Containment strategies and smart monitoring in solid oral dosage production

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Containment is critical in both active pharmaceutical ingredient (API) manufacturing and solid oral dosage form (SODF) production involving highly potent compounds. This article examines how containment valves and wireless monitoring can improve worker safety and manufacturing efficiency.

The global SODF market is expected to achieve a compound annual growth rate (CAGR) of 6.5 percent between 2017 and 2027, reaching $926.3 billion by the end of the forecast period [1]. In addition, rising incidences of hormonal imbalance disorders among the growing geriatric population is expected to lead to continued growth in the global hormone replacement therapy market. This market was valued at $15.1 billion in 2014 and is expected to grow at a CAGR of 8.2 percent over the next seven years [2].
Effective engineering controls are critical during material transfer. Worker safety is the primary focus, but it’s also essential to contain the material in a manner that causes minimal disruption to the manufacturing process. Hours lost in production can delay a product’s release and result in lost revenue, so it’s vital to choose production-line technologies and components that fulfill both safety and production needs.

Containment during production

SODF production is a complex, multi-stage process that involves transferring materials from one process to the next—such as from dispensing to granulation to blending to tablet compression to coating. Transferring powder in a contained manner that safeguards workers and complies with regulations can be a challenge [5].

The key difficulty is that powder transfer involves moving material from one closed system into a separate closed system that may or may not be compatible. It’s important to ensure that the design specifications of the transfer equipment meet accessibility, batch-size, and containment-performance requirements and that the

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Photo 1: A split butterfly valve (SBV) consists of a passive unit attached to a mobile container and an active unit attached to the processing equipment. When joined, the two units form a valve that enables contained and efficient powder transfer.

Photo 2: The passive SBV unit on the charge bottle shown here includes a GMP passive cover to prevent contamination and damage during storage and transport.
Ensuring that all containment technologies are functioning correctly is vital for keeping workers safe, maintaining compliance with regulations, and making production as efficient as possible. A number of approaches are available to monitor containment system performance, from modeling and manual checking to automated assessment via a fully integrated system [6].

Manual assessment relies on the judgment of skilled operators and their ability to inspect each containment system on the production line in question. This approach is very labor intensive and requires accurate data recording and interpretation.

SMEPAC is only intended to be used as a guide, as it demonstrates how a containment device performs in a laboratory environment. SMEPAC testing in an environment as close as possible to the real-world manufacturing facility is the only way manufacturers can fully understand the device performance outside of the laboratory. Despite these drawbacks, it's widely accepted that using SMEPAC ensures good practice when specifying the containment performance of transfer equipment.

Interpreting containment performance test results

The type of surrogate, or sample material, you use for performance testing has a major influence on the test results. SMEPAC suggests a variety of surrogate powders, including lactose, mannitol, naproxen, and riboflavin. Each of these has varying particle sizes and bulk densities, which can influence the material’s detection level and airborne characteristics, affecting the test results.

Containment equipment manufacturers commonly use a micronized lactose surrogate, but they may also use various other grades of lactose or alternatives, such as paracetamol, that may have a larger particle size distribution than micronized lactose.

The equipment end user should ensure that the surrogate in the laboratory test is comparable to the HPAPI in the product being manufactured. If the two are not comparable, the differences must be factored into the interpretation of the test results. More importantly, when comparing multiple containment solutions of the same technology, the end user should consider this same factor in the final result comparisons.

Also, it’s possible for test equipment with the same specification to show differing results in the same test due to differences in sampling methods, and different sampling devices used under the same test conditions, and even using the same surrogate, can provide significant variability in the sample result. Understanding how each containment solution has been tested and how the performance results were obtained can also help manufacturers interpret test results.

SMEPAC guidance states that there must be a sufficient quantity of surrogate being transferred through the device to ensure maximum coverage of product contact surfaces. This guidance is defined by a suggested weight range, which means that testing devices with a variation of powder mass will result in inconsistent results.

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Photo 3: Wireless monitoring technology provides real-time reporting and data monitoring at a lower cost than manual monitoring and easily accommodates changes to manufacturing setups.
Effective maintenance and operational performance monitoring are also important parts of any containment strategy. Monitoring the integrity of a containment valve using wireless technology enables maintenance, health and safety, and compliance teams to analyze performance data and make informed decisions about how to proactively manage their maintenance programs.

**Monitoring the integrity of a containment valve using wireless technology enables maintenance, health and safety, and compliance teams to analyze performance data and make informed decisions about how to proactively manage their maintenance programs.**

The modular nature of wireless monitoring technologies means that they can easily accommodate changes to manufacturing setups. Wireless monitoring also provides real-time reporting and data monitoring at a lower cost than manual monitoring.

**Operator intervention and potential exposure**

During solid dose production with HPAPIs, it's important to ensure full operator safety and minimize levels of environmental contamination. Countering the risks associated with human intervention is difficult, and containment mustn't affect equipment operation or productivity. Appropriate validation testing must accurately reflect the operator intervention. However, some aspects of performance can be reliant on operator technique, which further increases variability.

Decontamination and cleaning of process equipment, from milling to tablet compression, must also be carried out in a contained manner. SBVs can be fitted with integrated washing devices to maintain containment during the washing phase.

**Preventative maintenance**

Frequent monitoring and regular preventative maintenance help to ensure reliable operation of containment equipment. Manufacturers can minimize risk by immediately rectifying any damage that occurs during operation.

Wireless technology enables manufacturers to maximize up-time by maintaining product integrity. It increases operator safety and ensures optimal performance and productivity. The real-time feedback provided by wireless monitoring allows companies to proactively manage equipment maintenance, reducing unnecessary downtime.

**Disposable technology**

Many companies in the pharmaceutical industry are increasingly adopting disposable technologies, including SBVs, as a way to reduce costs by minimizing the handling of contaminated items as well as washing and cleaning activities. Disposable SBVs are an economical alternative to traditional containment valves and are increasingly being used in SODF manufacturing, but their performance must be equal to their reusable equivalent to avoid sacrificing the health and safety of workers.

**Conclusion**

Achieving containment in manufacturing processes handling HPAPIs can be challenging, but it is critical for both worker safety and regulatory compliance. Integrating disparate processing technologies from different suppliers into a single, contained production line is a highly complex task. Containment valves create common interfaces between the different technologies, providing a cost-efficient and flexible means of ensuring containment. In addition, wireless monitoring offers manufacturers an automatic and reliable risk control method, ensuring that the valves perform as they should and that workers handling potentially hazardous APIs are safe.

**References**

2. [www.grandviewresearch.com/industry-analysis/hormone-replacement-therapy-market](http://www.grandviewresearch.com/industry-analysis/hormone-replacement-therapy-market).

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