13.3. Nonchromatographic Methods

Approaches and guidelines used to develop and validate a chromatographic method can be applied to develop nonchromatographic methods (not stability-indicating) as well. It is equally appropriate to follow the guidelines of USP 23 General Chapter <1225>, Validation of Compendial Method (34), selecting and validating those analytical elements that are needed for a rugged method. These nonchromatographic methods include UV spectrophotometry, atomic absorption, infrared spectroscopy, and titrimetry.

Additional discussions on the validation of various nonchromatographic methods are found in Sec. 19.3.

Part II: Method Validation

14. REGULATORY AND COMPENDIAL BASIS OF METHOD VALIDATION—WHERE TO START

Analytical methods including chromatographic and nonchromatographic techniques are used to generate reliable and accurate data during drug development and post approval of the drug products. The testing, in general, includes the acceptance of raw materials and the release of drug substances and finished products, in process testing, and analysis of stability samples for establishing expiration dating. Therefore test methods that are used to assess the compliance of pharmaceutical products with established acceptance criteria must meet proper cGMP standards of accuracy and reliability as set forth by the regulatory agencies (35).

According to Section 501 of the Federal Food, Drug, and Cosmetic Act, assays and specifications in monographs of the USP and NF constitute legal standards. Under the Food Drug, and Cosmetic Act, the FDA can enforce the USP/NF standards of strength, quality, purity, packaging, and labeling. Therefore for compliance purposes, every analytical method should be validated according to pharmacopeial standard, because each method could be included in a drug monograph.

Method validation is a regulatory requirement. The Food and Drug Administration and the International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use have published a series of guidelines on the validation of analytical procedures (36,37). In USP 23/NF 18, General Chapter <1225> has been allocated for validation of compendial methods (34). This chapter describes in detail as well as in summary how to evaluate particular performance parameters. In general, it is assumed that this chapter is applied to chromatographic methods of analysis, and that for nonchromatographic procedures some alternate guidelines should be used. However, in USP 23/NF 18 no such distinction has been made. Therefore performance parameters given in General Chapter <1225> can be used to evaluate the performance of any analytical method. However, one needs to be careful in selection of performance parameters. Also, methods described in the current USP are not stability-indicating in nature. Therefore for monitoring of stability studies, guidelines given in General Chapter ⟨1225⟩ can be used to validate these methods.