ChargePoint TECHNOLOGY

Customer Case Study

North American CDMO selects ChargePoint Technology for Sterile API Transfer

The Ritedose Corporation are a North American Contract Development and Manufacturing Organisation (CDMO) producing sterile unit dose products.

Ritedose has over 20 years' of experience producing respiratory and ophthalmic products and a 1.7 billion unit capacity facility utilising the latest technology in formulation, Blow Fill Seal and high speed packaging, with a team of experts that manage programs from development through to commercialisation.

Challenge

Ritedose were looking to solve the issue of charging sterile drug substance into a mixing tank. This is a widespread problem in aseptic processing and particularly in formulation.

It was vital that sterile conditions were maintained whilst docking a container to the vessel and then transferring solid drug substance to form a liquid suspension. With a fully dissolved liquid, the product could typically be sterile filtered as it was passed to the filler. Although in this case, the product being passed to the filler was a suspension and so this option was not possible.

This required the process to be performed under aseptic conditions. As such, this would normally mean one of the following upgrades would be required:

- Upgrade the entire room to a grade A cleanroom from a grade C
- Introduce an over-pressurised grade A area around the point of fill and upgrade the whole room to a grade B environment
- Implement a laminar flow system around the point of fill, plus additional control due to the lack of a barrier
- Introduce a RABS system at the point of fill or full vessel and upgrade the room to a grade B environment
- Maintain the grade C cleanroom but introduce isolator technology around the point of fill or full vessel.

Generally, RABs and isolator technology would likely have been favoured in this situation, due to the benefits both technologies can offer. This includes improved sterility assurance, employing the fundamental techniques of separation and decontamination.

"We selected the ChargePoint AseptiSafe® Bio transfer valve because of its increased sterility assurance when handling sensitive ingredients."

Angie Koen, VP of Technical Services, The Ritedose Corporation

However, when considering some of the disadvantages associated with these technologies such as high initial investment, space, ergonomics and ongoing cost and energy consumption, the company decided to look for a solution that was more suited to the task.

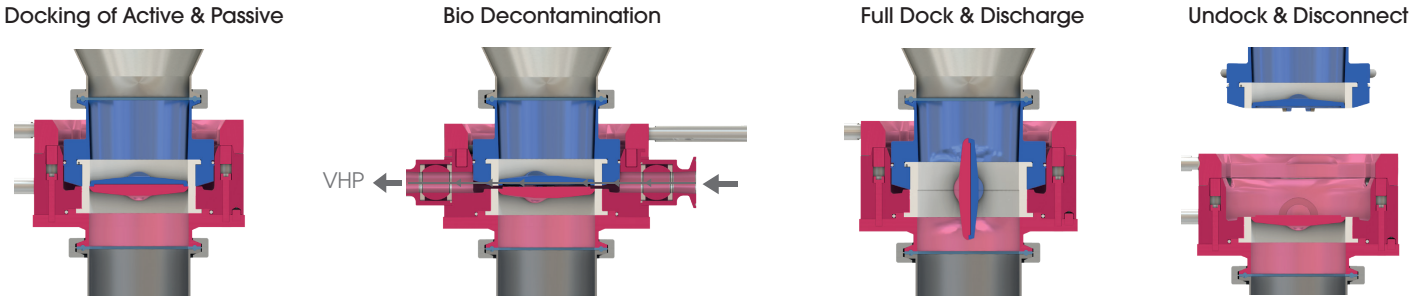
Solution

ChargePoint Technology presented its AseptiSafe Bio Valve as a solution to meet the challenge facing Ritedose due to its unique ability to provide a sealed powder transfer within a small footprint, by being mounted to the inlet port of the vessel.

The ChargePoint AseptiSafe® Bio Valve along with the vessel can be steam sterilised prior to transfer using a Steam in Place cap, unlike other traditional SBVs or other conventional transfer connections.
Once docked in place, the valve creates a sealed chamber between the passive section (transfer container) and the active section (vessel). The sealed chamber is bio decontaminated with vaporised hydrogen peroxide (VHP) when both halves dock together.
This removes any biological contamination to a validated 6-log reduction and leaves the space and mating faces clean and ready to dock together.

Once mated, the disc can be opened. This allows the product to be securely transferred from transfer container to vessel, eliminating the risk of contamination. Performing this transfer within the grade C space provided considerable cost and production benefits.

The ChargePoint AseptiSafe® Bio valve



The Validation Process

The first step in microbiologically validating the process was to generate a validated decontamination cycle for the VHP gassing stage. This consisted of four distinct phases, which the generator will run through to ensure a validated gassing cycle is performed each time.

- Dehumidification phase – The humidity is reduced within the chamber to provide ideal conditions for biological kill.

- Conditioning phase – VHP is introduced into the chamber to build up to levels to achieve good decontamination.
- Decontamination phase – VHP concentration is retained in order to deactivate any microbiological activity within the chamber.
- Aeration – On completion of the biological decontamination, the VHP is removed from the system so that no harmful levels of residue are left. In this instance, 0.4ppm was used as the acceptance level, as the client used a lower residue limit to ensure they had a robust system and no chance of contamination of their product due to gas residue.

The full decontamination cycle can be accomplished in as little as four minutes although 20 minutes is more typical. For this application the process was only being performed once a day. To ensure a robust cycle was produced, additional time was added to each of the critical phases, ensuring that decontamination was confirmed, and gas was aerated from the system. This resulted in a 41-minute full cycle.

Parameter/Phase	Dehumidification	Conditioning	Decontamination	Aeration
Time, hh:mm	00:10	00:00	00:06	00:25
Airflow, SCFM	16	N/A	9	16
Injection rate, g/min	N/A	N/A	4.0	N/A
Humidity, mg/L	2.3	N/A	N/A	N/A

Initial cycles utilised chemical indicators (CIs) to determine H202 distribution. When satisfactory CI results were achieved, biological indicators (BIs) were introduced to the process to confirm the process was successfully achieved. Upon completion of each cycle, all BIs and CIs were collected. The CI strips were then checked for colour change to ensure uniform vapor distribution. The BIs were transferred to a suitable growth media, in this case Spordex culture media and incubated at 55°C to 60°C for seven days. They were observed daily for any microbial growth.

Acceptance criteria for the cycle included:

- All CI strips used in the cycle must have changed colour.
- The positive control BI must demonstrate growth.
- At least one BI from each location must not demonstrate growth.

Once the cycle was developed it was then executed in triplicate to form the performance qualification (PQ) for this element of the process. In order to fully validate the system, the process was challenged with multiple media runs prior to validation. These successful media challenges were then carried forward with three media runs at PQ. The sterile hold was demonstrated at greater than 10 days with product transferred to the vessel and with the bio valve held in the closed interlocked position. The sterile hold period was demonstrated for the passive section (product in transfer container) for 48 hours, which was more than adequate as typically this would be at most half this time.

Outcome

The installation is now operational and in full production. The initial benefits predicted at the outset of the project, such as low capital equipment cost, smaller footprint and ease of installation, have been matched by improved sterility assurance, ease of use for operators, and low maintenance. The system is straightforward to use, easy to install and validate and has improved the CDMO's process.

One learning from this project was at the dispensing stage. At the time of validation, the system installed was a rigid reusable solution where pre-sterilised drug substance was supplied to the client in bags. These bags were opened and then subdivided and dispensed within an aseptic isolator to the pre autoclaved transfer container and bio valve. It would have been beneficial to sterilise the product, container and transfer connection in one step through gamma irradiation, although this was not possible due to the constraints associated with gamma sterilising stainless steel and elastomeric assemblies as one item.

With the release of ChargePoint's single use range, the ChargePoint AseptiSafe® Bio valve will be combined with Single Use Passive (SUP) and ChargeBag® will allow the client to purchase the drug substance, bag (container) and passive in a pre-sterilised, gamma irradiated form which can be docked directly onto the active vessel and discharged.

From the Customer

"It was critical that we chose the right solution for this project to prevent product contamination and expensive product loss. We selected the ChargePoint AseptiSafe® Bio transfer valve because of its increased sterility assurance when handling sensitive ingredients such as our drug substance. We have received considerable support during the project and are benefitting from significant cost reductions and process efficiencies."

Angie Koen, VP of Technical Services, The Ritedose Corporation.