

## Flexible Pharma Containment Solutions

Split valve technology has been the mainstay of pharmaceutical containment for many years; the current trend, however, is towards flexible, disposable containment solutions, and it is here that the most exciting innovations are being developed.

**By Martin Koch and Joachim Stoye at GEA Niro GmbH, and Dr Harald Stahl at Niro Pharma Systems**



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**The need for contained handling and processing of pharmaceuticals started to increase significantly about 15 years ago; the reasons for this were an increased focus on health and safety, and also the development of more highly potent active pharmaceutical ingredients (HPAPIs). The response from pharmaceutical equipment suppliers resulted in market improvements in the containment levels achievable, using both established solid-handling equipment and new innovative techniques.**

At the beginning of this development, attention was focused on the revolutionary split valve technology, which is now established as a standard for contained material handling and is offered by a number of suppliers. The current trend, however, is heading strongly towards flexible, disposable containment solutions, first, for cost reasons – no initial investment, no cleaning, safety (no cross contamination) – and second, because of its high flexibility. This market segment is still at the beginning of its development, and it is here where the most exciting innovations are starting to be launched onto the market.

This article presents a brief overview of the techniques available on the market, and concludes with an analysis

of the prospects for innovative flexible, disposable containment solutions.

### SPLIT VALVE TECHNOLOGY

Up until the early 1990s, it was usual practice to bring raw materials and intermediate products in an open state into a plant. Isolator technology was only brought into play for the protection of employees, or for the total protection of the operator in exceptional circumstances, such as when processing especially problematic substances. At this time, it was also common for various in-plant transfers to take place openly; for example, the movement of wet product from the reactor to the centrifuge and then on to the dryer, the partial milling of the product to the seeding of the crystallisation process, or the emptying of the dryer with downstream filling into containers, all took place openly. Employees were protected by ventilation measures or by personal, protective clothing. The pollution of the environment – with the risk of cross-contamination when changing over to the next product – could only be conditionally prevented by these measures.

This situation changed fundamentally with the development and introduction of the first split valve



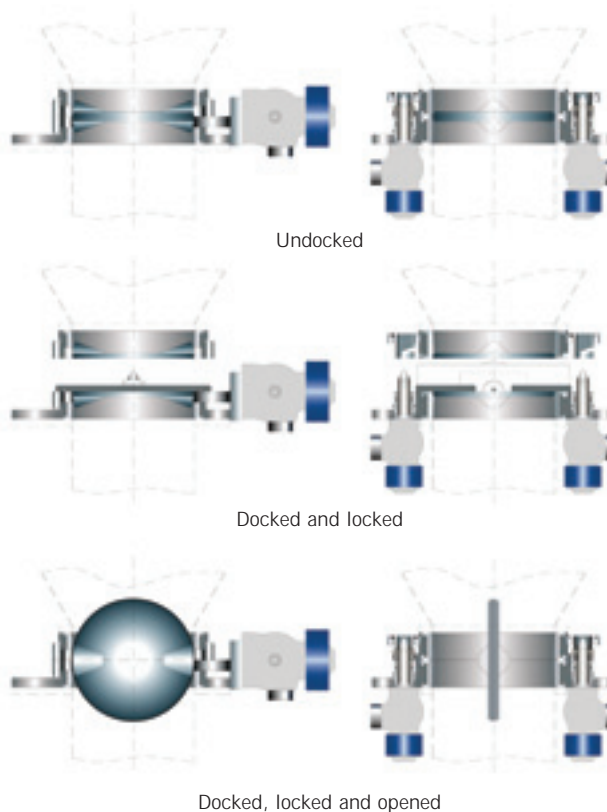
systems by various working groups (including the pharmaceutical industry and suppliers) in Europe and the US. An example of such a split valve system is shown in Figure 1. In the beginning, this development was driven by companies such as Buck Valve, Glatt and PSL. Further developments were made, but did not gain full market acceptance until companies such as Bohle and Andocksysteme also started to offer this technology.

A split valve system is made up of an active and a passive split valve; these seal two different container systems independently of one another in a dust-proof manner. The active valve is usually to be found on the production unit; 'active' means that this split valve is actuated either manually or automatically. The passive part, without actuation, is usually mounted onto mobile containers by various fixing methods. The docking procedure brings the active and passive valves together, whereby they lock on to each other. The outer surfaces of the valves – which could potentially be contaminated by the environment – lie hermetically sealed together and are also sealed on the product side. The discharging and filling procedures are brought about by the rotations of both valve halves. In this way, there is no connection between the outer and inner surfaces of the valves at any point during the transfer process, and so the transfer process is virtually contamination-free.

### FLEXIBLE SOLUTIONS

Split valve technology has established itself in the industry as a standard for contained material-handling when working with rigid containers. However, the demands of the pharmaceutical industry have changed yet again. In addition to containment – which is still considered to be the most important aspect – the equipment has to fulfil more and more requirements, such as low investment and production costs, full prevention of cross contamination, fast project realisation, full yield discharge capability, and so on. All these additional requirements should read strongly in one direction: flexible containment solutions.

Disposable flexible bag and in-liner solutions have been developed to meet these demands. Such systems have already been accepted by the pharmaceutical industry and their performances have been proven in many different applications. Companies such as ILC Dover, ATMI Life Science, Stedim, Hyclone, Wave Biotech, Hecht Anlagenbau, VISVAL AG and many others are providing the industry with continuous liners, powder handling bags and flexible process equipment. However, the most critical point in keeping a process closed – the



interface between the bag and the process – was not solved satisfactorily. Either rigid split valves are used in combination with bags, or heat-sealing solutions are applied, which only allow for material flow in one direction under contained conditions.

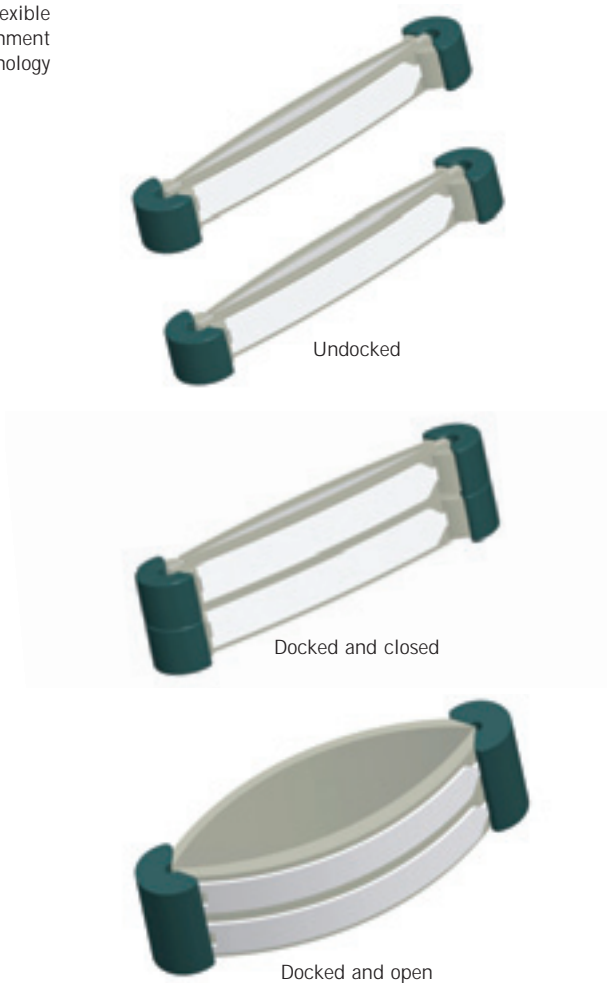
### A NOVEL APPROACH

A new technology (Hicoflex, Niro Pharma Systems) is based on the time-tested functional principle of split valve technology but is combined with the simple locking principle of a snap ring. An example of this principle can be found in the simple spectacle case; here, just like with the split valve technology, two complementary half-locks are docked onto each other. This means that mutual opening and closing can take place just as if it were a one-piece locking unit (see Figure 2, page 80). This process ensures that the medium to be transferred is protected from the environment during the transfer process. The two half-locks close after the transfer process and can be separated from each other without any contamination.

From the very beginning, attention was paid to the fact that plastic and GFK components were utilised exclusively during the Hicoflex technology development. These could be comparatively economically manufactured and disposed of thereafter in an

Figure 1:  
The split  
valve system

**Figure 2:** Flexible high containment technology



environmentally suitable manner. So for the first time a docking system has been developed that meets the stringent containment requirements (Short Term Time Weighted Average, STTWA, 1-10mcg/m<sup>3</sup>), and at the same time provides a disposable system for flexible transport containers and/or process containers.

The technology differs from existing flexible containment solutions (continuous liners, sacks with Triclamps, and so on) in one fundamental respect: it enables the docking on and off of flexible transport or process containers in a more or less repeatable manner, whilst complying with stringent containment requirements. The optimal unification of the characteristics of stainless steel and plastic brings a number of fundamental advantages in application of the technology. These can be summarised as: cost reduction, safety and flexibility.

**COST REDUCTION**

- ◆ Cleaning and cleaning validation are no longer necessary when using the technology as a

disposable system. Obviously, the components can also be used as a reusable system.

- ◆ The components are inexpensive and can be procured as required. The opening tools or devices clearly represent less of a capital outlay than comparable containment solutions made of stainless steel.
- ◆ The flexible transport and process containers allow the operator on site to support a very simple discharge procedure, ensuring total discharge.
- ◆ No intensive technical support service is required due to the simplicity of the system and the disposable nature of the components.

**SAFETY ASPECTS**

- ◆ There is no risk of cross contamination, as the components are either disposed of at once or only used during the same charge. The possibility of contact with other substances respectively during another charge is, therefore, completely excluded.
- ◆ The performance of the technology has been proven repeatedly with different readings based on the SMEPAC (Standardised Measurement of Equipment Particulate Airborne Concentration) Guidelines for stringent containment requirement with STTWAs of 1-10mcg/m<sup>3</sup>.

**FLEXIBILITY**

- ◆ The technology has a wide spectrum of standard solutions which enables its use in nearly every process step – from the initial weighing to the final packing.
- ◆ The re-fitting or the initial outfitting is possible at any time, since most of the components are in stock.
- ◆ The simple construction of the components enables easy handling without the risk of faulty operation.
- ◆ The use of transparent transport and process containers aids visual control – ensuring that discharge has taken place completely.

Apart from the original application areas of material transfer of potent substances in powder or granulate form, there are a variety of other application possibilities. One example is sample-taking, within the context of material identification in the stores area, as well as for product control within or between process steps. A special lance allows for the non-intrusive taking of samples from stock sacks or from a process unit via a relevant interface. Afterwards the sample can be



**Figure 3:** Hicoflex discharge with pneumatic opening tool

transported in a closed sample bag to any location where it can then be taken out and analysed when required.

The technology can be adapted relatively simply to individual requirements, meaning that it can offer a broad range of implementation and application possibilities, via one standard interface with flexible plastic containers.

## CONCLUSION

After 15 years of practical application, split valve technology developed into an industry standard for the contained transfer of potent materials. The technology did not always offer the optimal solution, however, leading to the development of a flexible and disposable containment interface. This can not only replace conventional split valve technology for certain applications, but is also able to satisfy demands that cannot be fulfilled by the use of rigid technology. Industrial use of the technology has only just started, so further developments can be expected in the future, opening up even broader fields of application.

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### *Note*

*Hicoflex® is a trademark of GEA Niro GmbH,  
part of the Niro Pharma Systems group.*