529c CFD Simulations for Scale-up of Anti-Solvent Crystallization Process

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Anti-solvent crystallization is one of the preferred ways of crystallizing from solution heat-sensitive materials, e.g., pharmaceuticals. In this process, mixing in conjunction with anti-solvent addition is of primarily importance to obtaining crystals of desirable quality. Care is taken to suppress sharp concentration gradients that prolong nucleation and result in crystals of small size.

CFD simulations capture the effect of mixing on anti-solvent crystallization of organic compounds and provide a means for controlled and inexpensive experimentation to determine optimum process conditions and rules for scale-up from laboratory to industrial scale. A DOE with CFD simulations is undertaken initially to determine the effect of (1) agitation rate, (2) position of anti-solvent feed, and (3) schedule of anti-solvent feed on the distribution of the anti-solvent concentration in the crystallizer. The results of the simulation scale-up with (NdD2)/q, where q is the volumetric flow rate of anti-solvent addition, N the agitation rate, d the diameter of the impeller and D the diameter of the crystallizer. A second DOE with CFD simulations will be conducted to formulate scale-up rules when crystallization kinetics are introduced.