for evaluating linearity. The determination of linearity should be done using the method of quantification specified in the procedure.

Evaluation of linearity for TLC may be performed by visual examination of the plate, if this is consistent with the method of quantification specified in the procedure. A linear relationship for the main standard spot may be confirmed visually by an increase in intensity with concentration. The sample concentration may then be "estimated" by comparison with the standards.

Recommended Linearity Acceptance Criteria:
The assay need not give results that are directly proportional to the concentration (amount) of analyte in the sample for the test method to be valid. However, the desire to have a linear relationship reflects a practical consideration, since a linear relationship should be accurately described with fewer standards.
A validated method may be sufficiently linear to meet accuracy requirements in the concentration range in which it is intended to be used. When inferring accuracy from a linearity study, linearity could be considered acceptable if results, as compared to a standard, meet the accuracy criteria. A plot of the data should visually appear to be linear. Suggested acceptance criteria (for API Raw Material, In Process Control, and early intermediate material tests) for an acceptable linear relationship may be a test method having a minimum correlation coefficient (r) of > 0.95.

Range:
The range is the interval between the upper and lower levels of analyte concentration for which acceptable linearity, accuracy (recovery), and precision are obtained. It is recommended that the range be established to include all specification limits for a method and the expected results. The range should include at least five points to establish linearity. Values outside of the validated range can be reported as estimates. Range should be established by summarizing the accuracy (where appropriate), the linearity, and the precision data.

The following minimum specified ranges are taken from ICH and may be considered as minimum start points for test methods within the scope of this document.

   o   For the assay, the ICH range is normally from 80% to 120% of the test concentration. If assay and purity are performed together as one test and only a 100% standard is used, linearity should cover the range from the reporting level of the impurities to 120% of the assay specification.

   o   For determination of an impurity; the range of concentrations used to evaluate the linearity should consist of the quantitation limit and at least 120% greater than the concentration that would be the impurity specification limit.

   o   For example, if the concentration at the specification limit was 0.2% w/w, and the limit of quantitation was 0.08% w/w then the range should span 0.08% (w/w) to 0.24% w/w. For example, the concentrations for the linearity experiment might be 0.08%, 0.12%, 0.16% 0.20% and 0.24%. More solutions may be evaluated if the linearity range must be extended.

   o   In cases where specified impurities/degradation products are not available a surrogate material such as a compound with similar structure or API may be used to demonstrate linearity. In these cases, a rationale for the use of a surrogate should be given.