To evaluate the potential effect of the physicochemical properties of the drug substance on the performance of the drug product, studies on drug product might be warranted. For example, the ICH *Q6A Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances* describes some of the circumstances in which drug product studies are recommended. The knowledge gained from the studies investigating the potential effect of drug substance properties on drug product performance can be used, as appropriate, to justify elements of the drug substance specification.

One purpose of these comprehensive guidelines is to prepare for compliance with process analytical technology (PAT), a recent initiative of the Food and Drug Administration (FDA; Ref. 1). Process analytical technology is intended to encourage drug makers to build quality into their development processes, so that they can anticipate the impact of changes on a final formulation. Although PAT is voluntary, the initiative is designed to promote a better understanding, among drug manufacturers, of the mechanics of their processes, so that they can avoid failures and minimize the amount of testing required at the end of production. Preformulation studies support PAT by providing more information on an active pharmaceutical ingredient's (API's) characteristics to facilitate downstream efficiency and success. Drug manufacturers can eventually submit their documents to a special PAT group within the FDA, which can expedite regulatory approval. Preformulation studies also support reference standard characterization. The regulations of the FDA require that the drug manufacturers establish a primary reference standard at a certain stage in drug development, whereby a compound is characterized as thoroughly and precisely as possible. Subsequent tests and analyses must be based on samples that meet this standard.

The FDA considers PAT to be 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 materials and processes, with the goal of ensuring final product quality. It is important to note that the term *analytical* in PAT is viewed broadly to include chemical, physical, microbiological, mathematical, and risk analysis conducted in an integrated manner. The goal of PAT is to enhance the understanding and control the manufacturing process, which is consistent with our current drug quality system: *quality cannot be tested into products; it should be built in or should be by design*. Consequently, the tools and principles described in this guidance should be used for gaining the process understanding and can also be used to meet the regulatory requirements for validating and controlling the manufacturing process.

Quality is built into pharmaceutical products through a comprehensive understanding of the following:

- The intended therapeutic objectives; patient population; route of administration; and pharmacological, toxicological, and pharmacokinetic characteristics of a drug.
- The chemical, physical, and biopharmaceutic characteristics of a drug.
- Design of a product and selection of product components and packaging based on drug attributes listed previously.
- The design of the manufacturing processes by using principles of engineering, material science, and quality assurance to ensure acceptable and reproducible product quality and performance throughout a product's shelf life.