

Standard Operating Procedure

Title: Method Validation Procedure

4.1.2. Determination

The accuracy of an analytical method may be determined by applying that method to samples or mixtures of excipients to which known amounts of analyte have been added both above and below the normal levels expected in the samples. The accuracy is then calculated from the test results as the percentage of analyte recovered by the assay.

4.2. Precision

4.2.1. Definition

The precision of an analytical method is the degree of agreement among individual test results when the procedure is applied repeatedly to multiple samplings of a homogeneous sample. The precision of an analytical method is usually expressed as the standard deviation or relative standard deviation (coefficient of variation). Precision may be a measure of either the degree of reproducibility or of repeatability of the analytical method under normal operating conditions. In this context, reproducibility refers to the use of the analytical procedure in different laboratories. Intermediate precision expresses within-Laboratory variation, as on different days, or with different analysts to the use of the analytical procedure within a Laboratory over a short period of time using the same analyst with the same equipment. For most purposes, repeatability is the criterion of concern in analytical procedures.

4.2.2. Determination

The precision of an analytical method is determined by assaying a sufficient number of aliquots of a homogeneous sample to be able to calculate statistically valid estimates of standard deviation or relative standard deviation (coefficient of variation). Assays in this context are independent analyses of samples that have been carried through the complete analytical procedure from sample preparation to final test result.

4.3. Specificity

4.3.1. Definition

The specificity of an analytical method is its ability to measure accurately and specifically the analyte in the presence of components that may be expected to be present in the sample matrix. Specificity may often be expressed as the degree of bias of test results obtained by analysis of samples containing added impurities, degradation products, related chemical compounds, or placebo ingredients when compared to test results from samples without added substances. The bias may be expressed as the difference in assay results between the two groups of samples. Specificity is a measure of the degree of interference (or absence thereof) in the analysis of complex sample mixtures.

4.3.2. Determination

The specificity of an analytical method is determined by comparing test results from the analysis of samples containing impurities, degradation products, or placebo ingredients with those obtained from the analysis of samples without impurities, degradation products, or placebo ingredients. The bias of the assay, if any, is the difference in test results between the two groups of samples. When impurities or degradation products are unidentified or unavailable, specificity may be demonstrated by analysis by the method in question of samples containing impurities or degradation products and comparing the results to those from additional purity assays (e.g. chromatographic assay, phase solubility differential scanning calorimetry). The degree of agreement of test results is a measure of the specificity.

4.4. Limit of Detection

4.4.1. Definition