ROYAL SOCIETY OF CHEMISTRY | APPROVED TRAINING

MTS MOURNE TRAINING SERVICES

TRAINING COURSE

Validation, Verification & Transfer of Methods for

COURSE OPTION 1: Pharmaceutical Analysis, or

COURSE OPTION 2: Biopharmaceutical Analysis

ANALYTICAL METHOD LIFECYCLE MANAGEMENT

[Total Learning time = 20 hours]

This course will provide you with the requisite scientific knowledge and understanding of analytical method lifecycle management, which includes the activities of validation, verification, transfer, and post-approval changes which affect methods, to allow informed interpretation of current regulatory guidance from ICH, EMA and FDA, and in particular, ICH Q2(R2) and Q14.

This course is approved by the Royal Society of Chemistry for purposes of continuing professional development.

This course is available in two versions; choose from either the pharmaceutical version (test methods used for small molecules) or the biopharmaceutical version (test methods used for large molecules, typically derived from biological or biotechnology processes).

The analytical techniques used to test traditional small molecule pharmaceuticals are typically different to those used for testing biopharmaceuticals, also known as biotherapeutics. Therefore, the key difference between the two versions of this course is that the examples and case studies used in the course are tailored to these different types of medicinal products. Additionally, since the typical acceptance criteria which is applied to each type differs, the most relevant guidance can be provided to attendees.

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Course overview

The data generated using analytical test methods is essential for many of the critical decisions made in the pharmaceutical industry. To be confident in the integrity of this data it is crucial that the methods are fit for purpose throughout their lifecycle. To demonstrate that a method is fit for purpose will require either a validation, verification or transfer study, depending on the source of the method in question.

This course provides a detailed explanation of how these studies are performed, enabling a full understanding of method performance characteristics and associated statistics, and how they are applied to the techniques used for analysing drug related samples.

Attendees are invited to bring along any real-life examples that they would like advice on during the training. These may be discussed during group exercises, or, where intellectual property is an issue, privately with the trainer.

Learning Objectives

1. Understand the purpose of analytical method validation and the principles of analytical error and measurement uncertainty, and how they link to acceptance criteria.
2. Define the performance characteristics evaluated during method lifecycle management studies, i.e., robustness, specificity/selectivity, range (including response and lower range limits), accuracy and precision.
3. Generate a suitable protocol for analytical method lifecycle management studies (i.e., validation, verification, transfer, and post-approval changes), including practically relevant experiments and suitable acceptance criteria.
4. Interpret the results of analytical method lifecycle management studies using appropriate statistics and statistical tools.
5. Be able to perform risk assessments associated with analytical method lifecycle management studies.

Delivery options for this course

This course is available either as an open enrolment option, where anyone can book onto the course, or as an in-house option where the course is run for employees in a specific company.

The open enrolment option is delivered as a 4 day 'virtual' live online training event which is delivered over a 6-hour period on each day, from 9am to 3pm, including a short break. The time zone is typically based on GMT (UTC) from November to March, and BST (UTC+1) from April to October.

The agenda is provided on (starting on page 5) and the full schedule of dates is available on the MTS website, click here.

The in-house option may be delivered either in the live online format or in a classroom-based format at your site. An agenda for the classroom-based option is provided (starting on page 9), it is typically delivered from 9am to 4:30pm but the timings are based on customer preference.

In-house training may include customisation to meet specific requirements. For example, it may be beneficial to use real case studies of validation/verification/transfer performed by your group, and/or to link the course content to your standard operating procedures in terms of experimental approach and acceptance criteria.

It is possible to attend just the method validation part of the course, if transfer and verification are not relevant for you. This would consist of the first 3 days (approximately) only for the live online option, and the first 2 days only for the classroom-based option resulting in a total learning time of 14 hours.

This course is suitable for

Anyone who needs to manage the lifecycle of analytical methods and/or understand how methods are validated, verified, or transferred, either to design and carry out the investigation, or to review and interpret the data generated.

For example:

- Development/Quality Control (QC) analytical chemists
- Development/Quality Control (QC) managers/ supervisors
- Quality Assurance personnel
- Regulatory affairs personnel
- Assessors and Inspectors from regulatory authorities

Included in the course fees

- Comprehensive course hand-outs - The training book is provided as an electronic copy (pdf) for both live online and classroom-based options.
- Certificate of Attendance
- Optional post training assessment (accessed in e-MTS, our learning management system) which leads to a Certificate of Training.
- Access to training materials via e-MTS
- Post training support – Attendees can contact the trainer with questions that may occur when they apply their learning to real life situations.

Course Agenda & Outline
Live Online Training Option

Day 1

Timings (approximate)	Content
0900 to 0930	Technical set-up & introductions
0930 to 1030	Introduction to method validation: • The purpose of validation in the pharmaceutical industry • Available guidelines for method validation, e.g., ICH Q2, etc. • Data quality and method validation
1030 to 1045	*Break (15 min)*
1045 to 1130	Introduction to method validation *continued* • Definition of analytical method validation characteristics.
1130 to 1230	Analytical method performance: • Analytical error • Random and systematic sources of error • Analytical Quality by Design (QbD), Analytical Target Profile (ATP) and analytical method lifecycle, as per ICH Q14 • Measurement uncertainty
1230 to 1315	*Lunch (45 min)*
1315 to 1335	Analytical method performance *continued*
1335 to 1415	Statistics for method validation: • Statistical tools for method validation • The mean, the standard deviation and confidence intervals – definition and calculation • Student's t-distribution for small sample sets
1415 to 1500	Performance characteristics, as defined in ICH Q2 and Q14: **Robustness:** • Relevance in validation studies vs development; factors and levels for investigation; experimental design for robustness investigations

Day 2

Timings (approximate)	Content
0900 to 0930	Review of Day 1
0930 to 1030	Performance characteristics continued: Robustness *continued.*
1030 to 1045	*Break (15 min)*
1045 to 1200	Performance characteristics continued: **Specificity/Selectivity:** • Discussion of specificity and selectivity for qualitative and quantitative analytical methods; practical investigation of specificity/selectivity and acceptance criteria; performing stress studies.
1200 to 1230	Performance characteristics continued: **Range:** • Reportable ranges to validate for different types of pharmaceutical related analytical methods; required reporting thresholds for impurities analysis.
1230 to 1315	*Lunch* (45 min)
1315 to 1500	Performance characteristics continued: **Range:** • Linear response – verification of the calibration method; single point and multi-level calibration; regression analysis and associated statistics; use of residuals; when to use weighting; experimental procedure and acceptance criteria.

Day 3

Timings (approximate)	Content
0900 to 0930	Review of Day 2
0930 to 1030	Performance characteristics continued: **Range:** • Lower range limits - Detection limit & quantitation limit – methods of determination; experimental procedure; acceptance criteria.
1030 to 1045	*Break (15 min)*

Timings (approximate)	Content
1045 to 1230	Performance characteristics continued: **Accuracy:** The relationship between accuracy and trueness; preparation of recovery samples for different types of drug-related samples and inherent problems; experimental procedure; recovery calculations; acceptance criteria.
1230 to 1315	*Lunch (45 min)*
1315 to 1430	Performance characteristics continued: **Precision** (repeatability, intermediate precision & reproducibility): • Choosing suitable samples for precision; options if homogenous material is not available; Horwitz equation; acceptance criteria; Analysis of Variance (ANOVA). Combining accuracy and precision
1430 to 1500	Validation protocol & report: • Choosing validation characteristics for different types of analytical methods • Execution of the validation protocol • Contents of the validation report Method validation by phase of drug development Method validation Q&A

Day 4

Timings (approximate)	Content
0900 to 0930	Review of Day 3
0930 to 1030	Introduction to analytical method lifecycle management. Review of available regulatory guidance for analytical method lifecycle management. Different possible approaches to analytical method lifecycle management. Statistical tools for comparative testing: Two one-sided t-tests (TOST)
1030 to 1045	*Break (15 min)*

Timings (approximate)	Content
1045 to 1130	The role of risk assessment in analytical method lifecycle management. Main steps in method verification and transfer.
1130 to 1230	Risk assessment and gap analysis review of methods in terms of: • The adequacy of the content and how it is written, • Potential technical challenges, • Existing method knowledge and robustness. Training requirements during method transfer studies.
1230 to 1315	*Lunch (45 min)*
1315 to 1500	Preparation of the analytical method lifecycle management protocol (verification/ transfer/post-approval change) in compliance with available regulatory expectations, to include: • Required materials, e.g., drug samples, reference standards, etc., • Experimental procedure, e.g., numbers of batches and replicates, • Method performance characteristics, • Suitable acceptance criteria. • Comparison of data Execution of the protocol Final Q&A

Course Agenda & Outline

Classroom Based Training Option

Day 1

Timings (approximate)	Content
0900 to 1030	Introductions Introduction to method validation: • The purpose of validation in the pharmaceutical industry • Available guidelines for method validation, e.g., ICH Q2, etc. • Data quality and method validation
1030 to 1045	*Refreshment break*
1045 to 1115	Introduction to method validation continued • Definition of analytical method validation characteristics
1115 to 1230	Analytical method performance: • Analytical error • Random and systematic sources of error • Analytical Quality by Design (QbD), Analytical Target Profile (ATP) and analytical method lifecycle, as per ICH Q14 • Measurement uncertainty
1230 to 1315	*Lunch*
1315 to 1335	Analytical method performance continued
1335 to 1415	Statistics for method validation: • Statistical tools for method validation • The mean, the standard deviation and confidence intervals – definition and calculation • Student's t-distribution for small sample sets
1415 to 1500	Performance characteristics, as defined in ICH Q2 and Q14: **Robustness:** • Relevance in validation studies vs development; factors and levels for investigation; experimental design for robustness investigations
1500 to 1515	*Refreshment break*
1515 to 1630	Performance characteristics continued: • Robustness *continued.*

Day 2

Timings (approximate)	Content
0900 to 1030	Review of Day 1 Performance characteristics continued: **Specificity/Selectivity:** • Discussion of specificity and selectivity for qualitative and quantitative analytical methods; practical investigation of specificity/selectivity and acceptance criteria; performing stress studies.
1030 to 1045	*Refreshment break*
1045 to 1230	Performance characteristics continued: **Range:** • Reportable ranges to validate for different types of pharmaceutical related analytical methods; required reporting thresholds for impurities analysis. • Linear response – verification of the calibration method; single point and multi-level calibration; regression analysis and associated statistics; use of residuals; when to use weighting; experimental procedure and acceptance criteria. • Lower range limits - Detection limit & quantitation limit – methods of determination; experimental procedure; acceptance criteria.
1230 to 1315	*Lunch*
1315 to 1500	Performance characteristics continued: **Accuracy:** • The relationship between accuracy and trueness; preparation of recovery samples for different types of drug-related samples and inherent problems; experimental procedure; recovery calculations; acceptance criteria. **Precision** (repeatability, intermediate precision & reproducibility): • Choosing suitable samples for precision; options if homogenous material is not available; Horwitz equation; acceptance criteria; Analysis of Variance (ANOVA).
1500 to 1515	*Refreshment break*
1515 to 1610	Performance characteristics continued: • Precision *continued* Combining accuracy and precision

Timings (approximate)	Content
1610 to 1630	Validation protocol & report: • Choosing validation characteristics for different types of analytical methods, • Execution of the validation protocol, • Contents of the validation report. Method validation by phase of drug development

Day 3

Timings (approximate)	Content
0900 to 1030	Review of Day 2 Method validation Q&A Introduction to analytical method lifecycle management. Review of available regulatory guidance for analytical method lifecycle management.
1030 to 1045	*Refreshment break*
1045 to 1230	Different possible approaches to analytical method lifecycle management. Statistical tools for comparative testing: Two one-sided t-tests (TOST) The role of risk assessment in analytical method lifecycle management. Main steps in method verification and transfer. Risk assessment and gap analysis review of methods in terms of: • The adequacy of the content and how it is written, • Potential technical challenges, • Existing method knowledge and robustness.
1230 to 1315	*Lunch*

Timings (approximate)	Content
1315 to 1500	Review of methods continued Training requirements during method transfer studies. Preparation of the analytical method lifecycle management protocol (verification/ transfer/post-approval change) in compliance with available regulatory expectations, to include: • Required materials, e.g., drug samples, reference standards, etc., • Experimental procedure, e.g., numbers of batches and replicates, • Method performance characteristics, • Suitable acceptance criteria, • Comparison of data.
1500 to 1515	*Refreshment break*
1515 to 1615	Preparation of the protocol continued Execution of the protocol Final Q&A