

PROCESS ANALYTICAL TECHNOLOGY FOR CRYSTALLIZATION – ALL IN ONE

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In 2004, the U.S. FDA published a guidance for industry on process analytical technology (PAT)¹. The most used techniques include attenuated-total reflectance Fourier-transform infrared spectroscopy (ATR-FTIR)², Focused Beam Reflectance Measurement (FBRM)^{2,3,4}, particle vision and measurement (PVM)^{3,4}, Raman spectroscopy⁵, near infrared spectroscopy (NIR)⁶ and ATR ultraviolet-visible spectroscopy⁴. Using PAT helps with better understanding of processes, improving quality of final products and improving manufacturing efficiency. Unfortunately, we are in the year 2022 and most PAT applications are mainly in research and development.

Final step in pharmaceutical production for separation and purification is crystallization. We can control and change crystallization conditions and thus drive the final product properties which are important for further downstream processes and formulations. We are focused on right polymorphic form, crystal shape, particle size distribution and yield during crystallization among properties. BlazeMetrics Co. developed one probe which is capable to capturing all of these parameters in real time. We are able to capture surface structure, track parameters like D10, D50 or D90 and particle counts, mean or median and turbidity. Thanks to this, crystallization process development and optimization are more effective. We do not need to take sample and wait for results. Using PAT reduces the amount of experiments performed to get the same goal. Probe was tested on actual developed project at different crystallizations (spontaneous, antisolvent and seeded crystallization) and on wet milling. Results were compared with SEM images and PSD obtained by a validated method. In the case of API salt, polymorphic transformation was studied in situ by Raman spectroscopy.

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