Innovative Approach to Conical Milling Addresses Challenges With Heat-Sensitive Products, Particle Size Distributions and Capacity Throughput

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Introduction

Pharma Oral Solid Dosage (OSD) manufacturers take a lot of care to produce good flowing granules, with the right particle size distribution range, and with the ideal bulk density to ensure they can produce robust tablets with all the efficacy properties the medication was designed to deliver (Gurvinder Singh et al). In OSD manufacturing, most tablets are produced by either Dry or Wet Granulation methods. Regardless of the process, once the granules have been made - either wet granulated and dried in a fluid bed dryer or made into ribbons with a roll compactor – manufacturers do not wish to destroy them and make "fine" particles again by adding too much energy during the milling step, as fines are detrimental to flowability and hence tableting (Jambhekar et al). Conical mills have traditionally been used in the Wet Granulation process for decades because of their gentle milling nature, the ability to minimize fines generation and to maximize the percentage of powders within target (Schenck et al). In addition to making better particles, containment is undoubtedly one of the most critical design safety requirements and with it, the growing need for clean-in-place (CIP) equipment, without adding significant capital investment.

This poster compares traditional conical milling technologies typically used for particle size reduction in Oral Solid Dosage processes with recent breakthrough developments in conical milling screen designs, impeller profiles and gearbox technology. This Study investigates the benefits from improved efficiencies during milling, including optimized PSDs without affecting validated distributions (results are within upper and lower limits). This Poster will take a closer look at the reduction or elimination of bi-modal distributions while concurrently exploring the capability to significantly reduce heat generated during milling. Containment safety measures including CIP performance and benefits of lubricant-free gearboxes is outside the scope of this Poster.

Objectives

A. To determine how changes in conical screen design can positively improve powder milling efficiencies – both in improved particle size distributions (PSDs) and capacities; without affecting validated distributions.
B. To ascertain how an improved milling force profile reduces overall heat generation during milling.

Methods and Materials

Tests for this Study were performed in the R&D Center of Excellence at Quadro Engineering Headquarters (Waterloo, ON, Canada). Three materials were selected: Acetaminophen, Urea Prills and Lactose for their varying product characteristics.

A Quadro® model U21 High Efficiency Comil® (Fig 1) was supplied with an AB PowerFlex 70 VFD set at standard 1400 RPM. Trials were performed with a 1 mm (0.039") diameter hole screen and a 1601 round arm impeller. PSD analysis were conducted with a Malvern Mastersizer 2000 (Malvern, United Kingdom).

Results

Fig 1: Model U21 High Efficiency Comil®

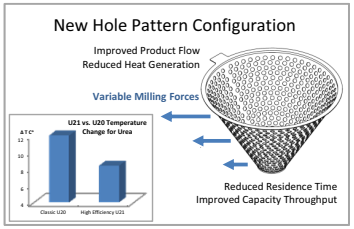

Fig 2: Patent-Pending High Efficiency Screen Design

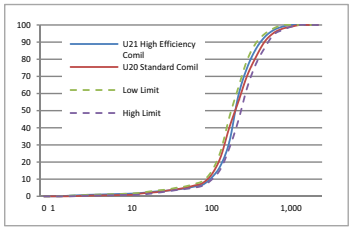

Fig 3: PSD Cumulative Comparison for Urea

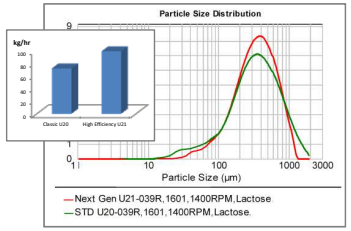

Fig 4: PSD Comparison U20 vs U21 for Lactose

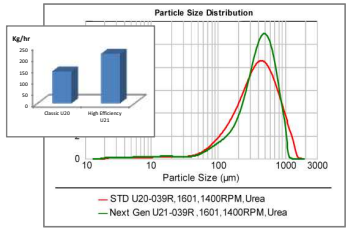

Fig 5: PSD Comparison U20 vs U21 for Urea

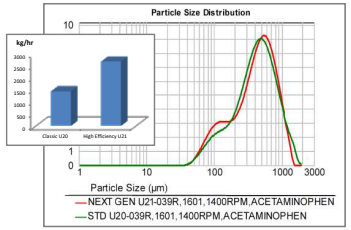

Fig 6: PSD Bi-Modal Comparison U20 vs U21 for Acetaminophen

Discussion

Quadro® High Efficiency Comil ® U21 model (Figure 1), was tested with a new patent-pending screen design (Figure 2) and compared to a previous generation U20 Comil® model The new screen hole pattern profile was tested with three separate materials for particle size distribution , capacity and heat generation comparison.

Three separate products were tested, each showing a markedly improvement in the reduction of heat generation (Figure 2) and particle size distribution as shown in Figures 4, 5 and 6.

Although the particle size distribution of materials processed through the Comil® U21 provided a markedly improvement in the amount of material within the ideal target range, tests revealed that the distribution was still within generally accepted upper and lower allowable limits (Figure 3), as determined by prior knowledge. Alternatively, manufacturers could rely on design of experiment (DoE) studies (Zhigang Sun, et al).

Figures 4, 5 and 6 show the overall improvement in PSD curves for Lactose, Urea and Acetaminophen, with the concurrent benefit of improved capacity throughput vs standard U20 Comils® by 37.5%, 54% and 86% respectively.

Furthermore, Figure 6 shows a significant reduction in the bi-modal particle size distribution of Acetaminophen, which is not a-typical in pharma oral solid dosage formulations.

Conclusion

The Model U21 High Efficiency Comil® presents a groundbreaking approach to pharma oral solid dosage size reduction. Improvements in PSDs resulting in more granules within target – potentially reducing or eliminating bi-modal particle curves – do not adversely affect validated processes, as the results do not stray outside of the typical upper and lower particle size limits. Concurrently, the new screen design improves capacities by as much as 85% without increasing the overall footprint of the industry standard Comil® U20 model. Furthermore, the improved product flowability through the screen offers the added benefit of a reduction in milling temperature – particularly critical for heat-sensitive products. Although this Paper did not focus on the additional benefits of the greaseless gearbox and the standard CIP design introduced with the model U21, the overall design of the High Efficiency Comil® offers solutions to pharma's most critical requirements.

References

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