18.1.2. Acceptance Criteria

For each step of the validation analytical parameters, acceptance criteria to determine success or failure of validation, are required. These acceptance criteria should be based on the intended use of the method. Also, regulatory implications should be taken into consideration. For acceptance criteria, it is imperative that responsible personnel with backgrounds in method development be involved. All validation steps should be evaluated against these acceptance criteria. Similarly, system suitability parameters should also accompany acceptance criteria. General acceptance criteria for each validation parameter have been discussed in Sec. 17.

18.1.3. Generation of the Test Method

Generation of the test method is the responsibility of the method's development group. The test method must include a detailed written procedure. For example, for a chromatographic procedure, preparation of mobile phase, column type, detector type, wave length, injection volume, flow rate, reference standard (USP/in-house), preparation of standard and sample solutions, reagent grade, and filters used for standard and sample solutions should be documented. If the method is designed to quantitate the main analyte and impurities simultaneously, then relative retention times for impurities should be given. If the main bulk active is light sensitive, then a precautionary note is required in the test method. Similarly, it should be reflected in the test method whether ambient or elevated temperature is required.

18.2. Revalidation

At some time during the lifetime of the method, for one reason or another, revalidation of the method may become necessary. For revalidation, reactive or proactive approaches may be used. Reactive validation will be required for changes in incoming bulk drug active, manufacturing batch changes, formulation changes, or other changes such as dilutions or sample preparation in the method. Recently, method change versus an adjustment has been the subject of discussion between regulatory agencies and industry (36,38,47).

This distinction is critical, as a process change requires method revalidation, whereas an adjustment does not. As a result of these discussions, limit changes for chromatographic changes do not require revalidation. Changes have been proposed under the following categories:

Aqueous buffer pH

1. Analytes without ionizable groups: ±1 unit
2. Analytes with basic or acidic groups and the buffer pH = pKa±2 units: ±0.2 unit
3. Analytes with basic or acidic groups and the buffer pH ⟨or⟩ pKa±2 units: ±1 unit

In each case a reference standard must be used to demonstrate that there is improvement in chromatography due to pH adjustment. No pH adjustment is allowed if standards are not available for all analytes of interest