the signal-to-noise ratio convention but also lists several other approaches for determining DL, depending on whether the procedure is instrumental or noninstrumental. These approaches are as follows.

A. BASED ON VISUAL EVALUATION. Visual evaluation may be used both for instrumental and noninstrumental methods. It requires analysis of samples with concentrations of analyte and establishing the minimum level at which analyte can be reliably detected. Visual noninstrumental methods can include DL determined by techniques such as TLC or titration.

B. BASED ON THE STANDARD DEVIATION OF THE RESPONSE AND THE SLOPE. The detection limit may be calculated based on the standard deviation (SD) of the response and slope (S) of the calibration curve (a specific curve should be generated by using samples containing analyte in the range of detection limit), according to the formula

$$\text{Detection limit (DL)} = 3.3 \times \text{SD}$$

The SD of the response can be determined from the SD of the blank, the residual SD of the regression line, or the SD of the y-intercept of the regression line. The detection limit and method used to determine the detection limit must be documented and supported, and a suitable number of samples should be analyzed at the limit to validate it. The FDA is of the opinion that expression of the detection limit in terms of a signal-to-noise ratio of 2 or 3 is not very practical. The reason for this is attributed to differences in the noise level on a detector during the method development phase and when samples are analyzed on different detectors. Detector sensitivity can vary with the model number or manufacturer.

17.6. Quantitation Limit (QL)

The quantitation limit is the lowest concentration of analyte in a sample that can be determined with acceptable precision and accuracy under the stated experimental conditions of the method. This is a parameter of the quantitative assays for low concentrations of compounds in sample matrices such as impurities in bulk drug substances and degradation products in finished products.

In the current USP General Chapter <1225>, the quantitation limit, QL, which is similar to the detection limit, is expressed as the concentration of analyte in the sample, and precision and accuracy of the measurements are also reported. The QL is dependent on the type of procedure, i.e., instrumental or noninstrumental. For instrumental methods, sometimes a signal-to-noise ratio of 10 : 1 is used to determine the QL. However, it is pointed out that the determination of the QL based on signal-to-noise ratio criteria is a compromise between the concentration and the required accuracy and precision. In other words, as the QL concentration level decreases, the precision increases. For better precision, a higher concentration must be reported for the QL. This compromise is dependent on the analytical method and its intended use.

As with to the limit of detection, the ICH has recognized using a signal-to-noise ratio of 10 : 1 for quantitation. However, this approach can only be applied to analytical procedures that exhibit baseline noise. Again, as with the DL, the ICH lists the same two options that can be used to determine the QL. They are visual evaluation for both noninstrumental and instrumental methods; the latter method can