CASE STUDY 3

Drug B is slightly soluble in water, and its water solubility is pH dependent with higher solubility at higher pH. Drug B has moderate permeability and is a BCS Class IV drug. The initial proposed dissolution method for drug B tablet was the USP apparatus 2 at 50 rpm in pH 6.8 phosphate buffer with the acceptance criterion of 80% in 30 min. However, during product development, three lots of products from the same formulation, but different manufacturing processes, were evaluated in bioequivalence/bioavailability studies. These three lots of products were bioequivalent, although Lot C failed to meet the dissolution acceptance criterion of 80% in 30 min and Lot B had to use S2 in order to pass the dissolution acceptance criterion. Therefore, the dissolution testing is more discriminating, as shown in Figure 6.4.

In order to establish an appropriate acceptance criterion, the additional dissolution studies with biorelevant dissolution media FaSSIF in Table 6.1 were conducted, and the results are shown in Figure 6.5. Figure 6.5 indicates that the dissolution rate has been uniformly increased, and all three lots pass the acceptance criterion of 80% in 30 min. On the basis of these biorelevant dissolution results along with the bioequivalence study data, the acceptance criterion was reduced to 70% in 30 min.

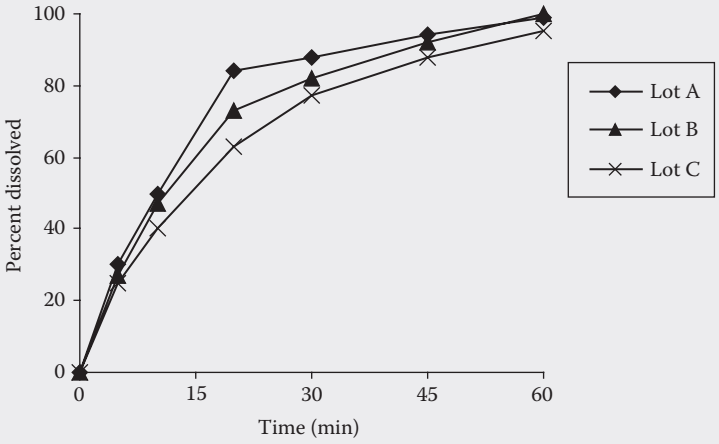

FIGURE 6.4 Dissolution of three lots of drug B tablet in pH 6.8 phosphate buffer.

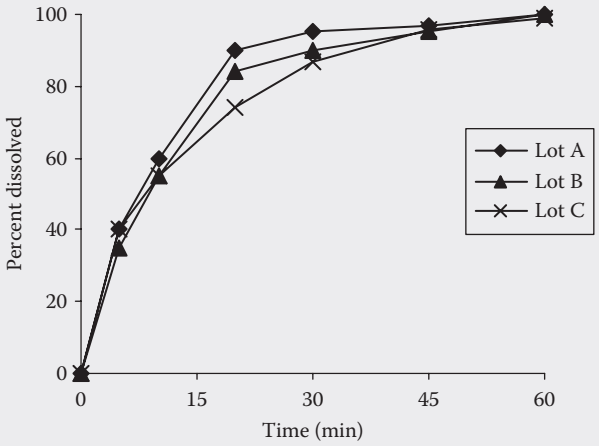

FIGURE 6.5 Dissolution of three lots of drug B tablet in pH 6.8 FaSSIF.