

pneumatic conveying

CONTAINED VACUUM TRANSFER OF HIGHLY
POTENT POWDERS

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When pneumatically transferring highly potent active pharmaceutical ingredients, containment is critical. This article discusses containment standards for highly potent materials, describes how modern vacuum conveying systems can help meet those standards, and provides two real-world examples of custom-designed vacuum conveying systems for high-potency applications.

Pharmaceutical manufacturers are increasingly developing new medicines that use highly potent active pharmaceutical ingredients (HPAPIs) and face a growing need for containment solutions that enable closed and dust-free transfer of these materials to protect employees, the material, and the production environment. In the past, employees were often equipped with only a full-body protection suit and generally worked in an open process. In this kind of work environment, the risk of contamination was very

high. Today, depending on the application, production is either integrated into an isolator or executed within a sealed and closed process to ensure the required dust-free and safe work environment. Such processes increasingly rely on pneumatic vacuum conveying systems to contain the highly potent powders during transfer.

Containment requirements for highly potent materials

The containment requirements for highly potent materials are always material specific and must therefore be redefined for every material. Acceptable emission levels are defined in a powder’s material safety data sheet (MSDS). The terms occupational exposure limit (OEL) and occupational exposure band (OEB) are generally used to define the maximum permissible emission levels in a work environment. A material’s specific OEL value along with characteristics such as granule size and fluidity play a significant role in determining the design of a process unit handling the material. Not every containment system is suitable for every material.

Throughout the world, there is a standard OEB chart, shown in Figure 1, with the corresponding OELs and the required system type for handling materials in each band. OEBs 4 and 5 (the dark orange and red bands, respectively) are the strictest containment levels typical for potent pharmaceutical or hazardous chemical applications. OEB 4 and 5 materials generally must be handled in highly sophisticated, custom-built isolators that use

high-efficiency particulate air (HEPA) filtration, push-push filters, and clean-in-place (CIP) designs. A push-push filter consists of a working filter and a standby filter. The working filter is inserted first and then pushed down into place by the standby filter, which rests on top of the working filter during operation. When the working filter needs to be replaced, a new standby filter is inserted on top of the existing standby filter, which pushes the old working filter out into a contained bag for disposal. The original standby filter then becomes the new working filter. OEB 4 and 5 materials may also require operators to wear full respiratory suits and other protective equipment.

International and US guidelines and regulations also provide direction on containment. The European Union’s Registration, Evaluation, Authorization, and Restriction of Chemicals (REACH) regulation established a chemical guideline for the EU that addresses the classification of hazardous and harmful substances. Chemical manufacturers and processing plant operators are obligated to disclose information about how hazardous or harmful a substance is and how users should handle the substance in order to protect themselves. In the US, there’s still no single standard that applies to powder transfer safety; however, there are the National Institute for Occupational Safety and Health (NIOSH) guidelines for containment standards; National Fire Protection Association standards 654, 652, and 70, which also cover explosion risks; and MSDSs that define hazards.

FIGURE 1

Occupational exposure limit (OEL) and containment system requirement for handling toxic materials in each occupational exposure band (OEB)



Secure, hygienic vacuum conveying

Vacuum transfer is inherently clean and contained because any potential leaks in the system leak inward, drawing outside air into the system rather than exhausting the hazardous material out into the workspace. Simple steps can be taken to minimize the potential for powder escaping and posing a danger to operators or the environment; examples of such steps include ensuring adequate venting at discharge or transfer points and using correctly designed connectors.

In a vacuum transfer system, filtration and separation of the material from the airstream is critical. Commonly used O-rings or felt seals can be ineffective as a means of sealing the connection between the vacuum pump and the material areas, as they aren't designed for this type of application. An O-ring is designed to seal a shaft and a felt seal is porous and compresses when the filter is secured, which undermines the seal. Some modern filter designs are rated to capture particles as small as 0.3 micron. For even greater security, some systems include a secondary HEPA filter or an exhaust air adaptor to pipe the filtered exhaust air from the rear of the vacuum pump away to a safe area.

Contained material handling isn't limited to preventing emissions during transfer. A safe environment includes being able to clean the equipment quickly and efficiently while avoiding the potential for cross contamination or dust explosions. Vacuum conveyors made from Type 316L stainless steel that use simple modules and feature tool-free disassembly are ideal for thorough and quick cleaning. Also, using common-size seals, nonadjustable clamps, and quick connects for everything from the valve actuators to the pneumatic connections will simplify standard operating procedures (SOPs) and save time during cleaning.



Photo 1: Lightweight sanitary hoses with molded cuffs provide simple connection to a vacuum receiver.

Some applications require more stringent cleaning, such as clean-in-place (CIP), wash-in-place (WIP), or wet-in-place methods. These techniques usually involve interior spray nozzles, conveyor flooding, or a combination of both, and are useful for containing dust when disassembling the equipment. The biggest challenge in the cleaning process, however, isn't wetting the unit but rather drying it such that a swab test can validate the cleaning. This is one area where conveyor parts that are manufactured for easy assembly and access without the use of tools become particularly beneficial. Hose design can also influence a vacuum system's effectiveness. Hoses should be light and sanitary for ease of use and cleaning. Recent advancements such as static-dissipative opaque hoses that include molded cuffs with sanitary fittings (Photo 1), have improved the practicalities of hose handling.

The following are two examples of how pharmaceutical manufacturing clients achieved high-containment material transfer using customized pneumatic vacuum conveyors.

Example 1: High-containment ingredient transfer and filling integrated into a containment facility

Objective: A pharmaceutical manufacturer in Switzerland needed to integrate a vacuum conveying system into a special containment facility for transferring and filling high-potency ingredients and excipients. The project's objective was to develop a closed-process concept that met OEB 4 exposure limits—1 to 10 $\mu\text{g}/\text{m}^3$, including WIP cleaning.

Solution: The system consisted of a material transfer compartment with an upstream material lock for inserting the various ingredient containers, a filling compartment integrated with a Type 316L stainless-steel pharmaceutical pneumatic vacuum conveyor sized to suit the demand of the packaging line (Photo 2), and a container station with a docked double-flap container system for filling the multiple containers with the ingredients.

Process: Containers with the high-potency ingredients are first positioned over the material lock in the transfer compartment. Using the integrated gloves in the transfer compartment, the operator opens the ingredient



Photo 2: This vacuum conveying system is integrated into a special containment facility for transferring and filling high-potency ingredients and excipients.

containers and uses a manual suction lance connected to the vacuum conveyor to transfer the ingredients into the vacuum receiver in the adjacent filling compartment. From there, the transferred ingredients are emptied into the docked container via the double-flap valve. The container is situated on a weighing system to ensure that the required amount of each ingredient is filled. The emptied containers of the hazardous active ingredients are fed through the side walls via foil ports. Harmless excipients, held in containers outside the unit, are also sucked into the vacuum receiver through a second suction lance and port to complete the operation.

Conclusion: The entire containment system fulfilled the OEB 4 requirement during filling and subsequent WIP cleaning and was suitable for dust-explosive powders in conformance with ATEX standards.

Example 2: High-containment material transfer between processing steps

Objective: A classic pharmaceutical application for vacuum conveying is transferring material from a fluidized-bed granulator to a downstream sieve mill. In this example, another global pharmaceutical client required such a system with OEB 5 containment (less than $1 \mu\text{g}/\text{m}^3$) to eliminate any risk to the employees or environment. For perspective, this dust concentration is akin to one six-hundredth portion of a small grain of sugar weighing approximately 0.6 milligram appearing in 1 cubic meter of air during an 8-hour timespan. This assignment required a sealed and closed process without an isolator as protective cover and required all material-contact surfaces to be fully cleanable within the manufacturer's customized WIP process. This meant that the entire surface in contact with the material, including the ports to the other process facilities in the closed procedure, needed to be WIP.

In the manufacturer's WIP process, the first step is to flood the entire facility with water, paying particular attention to the contaminated conveyor hoses and process lines. Wetting the material contact surfaces serves to prewash the vacuum receiver, the filters, and the valve. Once this initial cleaning is complete, the intensive cleaning begins, with rotating nozzles repeatedly washing the stainless-steel primary filter as well as the vacuum hose exiting the primary filter and a secondary filter, which may also be contaminated.

Solution: To fulfill these high demands, the manufacturer selected a Type 316L stainless-steel pharmaceutical pneumatic vacuum conveyor sized for the application. The conveyor was further developed and augmented with a HEPA 14 secondary filter level and suitable isolation valves. The conveyor's one-piece, gap-free vessel design lent itself readily to WIP.

Process: To verify that the vacuum conveyor met the OEB 5 requirement, the emitted particles needed to be measured. To accomplish this, the chosen conveyor was tested in a prepared clean room under conditions comparable to the actual production environment. The test



Photo 3: OEB 5 containment was verified in prepared clean room, with the vacuum conveyor mounted in a mobile frame and connected to an empty intermediate bulk container by a double-flap valve.

material was a commonly used, very fine-grained, dusty naproxen-lactose mixture that is well-suited for such tests because of its texture. The proposed system design called for the transported material to be located in an intermediate bulk container (IBC) transport vessel that was docked through a double-flap system on the feed hopper. The pharmaceutical pneumatic vacuum conveyor was in a mobile frame and was connected to an empty IBC by a double-flap valve (Photo 3).

The Volkmann team selected several statistically process-relevant measuring points for the test and placed the permitted air sensors with test filters for these measuring sequences within the test environment. The air sensors primarily record the fugitive dust content in the direct surroundings of the measurement points, while the person-related measuring point displays the cumulative, average burden of dust an operator will experience. The testing operator supervised the process during the measuring and changed the filled and emptied IBCs. The conveying process was performed three times for a representative result, and each individual process was measured separately. The measurements themselves were completed by special compact filter systems that were perfused by a defined amount of air with the aid of a small vacuum generator.

Conclusion: Particle concentration measurement occurred not only during the conveying process exclusively in the IBC change but also during the cleaning and subsequent disassembly of the vacuum conveyor. The evaluation of the particle measurements in the laboratory yielded that emissions were within the design limit of less than $1 \mu\text{g}/\text{m}^3$ in all three process steps, indicating that

the system was suitable for this high-containment application.

As these examples show, a vacuum conveying system can be an extremely versatile, safe, and clean method of containing powders and fine particles during transport. Systems handling highly potent materials can be designed to be ATEX-certified, equipped with secondary filters, and easily disassembled, cleaned, and reassembled. A high-containment project requires a closer and more-open-than-usual relationship between the conveyor supplier and the equipment end user because the consequences of any potent material escaping the system can be severe. The equipment end user doesn't just want to contain dust to keep a clean facility but also to protect the lives of the operators working with the equipment, so constant communication with the conveyor supplier is necessary. Before purchasing a vacuum conveying system to transfer highly potent powders, it's necessary to consult with a vacuum conveyor supplier to find the most suitable equipment to adequately contain the materials.

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