



## Method Validation Course Day 1 Essential statistics

**09:00** *Registration and coffee*

**09:30** Introduction to course

**09:40 Introduction to statistics**

- normal distribution
- population vs sample statistics
- degrees of freedom
- calculating mean, standard deviation, relative standard deviation, standard deviation of the mean

**10:00 Workshop A1:** Evaluating statistical parameters

**10:40** *Break*

**11:00 Significance testing 1:** Differences involving mean values – the *t*-test

- introduction to significance testing
- probability: level of confidence and significance
- one-tailed vs two-tailed tests
- hypotheses
- interpreting results from significance tests
- different *t*-tests (one-sample, two-sample, paired)

**11:30 Workshop A2:** Significance testing, *t*-tests

**12:05 Significance testing 2:** Differences involving standard deviations – the *F*-test

- calculating the *F* statistic
- obtaining critical *F*-values
- assessing the significance of *F*

**12:20** *Lunch*

**13:20 Workshop A3:** Significance testing, the *F*-test

**14:00 Analysis of variance (ANOVA)**

- what is ANOVA?
- uses of ANOVA
- key terms in ANOVA (sum of squares, mean square)
- ANOVA calculations
- interpreting the results from ANOVA

**14:35 Workshop A4:** ANOVA, types of hypotheses, interpretation of results

**15:15** *Break*

***Day 1 continued***

**15:35 Linear regression: Part 1**

- uses of regression
- principles of least squares linear regression
- assumptions in linear regression
- interpreting residual plots

**15:50 Workshop A5: Linear regression (I)**

**16:05 Linear regression: Part 2**

- interpreting regression statistics (correlation coefficient, residual standard deviation, etc)
- estimating the uncertainty in predicted values obtained from a linear calibration plot
- tests for non-linearity

**16:30 Workshop A6: Linear regression (II)**

**17:20 Close**

***All timings are approximate***

**Method Validation Course**  
**Day 2**  
**Providing the tools**

**09:00 Introduction to method validation**

- ISO definition of validation
- why is validation necessary?
- who validates a method and when?
- defining analytical requirements
- assessing fitness for purpose

**09:45 Workshop B1 (Part 1): Building a validation protocol**

**10:15** *Break*

**10:35 Performance parameter 1: Precision**

- definition of precision
- types of precision estimate (repeatability, reproducibility, intermediate precision)
- determining precision
- how many replicates?
- using ANOVA in precision estimation (pooling data)

**11:15 Workshop B2: Interpreting precision data**

**12:10** *Lunch*

**13:10 Performance parameter 2: Bias**

- definition of bias
- expression of bias
- using *t*-tests in bias assessment
- number of replicates required
- use of reference materials, spiking studies and reference methods in bias assessment

**13:35 Workshop B3: Interpreting data on bias**

**14:30** *Break*

**14:50 Performance parameter 3: Ruggedness testing**

- definition of ruggedness testing
- the need for ruggedness testing
- examples of parameters that can be studied
- planning a ruggedness test: the Plackett-Burman design
- evaluating results from a Plackett-Burman study

**15:10 Workshop B4: Interpreting ruggedness tests**

**15:50 Workshop B1 (Part 2): Validation protocol – plan experiments for precision, bias and ruggedness**

**16:45** *Close*

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**Method Validation Course**  
**Day 3**  
**Further tools**

- 09:00 Performance parameters 4: Selectivity, LoD and LoQ**
- definitions of selectivity and specificity
  - experiments to study interferences
  - definitions: critical value, limit of detection, limit of quantitation
  - false positives and false negatives
  - typical experiments for establishing LOD
  - statistical basis of limits
- 09:45 Workshop C1:** Examples illustrating lack of selectivity, how to evaluate LoD and LoQ
- 10:30 Break**
- 10:50 Performance parameters 5: Linearity and working range**
- definitions of working range and linearity
  - establishing working range and linearity
  - instrument versus whole method linearity
  - prediction (analytical) linearity
  - measures of linearity
- 11:10 Workshop C2:** Interpreting linearity and range data
- 12:10 Lunch**
- 13:10 Workshop B1 (Part 3):** Validation protocol – Plan experiments for selectivity, detection capability and linearity
- 14:10 Break**
- 14:30 Measurement uncertainty and validation studies**
- definition of measurement uncertainty
  - ISO approach to evaluating uncertainty
  - basic rule for combining uncertainties
  - ISO 17025 requirements
  - using data from validation studies in uncertainty estimates
- 15:00 Workshop C3:** Evaluating measurement uncertainty
- 15:45 Workshop C4:** Revision
- 16:30 Close**

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