529e Optimizing Powder Behavior through Crystallization Engineering

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The crystallization of Active Pharmaceutical Ingredients (API's) is a critical processing step, not only for polymorph and impurity control, but also for the design of the necessary bulk powder properties that can enhance powder performance during the formulation process. Powder properties such as particle size, morphology, surface properties, and bulk density can be engineered through the crystallization.

This presentation will describe the development process of an API crystallization, its focus on optimization of bulk powder properties, and its successful scale-up into kilo lab and pilot plant.

Particle size was identified as one of the critical parameters in the determination of powder properties. The particle size distribution of a crystallization batch showed strong dependence on seed properties (i.e., surface area), and seeding conditions. In this study, seeds from different types of milling equipment were examined. Additionally, seed amount, seeding temperature, and cooling profile were studied in order to design a rugged crystallization protocol which could provide the desired particle size distribution at different scales. FBRM (Lasentec, in-line) and LLS (Malvern, off-line) were used to monitor particle size throughout these development studies.

In order to determine the effect of the API's bulk powder properties on the formulation process, a kilo-lab study was conducted. Material was produced with varying bulk properties through alterations in seeding and crystallization protocols. This study made it possible to (1) establish the crystallization parameter ranges; and (2) define the desirable API powder property ranges based on subsequent formulation and drug product behavior.