

Crystallization development assisted by Lasentec FBRM®

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In development of crystallization processes as well as control of production processes it is of big interest to quantify changes in number and dimensions of crystals online and without sampling.

Lasentec® FBRM® probes (Focused Beam Reflectance Measurement) measure, in real time, the rate and degree of change in both the number and the dimension of crystals and crystal structures directly in process. This allows to track: nucleation and growth rates, secondary nucleation, seed control, morphology change, agglomeration/desagglomeration, endpoint, attrition.

Process goals are sometimes straightforward like filterability (reduction of fines), sometimes crystallization conditions have to be controlled to reach the desired morphology of the crystals.

We chose the cooling crystallization of ascorbic acid (Vitamin C) to show sensitivity of this measurement technique.

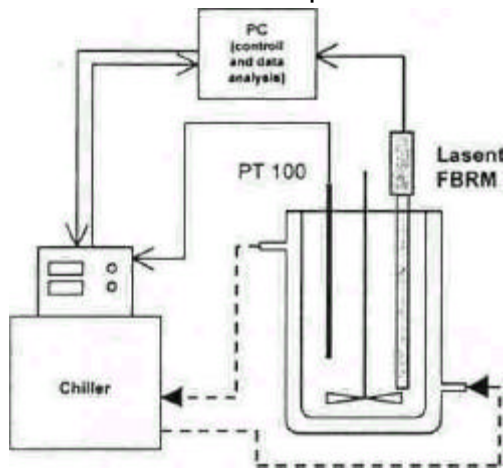


Figure 1: Setup for controlled crystallization

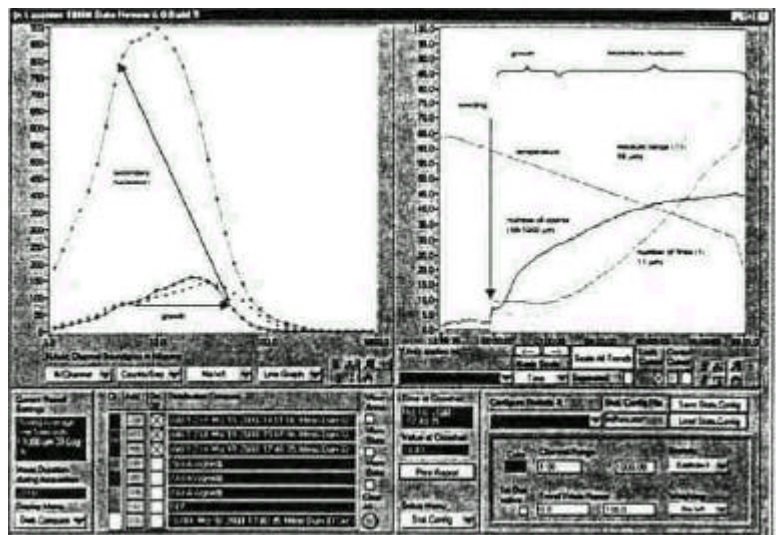


Figure 2: Seeded crystallization: growth phase followed by secondary nucleation (underseeding). Size distributions and trends over time..

Under investigation were different cooling curves (linear, quadratic etc.), seeded versus unseeded crystallization, different amounts of seed material. Best results towards good filterability could be obtained with seeded crystallization followed by temperature cycles to decrease the number of fines.

References:

1. M.W. Wood-Kaczmar, SmithKline Beecham, *The Control of Particle Size in the Batch Crystallization of Pharmaceutical Products by the Application of Statistical DOE Analysis to FBRM Data*, Lasentec User conference 28.2.-1.3 2000.
2. M. Cerreta, J. Liebel, Boehringer Ingelheim, *Crystal Size Distribution Control During Batch Crystallization*, Lasentec User conference 28.2.-1.3 2000.