Standards Qualification and Handling

The standard used for the method validation must be qualified. A vendor's certificate of analysis with the purity factor is needed for establishing quantitative relationships such as relative response factors. It is preferable to use compendial standards if available for method validation. A standard qualification report is part of the requirements for questions-based review document in ANDA submission in common technical documents format.

Optimization of the Experimental Sequence for Efficiency

Validation experiments should be designed that are efficient and optimized for resource utilization.

Resources and Timelines

The number of personnel needed for the validation should be well planned. The person involved in the method validation must be trained on cGMP compliance and method validation SOPs. The timeline for the method validation should be reasonable for full documentation, for data and notebook review and signature, and for quality review and approval process. Method validations must be completed before the methods' application for API testing in pilot bio-batch or exhibit batch release.

Validation Report

The validation report is a summary of the results obtained during execution of the validation protocol. The results are compared with the acceptance criteria. The validation report must discuss whether the results pass or fail the acceptance criteria and conclude if the method is suitable for its intended use.

The validation report must also discuss and document any deviation from the protocol, justify the deviation, and analyze the impact of the deviation.

During the method validation, some parameters of the test method may be required to be modified (such as system suitability parameters) or finalized (such as relative retention time and relative response factors). These suggestions should be documented in the method validation report along with the justification for the method change.

Method Equivalency Study

When an in-house method and a compendial method exist for the same test, a comparison with the compendial monograph test method must be established to demonstrate that the in-house method is equivalent or better than the compendial method. The assessment of method equivalency can be based on statistical principles such as *F*-tests and *t*-tests or approved acceptance criteria. One lot of the finished drug product can be chosen to compare both the in-house test method and the compendial test method. The sample with multiple preparations is assayed and the results from both methods are compared. If the results pass the preapproved acceptance criteria or the statistical analysis, the two test methods are considered equivalent.