sublingual tablets, water at about 37°C serves as the immersion fluid unless another fluid is specified in the individual monograph. For these tests, complete disintegration is defined as "that state in which any residue of the unit, except fragments of insoluble coating or capsule shell, remaining on the screen of the test apparatus is a soft mass having no palpably firm core" (7). Tablets must disintegrate within the times set forth in the individual monograph, usually 30 minutes, but varying from about 2 minutes for NTG tablets to up to 4 hours for buccal tablets. If one or more tablets fail to disintegrate, additional tests prescribed by the USP must be performed.

Enteric-coated tablets are similarly tested, except that the tablets are tested in simulated gastric fluid for 1 hour, after which no sign of disintegration, cracking, or softening must be seen. They are then actively immersed in the simulated intestinal fluid for the time stated in the individual monograph, during which time the tablets disintegrate completely for a positive test.

Tablet Dissolution

In vitro dissolution testing of solid dosage forms is important for a number of reasons (8):

1. It guides formulation and product development toward product optimization. Dissolution studies in the early stages of a product's development allow differentiation between formulations and correlations identified with in vivo bioavailability data.
2. Manufacturing may be monitored by dissolution testing as a component of the overall quality assurance program. The conduct of such testing from early product development through approval and commercial production ensures control of any variables of materials and processes that could affect dissolution and quality standards.
3. Consistent in vitro dissolution testing ensures bioequivalence from batch to batch. In assessing such bioequivalence, the U.S. Food and Drug Administration (FDA) allows manufacturers to examine scale-up batches of 10% of the proposed size of the actual production batch or 100,000 dosage units, whichever is greater.
4. It is a requirement for regulatory approval of marketing for products registered with the FDA and regulatory agencies of other countries. New Drug Applications (NDAs) submitted to the FDA contain in vitro dissolution data generally obtained from batches used in pivotal clinical and/or bioavailability studies and from human studies conducted during product development (9). Once the specifications are established in an approved NDA, they become official (USP) specifications for all subsequent batches and bioequivalent products.

The goal of in vitro dissolution testing is to provide insofar as is possible a reasonable prediction of or correlation with the product's in vivo bioavailability. The system relates combinations of a drug's solubility (high or low) and its intestinal permeability (high or low) as a possible basis for predicting the likelihood of achieving a successful in vivo–in vitro correlation (IVIVC) (9,10). Using this system, drugs are placed into one of four categories as follows:

I High solubility and high permeability	II Low solubility and high permeability
III High solubility and low permeability	IV Low solubility and low permeability

For a high-solubility and high-permeability Category I drug, an IVIVC may be expected if the dissolution rate is slower than the rate of gastric emptying (the rate-limiting factor) (11). In the case of a low-solubility and high-permeability Category II drug, dissolution may be the rate-limiting step for absorption, and an IVIVC may be expected. In the case of a high-solubility and low-permeability Category III drug, permeability is the rate-controlling step, and only a limited IVIVC may be possible. In the case of a Category IV drug with low solubility and low permeability, significant problems are likely for oral drug delivery (9).

As noted previously, tablet disintegration is the important first step to the dissolution of the drug in a tablet. A number of formulation