outside the quality specifications. This should result in better safety and efficacy of the product in the patient's hands.

PAT can be implemented in the vaccine space and will begin to become more common within the vaccine drug product development arena moving forward. Although beneficial, understanding where to implement is still being evaluated. Drug product operation that appear to fit well with PAT (i.e., lyophilization, moisture analysis, mixing times) across modalities will likely see more implementation in the future. Utilization of PAT will continue within the vaccine space and allow the formulation and process scientist a better understanding of the product and process.

Relevant PAT tools and principles, as described below can enable process optimization and control while improving efficiency and addressing the limitation of time-defined end points. PAT tools can be characterized into:

- Multivariate tools for experimental process design and ability to acquire data and analysis.
- Process analyzers for collecting process data relevant for QA and regulatory decisions.
- Control tools to aid in better understanding the link between the process design and CQA.
- Continuous improvement through data analysis and knowledge management for establishing understanding of multifactorial relationships.

Additionally, risk based, integrated systems and real-time release allow evaluation and builds quality in-process and final product.

For additional information, the reader is referred to the Guidance for Industry: PAT—A Framework for Innovative Pharmaceutical Development, Manufacturing, and Quality Assurance [54, 55, 57].

Scale-Up to Clinical Development/Early Launch Commercialization

A critical step in vaccine development is scale-up of the process from the laboratory-scale operations often used for preclinical studies to pilot and ultimately commercial scale operations required for the production of clinical supplies and marketed product. The scale-up and technology transfer from a developmental laboratory environment to a production environment increases capacity, assures compliance with GMP requirements, and preferably improves the consistency and overall robustness of the process. The primary objective at each stage of scale-up is to preserve the CQAs that assure the safety and efficacy of the product. Secondary objectives often exist to maximize facility throughput and minimize the opportunities for manufacturing deviations. Thus, the scale-up process includes careful consideration of both the technical aspects of each manufacturing unit operation as well as the GMP, quality, and operations systems within each manufacturing environment.