

470a Development of a Continuous Crystallization Technique to Produce Small Crystals of Pharmaceutical Compounds

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This talk illustrates a novel continuous crystallization process that is not commonly practiced in the pharmaceutical industry. The crystallization efforts to produce small crystals of two BMS compounds for improving the dissolution rate/bioavailability will be reviewed. Conventional batch crystallization and post-crystallization wet-milling cannot address the desired particle size requirement. One compound has strong dust explosion potential and cannot be milled and the other compound needs multiple passes to achieve the desired particle size by dry milling. A novel crystallization technique using a high-shear rotor-stator chamber to crystallize compounds at a high degree of supersaturation under good mixing was demonstrated to be effective in producing the desired small particles and was successfully scaled up in the pilot plant. The continuous design of the crystallization process eases the mixing requirement and improves the scalability. The rationale and design of this continuous process will be discussed.