A Guide to Analytical Method Validation

INTRODUCTION

Analytical method development and validation are two of the most important aspects of method development. These two processes are complementary and should be performed in concert. Method development is the process by which a method is designed and optimized, while method validation is the process by which the performance characteristics of the method are established. Method validation is critical to ensure that the method is fit for its intended purpose.

SPECIFICITY

Specficity is the ability of the method to determine accurately and specifically the analyte in the presence of other components that may interfere with the measurement of the analyte. Performance characteristics related to specificity include:

- The method's ability to distinguish between the analyte and its possible interferents
- The method's ability to detect the analyte in the presence of other components

REPRODUCIBILITY

Reproducibility is the precision of the method. Performance characteristics related to reproducibility include:

- The method's ability to produce consistent results across different analysts, laboratories, and instrument settings
- The method's ability to produce consistent results across different time points within a given day

ROBUSTNESS

Robustness is the capacity of a method to remain unaffected by small, deliberate changes in method parameters. Performance characteristics related to robustness include:

- The method's ability to produce consistent results across different conditions
- The method's ability to produce consistent results across different laboratories

LINEARITY AND RANGE

The linearity of a method is the ability of the method to provide a linear response over a specified range of concentrations. Performance characteristics related to linearity and range include:

- The method's ability to provide a linear response over the specified concentration range
- The method's ability to provide consistent results across different concentration levels

ACCURACY

Accuracy is the closeness of test results to the true value. Performance characteristics related to accuracy include:

- The method's ability to produce consistent results across different days
- The method's ability to produce consistent results across different analysts

PRECISION

Precision is the degree of agreement among individual test results when an analytical method is used repeatedly to measure the same substance under恒定条件。Performance characteristics related to precision include:

- The method's ability to produce consistent results across different days
- The method's ability to produce consistent results across different analysts

QUANTITATION LIMIT (LOQ)

The quantitation limit (LOQ) is defined as the lowest concentration of an analyte in a sample that can be quantitatively determined. Performance characteristics related to quantitation limit include:

- The method's ability to produce consistent results across different concentration levels
- The method's ability to produce consistent results across different analysts

DETECTION LIMIT (LOD)

The detection limit (LOD) is defined as the lowest concentration of an analyte in a sample that can be detected with a suitable degree of confidence. Performance characteristics related to detection limit include:

- The method's ability to produce consistent results across different concentration levels
- The method's ability to produce consistent results across different analysts

SYSTEM SUITABILITY

System suitability is the checking of a system to ensure system performance before or during the analysis of unknowns. System suitability parameters are established as a direct result of robustness studies.

- The method's ability to produce consistent results across different days
- The method's ability to produce consistent results across different analysts

INSTRUMENTAL METHODS

Instrumental methods are designed to provide a solution to a specific analytical problem. Performance characteristics related to instrumental methods include:

- The method's ability to produce consistent results across different concentration levels
- The method's ability to produce consistent results across different analysts

SOURCES OF ERROR

Sources of error are factors that can cause variation in the results of an analytical method. Performance characteristics related to sources of error include:

- The method's ability to produce consistent results across different days
- The method's ability to produce consistent results across different analysts

DATA ELEMENTS REQUIRED FOR ASSAY VALIDATION

When validating an analytical method, it is important to include the necessary data elements to ensure the method is fit for its intended purpose. Performance characteristics related to data elements required for assay validation include:

- The method's ability to produce consistent results across different concentration levels
- The method's ability to produce consistent results across different analysts

REFERENCES

The methodology presented in this guide is based on the guidelines outlined by the United States Pharmacopeial Convention (USP) and the International Conference on Harmonization (ICH). Performance characteristics related to references include:

- The method's ability to produce consistent results across different concentration levels
- The method's ability to produce consistent results across different analysts

Perfect Combination: Fast and Easy Validation with Superior Results

Waters Method Validation Manager (MVM) Option for Empower® 2 Software

- Manage method validation workflow in one automated application
- Calculate and store statistical results directly in Empower® 2 Software
- Trace validation back to raw data, methods or chromatographic results
- Save time with automatic data checking, reusable report templates

Waters ACQUITY UPLC® System

- Accurate, reproducible and robust Ultra Performance LC® methodology
- Methods are validated with substantial time savings over HPLC
- Significant ROI benefits are realized by validating new and existing methods with UPLC™