Reduce powder processing risks when outsourcing manufacturing

When outsourcing manufacturing for an oral solid dosage product, brand owners generally minimize risk by ensuring that the contract manufacturing organization’s (CMO’s) unit operations have the desired capability and have been tested with the target formulation and that the area has sufficient containment and environmental controls. They also typically confirm that the CMO’s site leadership team has a demonstrated commitment to quality, analytics, and regulatory compliance. An area of risk that is often overlooked, however, is powder transfer between unit operations.

Powder transfer has been described as the “forgotten unit operation” in solid dosage manufacturing, yet it can greatly influence the success of a process. Bulk solids processes have inherent weaknesses at the junctures between unit operations. These junctures include chutes, valves, intermediate bulk containers (IBCs), bins, drums, and other methods of moving in-process powder from point A to point B. The unit operations themselves may work well, but, at full scale, powder may not reliably flow through these connection points, often resulting in quality defects such as poor content uniformity.

The first step in de-risking powder transfers is to identify them. Consider where transfers need to take place and how the movements will be controlled. Relying on gravity flow is one aspect, as gravity is constant, and an assumption of success often exists as an equipment train is put in place. Unfortunately, gravity’s effect on powder flow can be highly variable and will depend on the powder’s properties. Unlike liquid flow, powder flow is influenced by variations in bulk density, wall friction and adhesion to surrounding surfaces, and cohesive strength within the material, which can all limit a powder’s ability to flow by gravity. Liquids can flow through very small openings, but powders often have a minimum outlet size requirement to avoid flow obstructions such as cohesive arches and ratholes.

Segregation is a separate area of concern and is defined as the separation of a powder into zones of similar properties (which are dissimilar zone to zone). Segregation potential is strongly influenced by particle size differences, but other properties such as particle shape and density can also play a role. Segregation can occur during transfer when forces on the particles are high and the material is in a dispersed state. Specific mechanisms include sifting, where interparticle motion occurs as a pile forms, and fluidization and dusting, which can occur due to air exchange as an open volume is rapidly filled in with free falling powder from above.

System components that are intended to control powder flow can be an additional source of concern. Feeders can contribute to flow behaviors where some portions of the connection above are stagnant, with areas of non-flowing powder within them when the system is running, making them more likely to experience a flow obstruction even when the inlet area is relatively large. Pinch valves and gates that do not fully open are further risk factors, as they inherently contribute to stagnation by restricting a portion of their throat area.

You don’t need to wait for a problem to arise to reduce the risks associated with powder transfer steps. Developing a basic suite of flow properties for the powders being handled at each stage allows for a technical evaluation of transfer steps. The goal of this effort is to develop a set of engineering parameters that you can use to evaluate a CMO’s actual production process. The most important properties include cohesive strength, to determine the minimum opening sizes a powder will pass through without arching or ratholing, wall friction, to determine hopper and/or chute angle requirements as a function of surface material of construction and finish; permeability, to determine critical opening sizes for steady flow rates; and segregation potential by sifting and fluidization, to consider the influence of forces during transfer that could give rise to content uniformity variations. If you know your material’s flow properties, you can quantitatively assess the powder flow performance of your CMO’s handling system, allowing you to solve or avoid problems at the outset based on equipment features.

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