MATCON®

www.matconibc.com

Case Study

Containment down to 1 µg/m^3 with full CIP

AstraZeneca

IDEX

AstraZeneca GmbH, Plankstadt

Containment down to 1 µg/m^3 with full CIP

AstraZeneca is one of the worlds leading pharmaceutical companies with a strong portfolio of drugs for treatment of cancer, cardiovascular, gastrointestinal, infection, neuroscience and respiratory conditions.

With over 30 manufacturing sites in 20 countries the Company is very focussed on effective use of its manufacturing assets. Central to this is the flexibility to respond to fluctuations in demand and minimising production lead times while at the same time ensuring regulatory compliance and the highest standards of health and safety in handling complex medicines.

Since it started manufacturing in Sept. 2003 the tablet production facility at Plankstadt, Germany has been a key part of AstraZeneca's future growth strategy to ensure unconstrained supply of some of the Company's most successful products, such as Casodex and Crestor. In order to safely manufacture a wide range of potent drugs the facility incorporates leading edge technology to provide an enhanced capability for process containment.

IBC High Containment Discharge Station with CIP

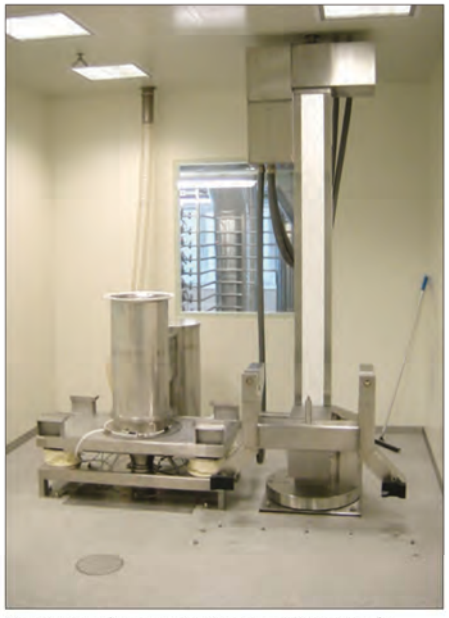
After extensive evaluation and testing, AstraZeneca selected the Matcon "Cone Valve" Intermediate Bulk Container system to handle the storage, movement and transfer of production batches across each step in the manufacturing process.

The manufacturing process contains the following steps:-

- Dispensing into IBCs using high containment barrier isolation technology;
- Granulation and Fluid Bed Drying - IBCs provide contained transfer into process;
- Milling - IBCs provide controlled feed to milling process;
- IBC Blending, incorporating NIR PAT for blend uniformity;
- Tablet Compression - IBCs provide mass-flow into tablet presses;
- Tablet Coating and Packaging - tablets are moved in bulk by IBCs and fed to process;

Key criteria in the selection of the Matcon Cone Valve system were:-

- Effective, controlled discharge from IBCs of all powders currently used in production or likely to be used in the future;
- Ability to completely and automatically clean in place (CIP) all equipment, without dismantling - this is vital in a multi-purpose facility;
- Ability to provide necessary levels of "containment" (see following notes);
- Avoidance of segregation;

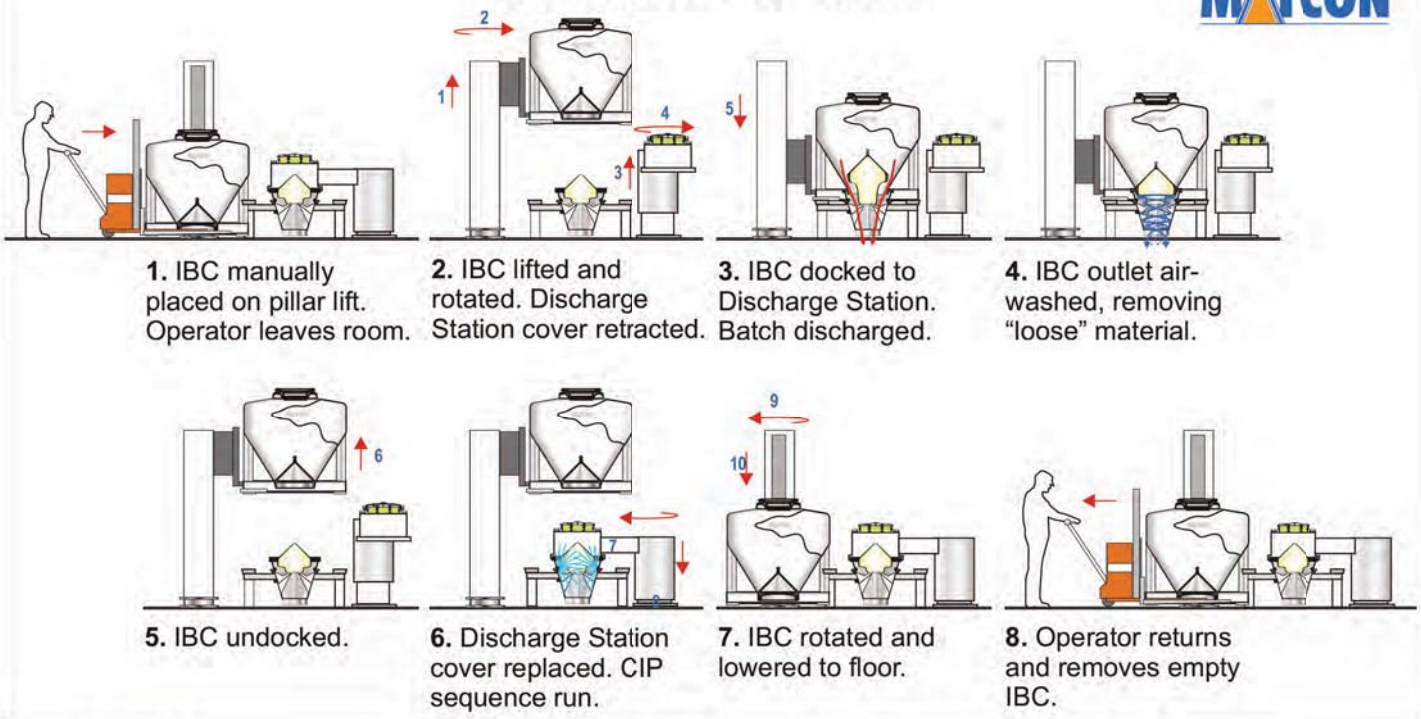


IBC Discharge Station in CIP Mode

Wall-mounted IBC "In-Bin" Blender

FEATURED STORY

PRINCIPLES OF OPERATION



1. IBC manually placed on pillar lift. Operator leaves room.

2. IBC lifted and rotated. Discharge Station cover retracted.

3. IBC docked to Discharge Station. Batch discharged.

4. IBC outlet air-washed, removing "loose" material.

5. IBC undocked.

6. Discharge Station cover replaced. CIP sequence run.

7. IBC rotated and lowered to floor.

8. Operator returns and removes empty IBC.

Containment

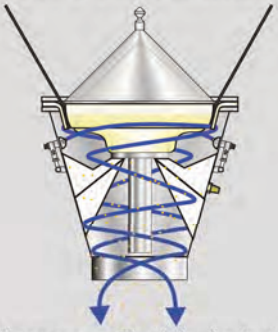
The Matcon Cone Valve was selected for effective discharge and containment at the outlet of IBCs. AstraZeneca selected a "Split Butterfly Valve" (SBV) as the means of containment at the inlet of the IBC. Matcon incorporated the SBV into the design of the IBCs and worked with the equipment supplier to ensure all interfaces were correctly designed.

The complete facility and all manufacturing processes were designed to achieve containment in the range of **1 - 10 µg/m³** (TWA / 8 hrs) and thus avoid the need for costly and cumbersome operator PPE. This was a key performance requirement of the project but was not so easy to achieve in practice. The early production runs failed to achieve this target due to a variety of equipment, control, interface and training issues.

AstraZeneca and Matcon were totally committed to realise the high standards specified and worked closely together to identify and overcome the various obstacles. Their efforts have been fully rewarded as the facility is now performing easily and robustly within containment specifications - in fact, the plant is now achieving **containment down to 1 µg/m³ and with full CIP**. It is one of the cleanest solid dosage plants anywhere in the world and a credit to the management and operators who run it.

Dr Johann Müller, production manager says *"Although it required a lot of effort by AstraZeneca and Matcon we are delighted with the excellent containment results and reliability we now achieve from the Matcon IBC system."*

HIGH CONTAINMENT



The Pharmaceutical Industry has a requirement to provide containment using 'closed' transfers when feeding solids to and from process. This is for both cGMP reasons to avoid cross-contamination as well as Health and Safety reasons to avoid operator exposure.

Matcon offer Cone Valve IBC systems for charging solids to process and Containment Transfer Systems for discharging solids from process into IBCs. Both operate on the Alpha/Beta principle of 'make before break' to achieve direct containment connections and disconnections without the use of glove box isolators or manual intervention.

Matcon Containment Solutions use direct connections to achieve OELs down to 10µg/m³. These solutions, when combined with local ventilation and/or secondary extraction, can further reduce OELs to just 1µg/m³. These levels are achievable using simple, robust solutions, built to normal fabrication tolerances with no requirement for high accuracy machining or precise mechanical guidance systems. These solutions also include integral wash nozzles for fully validatable CIP wash systems and Nitrogen intertion to "self-balance" displaced gas and remove the need for venting.

Matcon Test Centres provide full-scale containment monitoring of the discharging and filling of IBCs together with a "Clean Room" environment to provide background levels of <3µg/m³. These facilities have been used by major pharmaceutical organizations to conduct independent trials and have ultimately led to Matcon Technology being incorporated into a number of "state of the art" pharmaceutical facilities around the world.