TABLE 8.1

Study Factors for Various Prospective Dosage Forms

Prospective Dosage Form	Study Factors
Parenteral	Solubility, micellization, thermal stability, chemical stability, packaging component interaction (glass and stoppers), photostability, physical stress (particularly for protein drugs), buffer interactions, and viscosity
Oral solids	Solubility, dissolution, polymorphism, chirality, particle size, powder flow, chemical stability, photostability, compressibility, hygroscopicity, and excipient interactions
Oral liquids	Solubility, polymorphic conversions, chirality, excipient interactions, chemical stability, photostability, pH effects, and container interactions (e.g., type III glass)
Semisolids	Solubility, dissolution, particle size, polymorphism, chirality, chemical stability, photostability, viscosity, and excipient interactions

The experience and data accumulated during the preformulation stage prove pivotal to the development of the dosage form, based on the specifications developed. A specification is defined as a list of tests, references to analytical procedures, and appropriate acceptance criteria that are numerical limits, ranges, or other criteria for the tests described. It establishes the set of criteria to which a new drug substance or new drug product should conform to be considered acceptable for its intended use. Conformance to specifications means that the drug substance and/or drug product, when tested according to the listed analytical procedures, will meet the listed acceptance criteria. Specifications are critical quality standards that are proposed and justified by the manufacturer and approved by regulatory authorities as conditions of approval. It is possible that, in addition to release tests, a specification may list in-process tests, periodic or skip tests, and other tests that are not always conducted on a batch-by-batch basis. When a specification is first proposed, justification should be presented for each procedure and each acceptance criterion included. The justification should refer to relevant development data, pharmacopoeia standards, test data for drug substances and drug products used in toxicology and clinical studies, and results from accelerated and long-term stability studies, as appropriate. In addition, a reasonable range of expected analytical and manufacturing variability should be considered. Test results from stability and scale-up/validation batches, with emphasis on the primary stability batches, should be considered in setting and justifying specifications.

The U.S. FDA recommends the initiative process analytical technology (PAT), which applies to both drug substances and drug products (1). The PAT is a system for designing, analyzing, and controlling the manufacture 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 the final product quality. The goal of PAT is to understand 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.* 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. There are many current and new tools available that enable scientific, risk-managed pharmaceutical