17.9. Robustness

The robustness of an analytical procedure is a measure of its capacity to remain unaffected by small but deliberate variations in some parameters and provide an assurance of its reliability during normal usage. The robustness of the method is investigated by varying some or all conditions, e.g., organic composition of the mobile phase, pH, ionic strength, column temperature, age of column, column type. ICH guidelines recommend that robustness studies be performed during the method development stage. Also, if measurements are affected by variations in analytical conditions, the analytical conditions should be suitably controlled or a precautionary statement should be included in the test method.

Robustness can also be partly assured by good system suitability specification. Therefore, it is important to set tight but realistic system suitability specifications.

17.10. Application of Plackett–Burman Design to Ruggedness Testing

Ruggedness is normally defined as the lack of influence on test results by operational and environmental variables of the analytical method. Ruggedness is a measure of reproducibility of test results under normal operational conditions from laboratory to laboratory and from analyst to analyst. According to ASTM Guidance E 1169-89, "Standard Guide for Conducting Ruggedness Tests" (45), it is necessary to monitor the effects of environmental and experimental factors on the results obtained using the test method to assure method accuracy. Furthermore, the purpose of ruggedness testing is to determine which variables the method is susceptible to and how to control it. Ruggedness testing does not determine the optimum operational conditions for the test method. To determine the ruggedness of the method, the ASTM guidance recommends use of the experimental design as reported by Plackett and Burman. This guidance discusses effects of change on two levels per variable, as this design is easy to use and provide useful information needed for improvement of the test method. An example of ruggedness testing for an HPLC method is given in Tables 8 through 10.

Table 8 shows the various factors and their high and low limits to be considered in ruggedness testing. Table 9 shows the factors and their high and low limits in a +/− format. Lastly, Table 10 summarizes the results obtained when each of the eight combinations (rows across the spreadsheet) are experimentally performed.

Table 8 Ruggedness Testing—Typical HPLC Factors

Factor	Low value	High value
A. pH	3.0	4.0
B. Temperature	35°C	40°C
C. Mobile phase composition	45/55	55/45
D. Buffer concentration	0.05 M	0.1 M
E. Particle size	3 micron	5 micron
F. Column length	3 cm	5 cm
G. Flow rate	1.0 mL/min	1.5 mL/min