

PAT: ANALYSIS OF PROCESS INDUCED DISORDER OF API BY X-RAY POWDER DIFFRACTION

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Disordering of API material during processing can have a significant influence on final drug product performance, making the control of process induced disorder an ideal candidate for PAT and Quality by Design. X-ray powder diffraction provides a direct means to determine the degree and type of disorder occurring in API material during typical process steps (blending, milling, granulation, compaction etc) through off-line measurements. Characterizing the propensity for disorder per operational step allows the assessment of risk and appropriate design of downstream activities with at-line or near-at-line monitoring. Different types of structural disorder and their x-ray fingerprint will be discussed along with examples of expected changes in API physical properties like solubility. A ranking of manufacturing operations according to risk will be proposed along with the implied consequences for Quality by Design.