

Compact containment strategy

Plants that need to contain potent substances can now do so in a space conscious manner. Torsten Belger of Powder Systems Ltd explains.

In recent years, new drug developments have a recognised trend of increased potency which has resulted in the need to implement dramatic changes to plant design and operating procedures.

- 10 years ago, new plant design required 100 microgramme/m³ operator exposure level.
- 5 years ago, new plant design required 10 microgramme/m³ operator exposure level.
- Today, new plant design requires 1 microgramme/m³ operator exposure levels and some facilities handling drugs such as hormones have operator exposure levels of below 30 nanogrammes/m³.

In the past there are several layouts which have been used for plant design and these have tended to be quite spacious. Some designs involving separate rooms to contain compounds (and to help prevent cross contamination) with operators wearing airsuits. Whilst achieving good operator protection, they can lead to gross contamination of the working area, uncomfortable working conditions and the potential for product transfer from the contaminated suit.

New facility designs should attempt to ensure very compact arrangements and with efficient containment, the need for airsuits and individual rooms can be removed.

One way of achieving this compactness is to use split butterfly valve technology such as PSL's ChargePoint. There are a variety of split butterfly valves available on the market, all claiming to achieve between 1 - 25 micrograms/cu m. However, what these various designs actually achieve will be very much depends on:

- frequency of operations/transfers
- quantity of solids transferred
- size of split butterfly valve units used
- properties of the solids handled ie particle size, cohesiveness, etc.

Regular maintenance is also key considera-

tion in getting the best out of the containment system, including the split butterfly valve.

To obtain guaranteed containment results for any particular application, tests should be carried out, simulating the actual process conditions as closely as possible. A figure of around 10 micrograms/cu m is generally deemed to be achievable for most SB valves when used in suitable applications.

How do Split Butterfly Valves actually work?

Figure 1 shows the sequence of operation of a typical split butterfly valve. The valve consists of two parts, each essentially presenting a standard butterfly valve. Once the two parts are brought together, the discs join forming a 'single disc', sealing any surfaces which may be exposed to the compound during transfer. The two discs then operate as one disc, opening to permit compound transfer from one container to another eg during reactor charging which can consist of anything ranging from a small bottle to a large IBC or FIBC. Once transfer is completed the unit is closed and the two discs separated again. One part of the valve, *passive part*, then seals the container and the other part, *active part*, then seals the receiving vessel. None of the surfaces now exposed to atmosphere were exposed to the compound during transfer.

The ChargePoint Process.

Figure 2 shows a possible layout for a fully contained small scale pharmaceutical synthesis process, solely using split butterfly valve technology.

In step 1, raw materials are received in the plant from a variety of containers - such as bags, bottles, boxes etc. These raw materials have to be re-dispensed into containers of a suitable kind that attaches to the split butterfly valve passive unit. Normally this would take place within a down flow booth, glovebox or other type of location, appropriate to the overall containment requirements associated with the compound.

In step 2, these containers, already sealed with the split butterfly valve passive unit, are now moved to the processing area where they are docked to a split butterfly valve active unit connected to the first stage process reactor (see step 3 figure 2). Following synthesis, crystallisation, etc, the solids are normally separated from the mother liquors, this may take place

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within a filter dryer processing unit. After the required number of filtration and drying steps within the filter dryer, the solids are required to be discharged from the unit for further processing, this would be contained using the SBV on the solids discharge outlet of the filter dryer. Step 4 depicts an arrangement where the containment process is further enhanced by utilising a combined 'heel removal/discharge' glove box in conjunction with the SBV.

Most pharmaceutical processes require more than one synthesis step and solids have to be re-charged to reactors for further processing. In step 5, solids are transferred back from the filter dryer to step 3. The same size and type of container and SWV can be used, as for the original charging process, providing a significant simplification of the solids handling requirements within the plant.

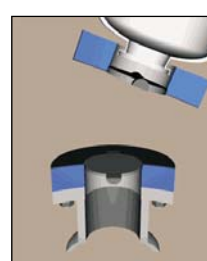
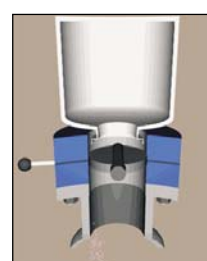
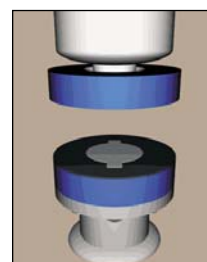
After the final processing step, solids are now discharged from the filter dryer (step 6) for further processing, ie particle size reduction, screening, dispensing, etc. Of course, the containment requirements for the compound do not stop here. The active contents of the compound has not been altered at this stage and in step 7, the SBV and the same type of charging container are again used to introduce the 'final' compound to the further processing unit. The exam-

ple here, shows a PSL MillBox, a milling system fully contained by an inerted glovebox. This is equipped with SBV active units on its inlet and outlet.

The chemical/pharmaceutical process investigated in this paper normally stops here, but the containment requirements for further handling and processing of the compound do not. In step 8, the compound is transferred in the SBV charging container to the secondary processing (tableting/formulation) facility. There SBV may again be employed to contain further solids handling steps, like charging to blenders, mixers, micronisers, etc.

SBV technology is a very useful tool in the design of a containment solution, but it is not the answer to every containment problem and application must be carefully assessed prior to selecting the most appropriate containment strategy. SBVs are a 'primary containment device', which means that they are used for containing any dust at the point at which it is generated. In conjunction with other 'secondary containment devices', SBVs can achieve the most extreme containment levels demanded by today's pharmaceutical compounds.

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1 Raw materials are subdivided into ChargePoint containers in a central dispensary

2 ChargePoint containers are transferred to process vessels

3 Actives and intermediates are charged to process vessels. For cohesive products, bags are available

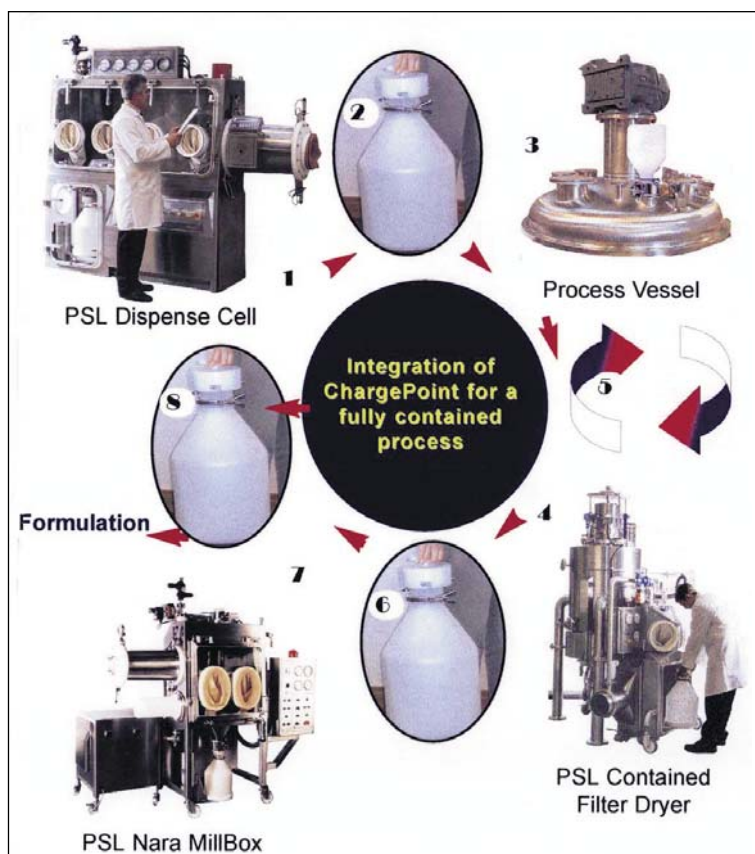
4 Intermediate products are discharged from final process step (eg filter dryer) into ChargePoint containers.

5 Steps 3 & 4 are repeated to complete the number of process steps required

6 Final product is moved to further processing (eg milling or sieving) using the ChargePoint containers.

7 Final processing

8 Final product is sent to formulation in closed ChargePoint containers ready to be received by ChargePoints in the formulation plant



PSL ChargePoint contained transfer. The sequence shows docking, the situation before product transfer, product transfer, the situation after product transfer and undocking.