

moisture level is often desired especially for LVV. Such optimal residual moisture and the corresponding glass transition for each product must be empirically quantified along with their drying yield, molecular mobility, and stability to ensure successful long-term shelf stability [53].

## PAT Development

In August 2002, the FDA announced an initiative, “Pharmaceutical Current Good Manufacturing Practices (cGMPs) for the 21st Century—A Risk-Based Approach,” to improve the overall understanding of the product and process better in the pharmaceutical industry [54]. The process would be for the addition of process analytical testing (PAT) to occur during development and in manufacturing.

PAT allows for quality to be a part of the process and product, rather than relying on testing during release. The definition of PAT is “a system for designing, analyzing, and controlling manufacturing through timely measurements (i.e., during processing) of critical quality and performance attributes of raw and in-process material and processes, with the goal of ensuring final product quality” [55]. PAT allows one to examine the process and determine the process performance by using risk-management tools as well as online sensors to monitor, control, and design the process [56].

Thus, PAT should improve the desired state of the manufacturing process and result in the following:

Manufacturing processes are designed efficiently and effectively, and thus improve the quality of the product and an improvement in the performance of the manufacturing process.

- A better mechanistic understanding of the formulation and process which results in improving the product performance and sets the product and process specifications based on knowledge learned during development.
- Continuous feedback during the formulation process by online monitoring improving the product quality. “Real-time” feedback loops.
- Based on the current level of scientific knowledge, regulatory policies and procedures are tailored to the product and process understanding.
- Using PAT allows a better understanding of the formulation and manufacturing process that impact product quality and consistency, as a result PAT allows for better risk-based regulatory approaches to be considered.
- PAT allows for better process control strategies to be implemented and improve the overall performance of the product and improve product quality.

PAT’s main goal is to improve the formulation process and product to ensure final product quality. This is accomplished through designing a system that analyzes samples in real-time and can control the manufacturing process. The PAT should not only consider the process but also understand the key inputs into the system including raw materials and in-process intermediates.