChargeBottle hoist to lift containers and dock the valve. A plastic (POM) material was selected for the Passive valve to reduce valve/bottle weight.
Pressure conditions of reactor (4 bar g)	ChargePoint valve pressure rated characteristic ensures the system holds a containment seal under pressure or vacuum up to 6 bar g.
In process cleaning of valves	The ChargePoint WIP Lance device achieves contained washing of the Active half of the valve. This features penetrating sprayballs that also move through the valve into the process vessel itself.
Smooth transfer of difficult to handle product	Vibratory clamp attached to ChargeBottles to aid product transfer. The clamp is mobile for cost-effective multiple container use.
Ability to clean ChargeBottle containers outside of the process	A specialist ChargeBottle Wash Station was installed for the fully automated and contained washing of the containers after use.
Ability to remove samples from vertical centrifuge in a contained manner	This involved a flexible bag and retractable sample basket thief coupled to the ChargePoint valve for contained sampling. A series of sensors and interlocks on the valve ensure this procedure is completed safely.

