

evaluated a particular approved product as therapeutically equivalent to other pharmaceutically equivalent products (first letter) and to provide additional information based on the FDA's evaluations (second letter).

## REFERENCE LISTED DRUG

In most countries, the RLD is generally the innovator drug product ("Brand"), which is marketed based on a full dossier that includes chemical, biological, safety, clinical efficacy, labeling, etc. The FDA identifies the RLD to which the *in vivo* bioequivalence (reference standard) and, in some instances, the *in vitro* bioequivalence of the applicant's product are compared (Table 1.4). By designating a single RLD as the standard to which all generic versions must be shown to be bioequivalent, the FDA hopes to avoid possible significant variations among generic drug products and their brand name counterparts. Such variations could result if generic drug products were compared with different RLDs.

At times, there may be two different NDA holders for the same active ingredient. In Table 1.4, Adalat CC (nifedipine ER tablet) is an RLD listed as AB1 and Procardia XL (nifedipine ER tablet) is an RLD listed as AB2. Because Adalat CC and Procardia XL have not established bioequivalence to each other, the ANDA sponsor must consider which RLD will be used. In the case of other domestic market places, such as European countries, the RLD is usually the brand name that has been approved and marketed domestically in that country.

**TABLE 1.4**  
**RLD—Nifedipine Extended-Release Oral Tablet**

TE Code	RLD	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
AB1	Yes	Nifedipine tablet	Extended release; oral	90 mg	Adalat CC	Bayer Healthcare
AB1	No	Nifedipine tablet	Extended release; oral	90 mg	Nifedipine	Actavis
AB1	No	Nifedipine tablet	Extended release; oral	90 mg	Nifedipine	Valeant International
AB2	Yes	Nifedipine tablet	Extended release; oral	90 mg	Procardia XL	Pfizer
AB2	No	Nifedipine tablet	Extended release; oral	90 mg	Nifedipine	Mylan
AB2	No	Nifedipine tablet	Extended release; oral	90 mg	Nifedipine	Osmotica Pharm
AB1	No	Nifedipine tablet	Extended release; oral	90 mg	Nifedipine	Mylan

*Source:* Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations ([www.accessdata.fda.gov/scripts/cder/ob/default.cfm](http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm).)