

active moiety is absorbed from a drug product and becomes available at the site of action. For drug products that are not intended to be absorbed into the bloodstream, bioavailability may be assessed by measurements intended to reflect the rate and extent to which the active ingredient or active moiety becomes available at the site of action [3]. Thus, drug product performance applies to both locally acting drug products, such as topical corticosteroids, and drugs intended for systemic absorption. The performance of each drug product must be consistent and predictable to assure both clinical efficacy and safety.

Defects in product quality can lead to poor drug product performance and affect safety and/or efficacy. Each component of the drug product and the method of manufacture contribute to quality. Quality is maintained by implementing systems and procedures that are followed during the development and manufacture of the drug product. Bioavailability, bioequivalence, and drug release/dissolution are important measures of drug product performance. Equivalent drug product performance is necessary to assure therapeutic equivalence. Thus, manufacturers of new and generic drug products must take into consideration drug product quality and drug product performance, so that each manufactured batch is equivalent and performs similarly *in vivo*. Likewise, both the generic drug product and its brand name alternative must also perform similarly, which is the basis of therapeutic equivalence.

GENERIC DRUG PRODUCT DEVELOPMENT

Generic drug product development uses a different approach and strategy compared with that used to develop a brand name drug product containing a new chemical entity. Generic drug product manufacturers must formulate a drug product that will have the same therapeutic efficacy, safety, and performance characteristics as its brand name counterpart. To gain market approval, a generic drug product cannot be “superior” or “better” than the brand name drug product. The key factor is that the generic drug product should meet all the necessary criteria to be therapeutically equivalent to the brand name (reference) drug product.

The manufacturer of a generic drug product has certain constraints in formulation development that differ from the formulation development of a brand name drug product. Generic drug manufacturers also face a variety of legal challenges from the brand name (innovator) pharmaceutical industry. For example, a generic drug manufacturer may not be able to use the same or similar inactive ingredients or excipients as in the brand formulation due to existing patents by the innovator. These issues will be discussed more thoroughly in subsequent chapters.

Initially, the generic manufacturer must find a source of the API and develop a finished dosage form (Figure 1.1). The method of manufacture of the API and its physical chemical characteristics, such as polymorphic (crystalline) form, should not infringe with patents filed by the innovator. In addition, an impurity profile for the generic API may be different from the brand due to a different synthetic routes of manufacture. The finished dosage form (e.g., an immediate-release or modified-release tablet) must also not infringe on formulation patents. To avoid patent infringement, the dosage form manufactured by the generic drug product manufacturer may use a different drug release mechanism compared with the brand; therefore, the