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Abstract

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Particle Engineering of a Pharmaceutical Intermediate via Crystal Agglomeration

The filtration of a pharmaceutical intermediate was historically challenging due to the intrinsic needle-like morphology of the crystals. Attempts were made in the past to change the crystal morphology to facilitate filtration. Micronized seeds, either jet or wet-milled, were found to be efficient in growing larger particles with improved filtration rate, and a process based on this approach has been demonstrated in multiple pilot plant scale batches. However, implementation of the process requires a solvent swap from acetonitrile to ethanol, and use of 5% wet-milled seeds to achieve desirable filtration rate. An alternative crystallization was recently developed that eliminates the need for distillation and wet-milled seeds. Crystal agglomeration, enabled by a specific by-product of the reaction and triggered by solvent composition during antisolvent charge, significantly changes the filtration characteristics of the material. This crystallization offers particle engineering opportunities to optimize the process by reducing the number of unit operations and solvent consumption. Additional washing is needed to remove the by-product and other impurities to ensure product quality. The design of this crystallization through particle agglomeration, and the challenges encountered for efficient washing will be discussed in this presentation.

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