of different parameters on selectivity is studied. Method robustness can be evaluated in a stepwise univariate approach or as a part of an experimental design incorporating multivariate parameters.

Next, a linearity test over five levels for both the drug substance and the dosage form is performed. The range is determined according to the test method's intended use (34,36,38,39). Comparison of the results between the drug substance and the dosage form fulfills the accuracy requirements. A minimum of three measurements at each level should be made.

At the end of day 1, a minimum of six repetitions are performed at the 100% level of the drug substance for repeatability.

Steps 1 and 2 are repeated over additional days for intermediate precision. The detection limit (DL) and quantitation limit (QL) can then be determined if required. For calculation of these performance characteristics one can follow criteria given in the USP or ICH guidelines (Q2B). It is stated that this protocol is merely a generic example, and specific protocols or SOPs should be documented and followed for the particular method and its intended use.

16. VALIDATION PARAMETERS

Prior to conducting validation studies it is imperative to decide which parameters are required to be studied. These parameters are termed "analytical performance characteristics" or sometimes "analytical figures of merit." Most of these terms are familiar and are used daily in the laboratory. However, some may mean different things to different laboratory groups. Therefore a complete understanding of the terminology and definitions of these characteristics is important.

The selection of desired performance characteristics would depend on the type of analytical method and its intended use. For example, an assay method designed for finished product release should not be used for the determination of detection or quantitation limits of an active ingredient. However, if the method has been designed to monitor trace quantities of the active ingredient in cleaning validation samples, then knowledge of the detection and quantitation limits are appropriate and necessary.

Therefore, selection of validation parameters for each assay or test method should be made case by case, to ensure that parameters are appropriate for the intended use. This is even more important when validating stability-indicating methods, because such validations are complex, as these involve forced degradation studies, spiking of samples with known degradants and literature searches.

16.1. USP General Chapter <1225>, Validation of Compendial Methods

General Chapter <1225> (34) describes typical analytical performance characteristics, how they are determined, and which subset of data elements is required to demonstrate validity, based on the method's intended use. These performance characteristics can be referred to as the "Eight Steps of Method Validation." These analytical performance characteristics are

Accuracy
Precision
Specificity