

## **Exploring Vacuum Technology in Pharmaceutical Processing**

*FDA Eases-the-Way for Processors to  
Automate Processing Lines with Safer, Faster and  
Adaptable Vacuum Transfer Equipment*



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## *FDA Eases-the-Way for Pharmaceutical Processors to Automate Processing Lines with Safer, Faster and Adaptable Vacuum Transfer Equipment*

Pharmaceutical manufacturers are implementing vacuum conveying technologies to deliver drugs to consumers faster, safer and more economically. Vacuum technology provides safer transfer of dry bulk materials and allows pharmaceutical processors to meet tight industry standards for sanitation and environmental safety.

The increasing use of vacuum conveying systems, is due in part, from FDA guidance and clarifications that allow pharmaceutical manufacturers to implement new production technologies by documenting them in annual reports rather than filing for post-approval manufacturing changes in time-consuming supplements.

The FDA clearly indicates that automated material transfer systems are the preferred method for delivering dry bulk powders and solids in pharmaceutical environments and that methods such as use of vacuum conveying are unlikely to have an adverse effect on drug product quality. Adding productivity-enhancing material handling equipment, such as vacuum conveying systems, is a level one change that is eligible for submission in annual reports.

Appendix A in the Guidance *CMC Post-approval Manufacturing Changes to Be Documented in Annual Reports* states that a “decrease in the number of open-handling steps or manual-operation procedures,” has “minimal potential to have an adverse effect on product quality.”

That statement correlates with the assertion in the Guidance *Immediate Release Solid Oral Dosage Forms: Scale-Up and Post-approval Changes: Chemistry, Manufacturing, and Controls, In Vitro Dissolution Testing, and In Vivo Bioequivalence Documentation* that “change(s) from non-automated or non-mechanical equipment to automated or mechanical equipment to move ingredients,” are “are unlikely to have any detectable impact on formulation quality and performance. [2]”

Although the Guidances opened the door for change, some confusion still existed about how vacuum conveying systems that operate in semi-continuous and continuous modes, coincided with batch processing as well as where that process fit into reporting changes. The term continuous brought about serious debate about its true meaning because the idea that continuous operation was most often associated with a mode



VAC-U-MAX Sanitary Receivers for Pneumatic Conveying of Excipients and API's for Pharmaceutical Processes

of manufacturing. In some instances, it means 24 hour per day, 7 days per week operation, while in other industries it refers to the mode of manufacturing.

Although this opened the door for pharmaceutical companies to make changes that increased production or protected product and employees, some confusion still existed about how vacuum conveying operating in semi-continuous and continuous modes coincided with batch processing, as well as where that process fit into reporting changes.

To move away from the definition of batch being tied to a mode of manufacturing, the FDA changed the definition in CFR Title 21 210.3(b)(2) to read: “CFR (2): Batch means a specific quantity of a drug or other material that is intended to have uniform character and quality, within specified limits, and is produced according to a single manufacturing order during the same cycle of manufacture. [3]”

The process can be continuous or semi-continuous depending on the level of automation employed. Vacuum transfer is the heart of continuous processes that move dry bulk materials from one processing machine to the next, including mixers, reactors, hammer mills, tablet presses, gel caps, and packaging machinery.

While it's possible to automate drug manufacturing completely, manufacturers, in lieu of complete infrastructure overhauls, are investing in vacuum conveyors, which are more accurate, cleaner, and safer and cost less than manual handling methods.

Vacuum conveyors can fit into existing processes through the routing of conveying lines between floors, through partitions, and around machinery, and they are easily re-routed to accommodate process modifications.

Whether you employ vacuum technology for dust containment, labor savings, cleanliness, or safety and environmental reasons, your success in adding that technology lies in an understanding of powder's characteristics, including how those characteristics interact with your equipment's design and your specific processes. Experts can provide access not only to industry-specific know-how but also to expertise in powder's characteristics that transfers from industry to industry, and can assure you, through written guarantees, that your equipment will perform the way it should.

### Mass flow and Material Separation

The pharmaceutical industry has given a great deal of attention to segregation, especially as it applies to manual transfer of materials in drums or other containers during production. Vibrations, caused by moving containers, promote segregation and threaten quality of batches. Therefore, companies have sought mass-flow methods that move particles at the same velocity, minimizing segregation.

Vacuum conveyors, with virtually no moving parts, use mass flow for the most part. They generally use standard components, but some manufacturers offer fabricating services to customize systems and provide unique solutions for distinctive environments and equipment.

### Dust Containment

Dust containment is a principal reason that manufacturers add vacuum conveyors to production lines. Manually dumping feeders creates small dust clouds with each scoop, creating fugitive dust—particulate matter (PM) that is any solid or liquid suspended in the air through wind or human interaction. While half of fugitive dusts are larger than 10 microns—a human hair is 70 microns—and settle on surfaces rather quickly, the other half are smaller—not visible to the naked eye—and can remain suspended in the air for days or weeks.

Fully enclosed systems protect drug product from air, dirt, and waste. As air moves through the system, it cycles through filters before being exhausted. Because materials don't escape, vacuum conveyors prevent particulates from entering the environment, where they can endanger workers' health; settle on equipment and surfaces, causing cross-contamination from dislodged fugitive dust; or create explosion hazards.

For ingredients that require higher levels of containment to protect workers' health, minimizing exposure requires additional scrutiny in conveyor design. One method that offers some additional guarantee of safety for exhaust air is HEPA filtration.

### Safety Hazards and Ergonomics

Automatically feeding materials into and removing them from hammer mills, mixers, reactors, and other equipment has multiple advantages beyond dust containment, such as reducing the amount of manpower needed to feed a hammer mill and eliminating safety hazards.

Generally, most processing equipment stands taller than workers do, requiring the addition of ladders or stairs to access feeders and often warranting a second worker for safety.

Automated or semi-automated systems eliminate the need for workers to climb stairs or haul heavy containers of material away, alleviating fall hazards. They also are cost-effective because only one operator needs to monitor the equipment's functioning.



Pneumatic Conveying System with Small Footprint, Eliminating Need for Workers to Climb Steps to Manually Dump Materials into the Process, Making it Safer for Workers

Automatic feeding also eradicates ergonomic issues that can occur with repetitive motion, lifting, and climbing to dump materials manually into feeders. If a manufacturer is paying \$250,000 a year in disability suits from manual-transfer injuries, investing in a vacuum conveyor can produce a near-instant return on investment, depending on the level of automation added.

Employing automated, or semi-automated, pneumatic conveying systems to deliver product to and from process equipment including hammermills and screeners eliminates the need for workers to climb stairs or haul heavy containers of material away from the hammermill, alleviating fall hazards and repetitive motion injuries.

## Direct Charge Blender Loading

Blenders, mixers, and reactors are common types of equipment used in pharmaceutical manufacturing and often require a mezzanine level for manual loading or specialized equipment like drum loaders or vacuum conveyors. Although better than manual loading, drum loaders have limitations, such as allowing operators to load only one drum at a time, which makes the delivery of materials to a blender or reactor time-consuming. In some circumstances, an operator must load multiple ingredients into drums prior to loading blenders and reactors, further slowing the process by increasing manufacturing steps.



Direct Charge Blender Loading System - a "Better Way" to Move a Variety of Bulk Materials, Eliminating Manual Handling

Vacuum conveying systems designed specifically for direct charge loading can efficiently load equipment that is capable of withstanding a vacuum. With a blender or mixer as the primary receiver, the conveying manufacturer provides the rest of the system—power source, filters, controls, and adapters.

Configured specifically for each application with standard equipment, such systems offer the option of either floor-standing or suspended blender loaders and can reduce the amount of carry over significantly, eliminating product loss and ensuring batch integrity. During the loading process, carry over is the amount of product collected in the filter separator that separates the air from solids (dust) inside a vessel to prevent solids from reaching the vacuum pump. Standing units are easy to clean, and those units with casters can service more than one blender. After the blender is loaded via the pneumatic conveyor system and the load equalizes, the carry over automatically releases into an airtight vessel that preserves product integrity, allowing reuse or safe disposal. Suspended units

automatically discharge material back into the blender, eliminating the need to handle product manually. Because such units come apart easily without tools, washing equipment and changing bags, filters, and hoses between batches and drug products takes only 30-45 minutes

## Vacuum Tablet Press Loading Systems

Vacuum tablet press loading systems allow pharmaceutical processors to automate batch process. These turnkey systems mount on customers' presses and are available for single or dual-hopper tablet presses. The equipment's construction is USDA accepted.

The systems automatically convey tablet granulations from drums or other containers or equipment to surge bins over tablet presses. A tube-hopper material receiver, with vertical sides to minimize material hang-up, lies over each surge bin, and the control panel and vacuum pump reside in an adjacent room. The systems apply a vacuum to all material receivers using one vacuum pump. A full opening discharge valve assures complete discharge of material.

The modern electronic technology of vacuum tablet press loading systems, with mechanical and pneumatic designs and programmable control panels with microprocessors, can be the nerve centers for manufacturing and can provide reserve capacity to handle a total of sixteen presses.



Vacuum Conveying System for Loading Tablet Presses, Available in Complete, Ready-to-Operate Systems for Mounting on Single or Dual-Hopper Tablet Presses

The microprocessor constantly scans level controls on the surge bins and initiates conveying of tablet formulation to the receiver over any press requiring material, insuring that no press runs dry, which could cause costly tooling damage.

## Gel Cap Conveying

Another type of turnkey conveyor package is the gel cap conveyor that delivers material from inspection machines to packaging lines at a transfer rate of 500 to 1000 pounds per hour (photo). Gel caps, soft gels, or tablets spill from the inspection machine into the hopper and then convey into the vacuum receiver above a packaging or sorting machine. The manufacture of delicate gel caps is an expensive process, and gel cap conveyors can protect a drug product's integrity and often also incorporate environmental improvements. For example, gel caps can sound like bullets when hitting the side of a hopper, creating additional noise in a facility. Tangential inlets can eliminate noise and protect delicate drug product from damage.



Gel Cap Conveying System Conveys up to and over 2,500 units per minute, delivering product to packaging lines

## Collection of Wastes / Wastewater

In addition to providing cleaner, safer, and quieter environments, vacuum technology is also integral to complying with FDA and EPA guidelines, especially in the collection of wastewater. Wet, central, pharmaceutical vacuum systems can assist manufacturing facilities in complying with regulations that prohibit disposal of liquids containing active pharmaceutical ingredients (APIs) and non-regulated pharmaceuticals and personal care products (PPCPs) into municipal wastewater sewer systems and municipal wastewater treatment plants (WWTP).

Such a system can provide multiple hose connections throughout a facility where wash-down processes occur, and when a network needs to move vertically, special tubing valves are available to prevent water from falling back into the network if the system shuts down. The system can move the liquid generated from a wash-down into a sanitary-tubing network and then collect it in a wet separator. A washable, corrosion-resistant filter media then separates the liquid from the airstream, and an integral pump transfers the solution to an in-house treatment system to address the APIs and PPCPs prior to discharge to the local municipal

WWTP. Depending on the treatment process, the liquid may be suitable for re-use within the pharmaceutical facility via a closed-looped treatment system. Other features of that type of industrial vacuum system include a full control package, liquid level sensors, sanitary construction, and protective secondary containment in the event of a release during maintenance or normal operations.



Air-Driven Industrial Vacuum Cleaner - "Intrinsically Safe"  
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Vacuum technology is also ideal for preventing solids from being delivered to WWTPs, which can cost processors upward of \$10,000 per month in back charges. To keep solids from entering drains, vacuum-technology experts have borrowed techniques from other industries and have applied them to pharmaceutical and food applications to separate materials in the vacuum stream. Constructed of stainless steel, these systems are built to be explosion proof.

## Conclusions

Whether employing a central vacuum system to eliminate harmful waste from the wastewater stream or using vacuum conveyors to eliminate hazards, increase the speed at which a processing line operates, or streamline production through automation, working with a manufacturer who has extensive experience in the delivery of powders ensures that pharmaceutical manufacturers get the right equipment for the job.

## References

1. Guidance for Industry, *CMC Post-approval Manufacturing Changes to Be Documented in Annual Reports*, Appendix A. Guidance for Industry, *Immediate Release Solid Oral Dosage Forms: Scale-Up and Postapproval Changes: Chemistry, Manufacturing, and Controls, In Vitro Dissolution Testing, and In Vivo Bioequivalence Documentation*.
2. CFR Title 21 210.3(b)(2)

