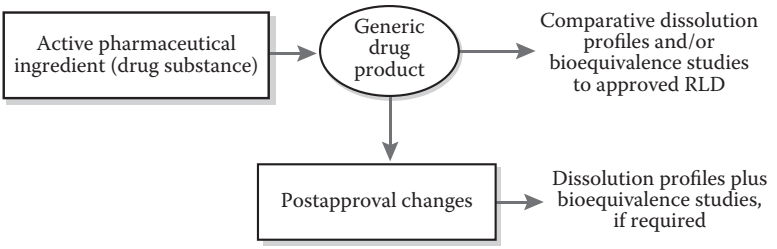

FIGURE 1.1 Drug product performance and generic drug product development. Reference listed drug (RLD) product performance may be determined in vivo by bioequivalence studies or in vitro by comparative drug/release dissolution studies. (From Shargel, L. et al. *Applied Biopharmaceutics & Pharmacokinetics*, 6th edition. McGraw-Hill, New York, 2012, Chapter 15.)

relationship between drug release and bioavailability may not be predictable in vitro. After drug approval, any scale-up, post-approval changes, including a site change, may also require comparative bioavailability studies to confirm bioequivalence.

SELECTION OF A GENERIC DRUG PRODUCT FOR MANUFACTURE

The main driving force for the selection of generic drug products for manufacture is the estimated sales volume for the branded product and the potential market share that the firm expects to have once the generic drug product is manufactured and approved for marketing (Table 1.1). Patent and legal considerations are also very important and are discussed more fully in Chapter 15. The generic drug manufacturer must consider the expiration date of the patent for the active ingredient and any other patent claims and exclusivities that the innovator firm has filed. In addition, the generic drug manufacturer needs to consider the lead time that is needed to make the product and submission of an Abbreviated New Drug Application (ANDA) to the FDA for approval. Timing is important, because the generic manufacturer would like to have their product submitted and approved just before patent expiration of the innovator's drug product. There is a large financial incentive to being the first generic drug product filed and approved by the FDA. The Hatch–Waxman Act, as

TABLE 1.1
Considerations in the Selection of a Generic Drug Product for Manufacture

Sales and potential market share
Patent expiration and exclusivity issues
Availability of API
Timing
Available technology
Formulation and dosage form
Experience
Development costs