

## **Towards a Robust, Greener API Process Via Cooling Crystallization**

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Abstract:

A late stage API candidate had been purified via antisolvent crystallization from IPA/MeOH. The antisolvent process was characterized by nucleation of undesirable crystal forms, large processing volumes, and small particle sizes (needles). A greener cooling crystallization from EtOH/water was developed to address these issues. FBRM and mid-IR PATs were used along with traditional HPLC methods to investigate supersaturation effects and gain insights into the nucleation and growth. The latter two phenomena were sensitive to mixing energy input. The cooling crystallization provides robust polymorph control, larger particles with smaller aspect ratio, lower processing volumes (higher throughput), and robust scalability as evidenced by runs at 200x and 2000x the lab scale (100 KG vs. 50 g.).