

What constitutes validation? The validation of analytical method is the process in determining the suitability of a given methodology by laboratory studies that the method in question can meet the requirements for the method's intended use. Method validation is not simply a measure of procedure; method validation is a measure of performance of the total analytical system. Sections 211.165(c) and 211.194(a)(2) of the cGMP for method validation specify that any method adopted at the product development stage be verified under actual conditions of use, and that subsequent variations on existing methodology are subjected to validation.

General Chapter <1225> states, "Validation is the process of providing documented evidence that the method does what it is intended to do." In other words, the process of method validation ensures that the proposed analytical methodology is accurate, specific, reproducible, and rugged for its intended use.

The articles in the current revision of the Compendia are also recognized to be legal standards when determining compliance with the Federal Food, Drug, and Cosmetic Act. Regulated industries must perform method validation to comply with Compendial or other regulatory requirements, and the data generated becomes a part of the methods validation package submitted to the FDA.

Similarly, the general regulation, which is currently represented in 21 CFR 2.19, states, "Where the method of analysis is not prescribed in a regulation, it is the policy of FDA, in its enforcement programs to utilize the methods of analysis of AOAC as published in the current edition." Further, it is stated in the FDA's current Good Manufacturing Practices for Finished Pharmaceuticals regulations 21 CFR 211.165(e) and 21 CFR 211.194(a)(2) that if a firm is using AOAC-OMA or USP/NF methods of analysis, only minimal additional validation data is required (35).

## 15. VALIDATION PROTOCOL

While the text of Title 21 CFR Part 211, ICH Guidelines, and General Chapter <1225> all provide terms and definitions, there is no specific discussion of validation protocol and methodology. In ICH Guidelines (Q2B) on Method Validation Methodology, the applicant has been made responsible for the appropriate validation protocol and procedure suitable for their product. Therefore prior to initiating a validation study, a well-planned validation protocol is required. This protocol should consist of experimental design and elements required for validation of the proposed test method that have been reviewed for scientific soundness and completeness by qualified individuals and approved by appropriate company management authority. The validation protocol should include a detailed test procedure, basic experimental design, elements for validation, predefined acceptance criteria, reference of related methods, and management approval.

As mentioned earlier, description of the test method is very significant for successful validation. Therefore a test procedure is a description of the "analytical method" to be used as a guide in validating the method and serves as a basis for the preparation of the validation protocol. It should include

1. A listing of reagents, solvents, and other supplies
2. Instructions for the preparation of standards, samples, and solutions
3. A listing of equipment to be used or equivalents
4. Instrumental parameters and chromatographic conditions