

Process Analytical Technology (PAT) in Crystallization

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Abstract:

Process Analytical Technology (PAT) has been defined by the United States Food and Drug Administration (FDA) to design, analyze, and control pharmaceutical manufacturing processes by measuring critical process parameters (CPP) that impact critical quality attributes (CQA). PAT plays an important role in crystallisation processes, which is a critical purification process in pharmaceutical manufacturing.

This comprehensive tutorial will delve into the role of Process Analytical Technology (PAT) in deepening our understanding of complex crystallisation processes. We will explore a range of analytical techniques including focused beam reflectance measurement (FBRM), particle video microscopy (PVM), and in-situ infrared (IR) and Raman spectroscopy. FBRM can be employed to estimate particle size distribution, providing insights into the growth dynamics of crystals. PVM offers a visual observation of the solution conditions, allowing for real-time monitoring of crystal formation and behavior. In-situ IR and Raman spectroscopy can be utilized to measure concentrations within the solution, helping to determine the supersaturation levels and the presence of impurities.

The tutorial will include some case studies demonstrating how these analytical tools are applied in various systems. We will examine the crystallization processes of small organic molecules in both homogeneous environments and complex scenarios involving oiling out and liquid-liquid phase separation systems. Additionally, we will explore the crystallization of protein molecules, highlighting specific challenges and observations unique to biological substances.

We will also discuss the limitations of these PAT tools. This includes potential issues with sensitivity, resolution, and the interpretability of data in complex mixtures, as well as the practical aspects of integrating these technologies into existing pharmaceutical manufacturing processes. Finally, we will look ahead to the future developments and potential advancements in PAT tools. This tutorial aims to help researchers and practitioners to effectively employ PAT in enhancing product quality and consistency in pharmaceutical crystallisation development.

Keywords: Crystallization; PAT; FBRM, PVM, in-situ IR, Raman