line calculated according to an established mathematical relationship from test results obtained by the analysis of samples with varying concentrations of analyte. The linear range of detection that obeys Beer's law is dependent on the compound analyzed and the type of detector used.

USP General Chapter <1225> gives general directions on the determination of linearity along with handling of the data. However, there are no concentration levels specified to monitor linearity. The ICH also has adopted an approach similar to that of the USP for the determination of linearity and data interpretation. The least squares method is recommended for evaluation of the regression line.

The correlation coefficient, y-intercept, slope of the regression line, and residual sum of squares should be reported. For linearity studies, a minimum of five concentrations is recommended. According to the FDA Reviewer Guidance, the linearity range depends on the intended use of the test method. For content assay, linearity should be performed between 80% and 120% of target concentration. The linearity range for the assay/impurities combination method based on area percent (for impurities) should be greater than 20% of the target concentration down to the limit of quantitation of the drug substance or impurity. A coefficient of correlation (r^2) value, an intercept, and a slope should be reported.

17.8. Range

The range of an analytical method is the interval between the upper and lower concentration levels of analyte (including these concentrations) for which the method as written has been shown to be precise, accurate, and linear. The range is usually expressed in the same units as test results obtained by the analytical method. According to USP General Chapter <1225>, the range of method is validated by verifying that acceptable precision and accuracy is obtained by the analytical method when actual analysis of samples containing analyte is performed throughout the intervals of the range.

The ICH recommends an approach similar to the USP for validation of range. It recommends specific ranges based on the intended use of the method, as follows.

1. For assay of a drug substance or drug product, the minimum specified range is 80% to 120% of the target concentration.
2. For content uniformity testing, the minimum range is 70% to 130%.
3. For the determination of impurity, the minimum range is from the reporting level of an impurity to 120% of the specification.
4. For a combination assay procedure for both active and impurity, where a 100% standard is used, linearity should cover the range from reporting level to 120% of the assay specification.
5. For dissolution testing, the recommended range is ±20% over the specified range of the test. That is, in the case of an extended release product dissolution test with a Q value of 20% after 1 hour, up to 90% in 24 hours, the range for validation will be 0 to 110% of the label claim.
6. For toxic or more potent impurities, the range should be commensurate with the controlled level. FDA recommendations for range are as discussed under the Linearity and Accuracy sections. These ranges can also be applied to other substances such as preservatives.