Method Development Performance Characteristics

Accuracy, or bias, is a measure of the agreement between an experimental result and the underlying true (or accepted) result. Accuracy is established by analyzing standard samples and spike recoveries, and is reported as a percent error and by significance testing. As accuracy may vary across a range of analyte concentrations, it typically is evaluated at high, medium, and low concentrations of analytes using at least three replicates—but preferably more—at each concentration.

Precision is a measure of consistency in results when using an analytical method, and is reported as a standard deviation, a relative standard deviation, a variance, and/or a confidence interval. Precision is divided into repeatability (variation in multiple analyses obtained using single set of conditions) and reproducibility (variation in results over multiple analyses that differ in the sample, analyst, lab, day, and/or snother variable that might introduce uncertainty). As precision may vary across a range of analyte concentrations, it typically is evaluated at high, medium, and low concentrations of analytes using at least three replicates—but preferably more—at each concentration.

Selectivity, or specificity, is the ability to determine the analyte's concentration, with acceptable accuracy and precision, when in the presence of another species that might reasonably be present in the sample. A method's specificity for the analyte is determined by analyzing samples that contain known concentrations of an analyte and an interferent, and determining the maximum relative amount of interferent that allows for acceptable accuracy.

A method's **limit of detection** is the smallest concentration of analyte that allows for a confirmation that the analyte is present even if its exact concentration is too small to report with confidence. The limit of detection typically corresponds to the concentration of analyte yielding a signal that is at least three times greater than the standard deviation for a method blank.

A method's **limit of quantitation** is the smallest concentration of analyte that is reported with an acceptable precision and accuracy. The limit of quantitation typically corresponds to the concentration of analyte yielding a signal that is at least ten times greater than the standard deviation for a method blank.

Linearity is the ability to establish a mathematical relationship between the analyte's signal (or a transformed version of the analyte's signal) and its concentration. Although a straight-line relationship is preferred—and, thus, the use of linearity—it is not a strict requirement. To establish linearity, use a minimum of five standards, determine the regression equation, and evaluate statistically and visually the regression equation and data.

Range is the interval between the smallest and the largest concentration of analyte that allows for acceptable precision, accuracy, and linearity. The ideal range spans the analyte's presumed concentration in samples without requiring the concentrating or diluting of samples prior to their analysis; however, the need for acceptable precision, accuracy, and linearity is more important than minimizing sample preparation.

Ruggedness is the ability of an analytical method to produce results of acceptable accuracy and precision in the presence of reasonable variability in how individual analyst's will carry out the procedure. An analytical method's ruggedness is tested by intentionally introducing multiple small, but reasonable, variations to the procedure and examining the results using a factorial design.