

degradation products formed, although it may not be possible to account for 100% of degradation products by the observed loss in actives. This mass balance checking should be performed for method validation study. It should also be considered when the method is applied to product stability study so that the decrease in assay value for the active(s) is mass balanced with the amount of impurities observed. The method specificity becomes more challenging when the product contains multiple actives and the strength of these actives differs in orders of magnitude.

In developing a dissolution method, one should consider that the medium used for the test should meet the sink condition for the *in vitro* test. For water-insoluble compounds, the dissolution medium may contain surfactants or organic solvents, although the latter should be avoided if possible. The assay for the drug release method can be a chromatographic procedure such as HPLC, a spectrophotometric procedure such as UV, or other suitable procedures. Shorter run times for chromatographic procedures are necessary due to the large number of samples to be analyzed for dissolution profiling studies. As mentioned earlier, compendial dissolution method should be considered first. Because the dissolution is formulation dependent, the alternative dissolution method can be submitted in the ANDA application and subsequently to the USP for monograph update if the drug product is shown to be bioequivalent to that of the innovator.

METHOD VALIDATION

Method validation is the process of demonstrating that the analytical method is suitable for its intended use. The validation process establishes documented evidence that provides a high degree of assurance that the test method will consistently provide accurate test results that evaluate a product against its defined specification and quality attributes.

OBJECTIVES OF METHOD VALIDATION

Validation of analytical methodologies is considered as an important task, occurring after method development and before method utilization, and is required in support of product registration applications such as ANDA and NDA applications to the FDA.

METHOD VALIDATION REQUIREMENTS

Compendial Analytical Procedures

The validation of a test method normally depends on whether the test method is a compendial method or a noncompendial method. The validation of compendial methods is described in USP <1225>. Users of analytical methods described in the USP and the NF are not required to validate accuracy and reliability of these methods but to merely verify suitability under actual conditions of use. The methods provided in official monographs have been validated by the laboratory submitting the monograph and may have also been verified by other laboratories designated by the