Method Procedure.

1. Choose the number of variables required and select a run design template.

2. Assigning the minus (-) or plus (+) values**:** These are arbitrary designations. As a standard rule assign a 'minus' (-) to **I** or a lower limit and a 'plus' (+) to **II** or a upper limit. Evaluate a range limit by assign (-) value for lower and (+) value for higher (i.e. Flow rate 1.2 mL/min assign (-) and 1.8 mL/min assign (+)). Likewise Day I assign (-) and Day II assign (+) and so on…

3. Perform the HPLC assays in a random order.

4. Tabulate the assay results in the template.

5. Calculate the Effects (Figures 1 and 2).

6. Rank the Effects from smallest to largest.

7. Plot the Effects against the M values.

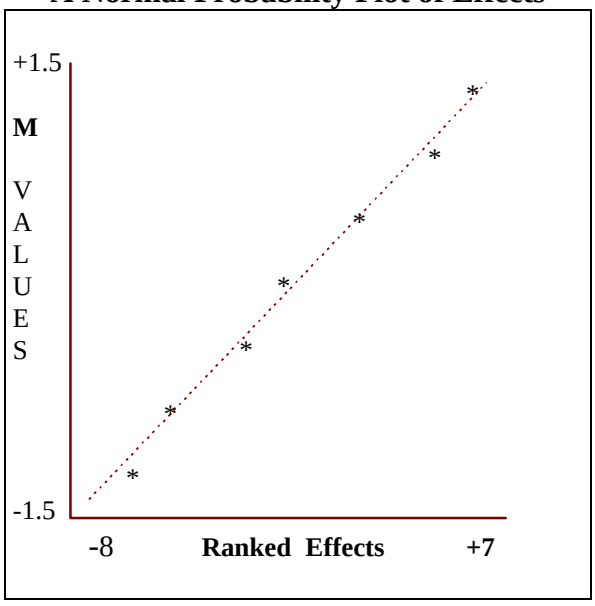
8. Evaluate the plot.

Conclusion.

The results from the plot form a near straight line. It can be concluded that the analytical method is (a) rugged for the *external* factors over the tested range and (b) robust for the *internal* factors over the tested range in the 12 run design.

Figure 3.

A Normal Probability Plot of Effects



Process Qualification Stage.

The evaluation of ruggedness and robustness should be finalised at the end of the development phase - around the time of the process qualification lot manufacture. The ruggedness/robustness evaluation should be developed with the commercial laboratory equipment in mind. It should show the reliability of an analysis with respect to deliberate variations in the method parameters.

Ruggedness/robustness determinations are essential when transferring analytical methods from the development laboratory to the commercial plant quality control laboratory. There may usually be a difference in columns or HPLC machine models used.

A consequence of ruggedness / robustness evaluation is that a series of system suitability parameters are established to ensure that the validity of the analytical procedure is maintained whenever used.

References:

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6. ASTM Standard Guide For Conducting Ruggedness Tests E1169 American Society for testing Materials Philadelphia 1989.
7. Kateman and L. Buydens, T*he Ruggedness Test Quality Control in the Analytical chemistry* John Wiley and Sons NY 2nd Edition 1993, pp118 125.