TRAINING COURSE

How to Develop Stability Indicating HPLC Methods

[Total Learning time = 13 hours]

This course will enable you to understand how HPLC methods work, how to develop a new HPLC method, with consideration of the principles outlined in ICH Q14, and how to ensure and demonstrate that a new or existing HPLC method (e.g., a pharmacopoeia method) is stability indicating.

Course overview:

Pharmaceuticals need to be assessed for stability to support the assigned shelf life. Therefore, when analysing stability samples obtained from these studies, analytical methods are required which are stability indicating, i.e., there is a measurable response which correlates with degradation (if present).

HPLC is a popular technique for monitoring the decrease in drug and corresponding increase in degradation products due to its separating abilities. However, the HPLC method must be developed carefully to ensure that degradation products are both separated and detected appropriately.

This training course is designed to provide a thorough understanding of how to develop HPLC methods specifically designed for stability indicating analysis of pharmaceuticals, following the principles outlined in ICH Q14. The course will describe strategies for performing forced degradation studies and selecting optimal HPLC method parameters to ensure that all relevant degradation products are separated, and that mass balance has been achieved.

The same strategies may be applied to existing methods to demonstrate that they are stability indicating.

This course focuses on reversed phase mode separations.

Learning Objectives:

1. Define the objectives for the development of a stability indicating HPLC analytical method.
2. Effectively assess all the available relevant information relating to the desired method.
3. Perform forced degradation studies to prepare samples that will be used for the method development.
4. Select suitable scouting conditions to find a suitable column and mobile phase system for an investigation of stressed samples and an evaluation of mass balance.
5. Optimise the chromatographic conditions to result in the best possible separation.

Case studies are employed to allow consideration of real-life scenarios. Delegates 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.

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 3 day 'virtual' live online training event which is delivered over a 6-hour period, from 9am to 3pm, including breaks, on days 1 and 2, and over a shorter 3.25-hour period, from 9am to 12:15pm, including a short break, on day 3.

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 4) 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 7), it is typically delivered from 9am to 4:45pm but the timings are based on customer preference. In-house training may include customisation to meet specific requirements.

This course is suitable for:

Anyone who has some experience of using HPLC and wants to know more about how HPLC methods work, and specifically how to develop new HPLC methods which are aimed at stability indicating capability.

For example:

- Development/Quality Control (QC) analytical chemists
- Development/Quality Control (QC) managers/ supervisors

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 1030	Introduction: Stability indicating methods for pharmaceuticals • The stability of pharmaceuticals and the concept of a stability indicating method. • Common strategies for HPLC method development are compared. • Available regulatory guidance relating to stability indicating methods is reviewed and in particular, the principles of ICH Q14, which includes the 'enhanced' approach, and use of an Analytical Target Profile (ATP).
1030 to 1045	*Refreshment break*
1045 to 1130	Step 1: Setting suitable objectives for the HPLC method • Defining the requirement for a stability indicating HPLC method: the analytes; the sample to be tested; the type of test required; and the purpose of the test. • Setting appropriate criteria for the method: Goals for the separation in terms of resolution (R), efficiency (N) and capacity factor (k'). • Designing an ATP.
1130 to 1230	Step 2: Assessing all available information • Identifying potential sources of information which may be useful during method development. • Assessing the effects of the structure of the analyte and in particular: how molecular weight and polarity (including assessment of Log P) of analytes are related to the most suitable type of HPLC and why reversed phase mode is preferred; how pKa affects the choice of mobile phase; analyte solubility.
1230 to 1315	*Lunch*
1315 to 1500	Step 2 continued: • How the properties of the analyte impact on the choice of detector; detector options for stability indicating HPLC methods. • Assessing available information relating to interferences which are likely to be encountered for the method.

Timings (approximate)	Content
	• Determination of what is known regarding the degradation profile of the active pharmaceutical ingredient.

Day 2

Timings (approximate)	Content
0900 to 0915	Review of Day 1
0915 to 1030	Step 3: Selecting suitable samples • Identifying suitable samples for the HPLC method development. • Performing forced degradation studies: Selection of suitable samples, stress conditions and timings. • Preparation of the test sample(s) to be used for method development.
1030 to 1045	*Refreshment break*
1045 to 1230	Step 3 continued Step 4: Performing scouting experiments to select suitable initial conditions • Separation theory for reversed phase HPLC including discussion of the parameters which affect selectivity, e.g., mobile phase composition, %B, gradient time and steepness, temperature, pH etc. • Selecting columns which give different selectivity – tools for column comparison. • The effects of HPLC method chromatographic parameters: e.g., column attributes, mobile phase composition, temperature, flow rate, injection volume, etc.
1230 to 1315	*Lunch*
1315 to 1500	Step 4 continued • Selecting initial conditions for stability indicating HPLC method development: stationary phase and mobile phase. • Designing scouting experiments: consideration of the requirements of the method, selection of suitable stationary phase and mobile phase combinations and set-up of the scouting experiments. • Interpretation of scouting experiments: how to identify promising potential conditions for the method, e.g., measurement of resolution, peak shape, etc., and calculation of mass balance for the stress conditions investigated.

Day 3

Timings (approximate)	Content
0900 to 0915	Review of Day 2
0915 to 1030	Step 5: Optimising the method to define method parameters which achieve the desired separation • Adjusting method parameters to achieve the desired separation, i.e., optimising the separation. • Investigation of peak purity.
1030 to 1045	*Refreshment break*
1045 to 1215	Step 5 continued: • Using computer modelling to optimise the separation. • Assessing the robustness of the method and consideration of set-points, proven acceptable ranges (PARs), and method operable design region (MODR) for method parameters. • Designing an appropriate system suitability test.

Course Agenda & Outline

Classroom Based Training Option

Day 1

Timings (approximate)	Content
0900 to 1030	Introduction: Stability indicating methods for pharmaceuticals • The stability of pharmaceuticals and the concept of a stability indicating method. • Common strategies for HPLC method development are compared. • Available regulatory guidance relating to stability indicating methods is reviewed and in particular, the principles of ICH Q14, which includes the 'enhanced' approach, and use of an Analytical Target Profile (ATP).
1030 to 1045	*Refreshment break*
1045 to 1130	Step 1: Setting suitable objectives for the HPLC method • Defining the requirement for a stability indicating HPLC method: the analytes; the sample to be tested; the type of test required; and the purpose of the test. • Setting appropriate criteria for the method: Goals for the separation in terms of resolution (R), efficiency (N) and capacity factor (k'). • Designing an ATP.
1130 to 1230	Step 2: Assessing all available information • Identifying potential sources of information which may be useful during method development. • Assessing the effects of the structure of the analyte and in particular: how molecular weight and polarity (including assessment of Log P) of analytes are related to the most suitable type of HPLC and why reversed phase mode is preferred; how pKa affects the choice of mobile phase; analyte solubility.
1230 to 1315	*Lunch*
1315 to 1500	Step 2 continued: • How the properties of the analyte impact on the choice of detector; detector options for stability indicating HPLC methods. • Assessing available information relating to interferences which are likely to be encountered for the method.

	• Determination of what is known regarding the degradation profile of the active pharmaceutical ingredient.
1500 to 1515	*Refreshment break*
1515 to 1645	Step 3: Selecting suitable samples • Identifying suitable samples for the HPLC method development. • Performing forced degradation studies: Selection of suitable samples, stress conditions and timings. • Preparation of the test sample(s) to be used for method development.

Day 2

Timings (approximate)	**Content**
0900 to 1030	Step 4: Performing scouting experiments to select suitable initial conditions • Separation theory for reversed phase HPLC including discussion of the parameters which affect selectivity, e.g., mobile phase composition, %B, gradient time and steepness, temperature, pH etc. • Selecting columns which give different selectivity – tools for column comparison. • The effects of HPLC method chromatographic parameters: e.g., column attributes, mobile phase composition, temperature, flow rate, injection volume, etc.
1030 to 1045	*Refreshment break*
1045 to 1230	Step 4 continued • Selecting initial conditions for stability indicating HPLC method development: stationary phase and mobile phase. • Designing scouting experiments: consideration of the requirements of the method, selection of suitable stationary phase and mobile phase combinations and set-up of the scouting experiments. • Interpretation of scouting experiments: how to identify promising potential conditions for the method, e.g., measurement of resolution, peak shape, etc., and calculation of mass balance for the stress conditions investigated.
1230 to 1315	*Lunch*
1315 to 1500	Step 5: Optimising the method to define method parameters which achieve the desired separation

	• Adjusting method parameters to achieve the desired separation, i.e., optimising the separation. • Investigation of peak purity.
1500 to 1515	*Refreshment break*
1515 to 1645	Step 5 continued: • Using computer modelling to optimise the separation. • Assessing the robustness of the method and consideration of set-points, proven acceptable ranges (PARs), and method operable design region (MODR) for method parameters. • Designing an appropriate system suitability test.