Analytical Methods for Cleaning Validation
Development, Validation & Control
03/04 June 2020, Heidelberg, Germany

Highlights
- Cleaning Method Characteristics
- Calculation of MAC
- Sampling Techniques of Cleaning Residues
- Method Validation for Cleaning Residues
- Documentation of Method Validation

With practical Excel® exercises
Objective

This course consists of two parts.

The first part revolves around the development of suitable analytical methods. The characteristics of these methods (HPLC, HPTLC, TOC, conductometry, pH, total protein, visual inspection etc...) will be discussed in the light of their capability of detection and quantitation of residues. In particular, the advantages of the TOC method in accurately detecting and quantifying low levels of non-specific residues (such as detergents, drug excipients and active ingredients) which may not be determined by HPLC, will be highlighted. Prior to this, setting Maximal Carry Over (MAC) limits according to PIC/S, FDA and WHO guides will be presented along with the new EMA approach based on toxicity thresholds. Finally, a pre-requisite requirement for a well-developed method is an efficient recovery and therefore, the first part of the course will highlight the various techniques of sample recovery.

The second part of the course will address a systematic validation of the analytical method for cleaning residues. Performance characteristics of the analytical method will be systematically presented, discussed in parallel to guided calculations of examples with Excel.

Background

Initiating the manufacturing of a pharmaceutical in shared equipment requires demonstrating that no cross-contamination from previous product takes place. Optimally, residues from a previously manufactured product or API or residues from the cleaning agent itself should be absent or very low. However, here lies the challenge facing an analytical chemist: the need to develop and validate an analytical method that is sensitive enough to detect and reliably quantify well recovered trace amounts of chemicals and practical enough to rapidly deliver results.

Target Audience

The addressees of the event are analytical chemists testing the residues, quality control personnel, quality assurance personnel, regulatory affairs professionals and validation personnel also involved in cleaning validation.

The participants should bring a laptop with Excel.

Programm

Introduction

- Regulations (FDA, EU, PIC/S, APIC, WHO)
- Types of analytical methods
- Preparing a method to a validation process
- Life cycle approach to analytical methods
- Roadmap to development of analytical methods for cleaning residues

Cleaning Method Characteristics

- Cleaning procedures in pharmaceutical processes
- Types of cleaning residues and their identification
- Development of method for cleaning residues
- Analytical methods for cleaning residues (HPLC, HPTLC, TOC, Conductometry, pH, total protein, visual inspection etc...)
- Testing methods for cleaning agents
- What should you know about a Cleaning Agent

Sampling Techniques of Cleaning Residues

- Swab and Wipe Sampling
- Requirements from Swab
- Rinse Sampling
- Solvent Sampling
- Placebo Sampling
- Product Sampling
- Visual examination of cleaned equipment

Calculation of Allowable Carryover (MAC)

- Common MAC limits (PIC/S, FDA and WHO guides)
- New approach of EMA guide (NOAEL and PDE)
- Residues limits on swab and rinse samples and in analytical samples
- Formulas for calculating MAC

Workshop

- Exercises in calculations of API or drug product residues
- Exercises in calculations of cleaning agent residues

Specificity of measurement method

- Interference with excipient residues, degradation product, and cleaning residue
- Interference with swab extractables
- Interferences in analytical samples
- Quantitative aspect of specificity
**Accuracy (incl. exercises with Excel)**
- Swab Recovery Studies on coupons
- Rinse Recovery Studies on coupons
- Solvent Sampling from hoses
- Accuracy of the Measurement Method

**Precision of measurement method (incl. exercises with Excel)**
- Method Repeatability
- Intermediate Precision
- Combined analysis of Repeatability/Intermediate Precision with One-way ANOVA

**Detection and Quantitation Limits of measurement methods (incl. exercises with Excel)**
- By ICH, EP and USP methods
  - Of TOC method
  - Of HPLC method
- Visual detection Limit (VDL)

**Linearity of measurement method (incl. exercises with Excel)**
- ICH requirements (Correlation coefficient, residual SS, residuals plot)
- Considerations (number of data points, of repeats, quality of fit to linearity, etc.)
- Analysis of plot of measured vs. actual concentrations
- Correlation between Cleaning Validation and Monitoring: Relative TOC response factor of Target Residue/Reference Standard in TOC method

**Range**
- Range on swab and rinse samples
- Range of analytical samples

**Robustness**
- Robustness factors for sampling recovery
- Robustness factors for measurement method
- by DOE matrix Solvent Sampling from hoses

**Documentation of method validation**
- Writing a protocol
- Writing a report

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**Speakers**

**Dr Raphael Bar**
BR Consulting, Israel
Dr Bar headed the Analytical R&D Laboratories at Teva Pharmaceuticals and the analytical QC Laboratory at Pharmos. For the last ten years, Raphael Bar has been a pharmaceutical consultant for the Pharma and Bio-Pharma industries.

**Walid El Azab**
STERIS Cooperation, Belgium
Walid El Azab is an Industrial pharmacist, a Qualified Person and Lean Six Sigma green belt. He provides technical support related to cleaning, disinfectants and sterility assurance.

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**Social Event**
In the evening of the first day, you are cordially invited to a social event. This is an excellent opportunity to share your experiences with colleagues from other companies in a relaxed atmosphere.

**Heidelberg – Optimal Accessibility via Frankfurt**
As one of the most beautiful cities in Europe, Heidelberg is at first sight an interesting venue – but is it also easily accessible? The answer is: Yes! The connection to Frankfurt Airport is convenient and fast. Next to London, Frankfurt Airport offers the most frequent air connections in Europe. It takes only about 45 minutes to get from Frankfurt to Heidelberg.

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HLS: http://www.hls-online.com/PCS-Flughafentransfer.html
Train: You can also take a train to get from/to the airport, which takes less than one hour.
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Reservation Form (Please complete in full)

Analytical Methods for Cleaning Validation, 03/04 June 2020, Heidelberg, Germany

Title, first name, surname

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Important: Please indicate your company’s VAT ID Number  Purchase Order Number, if applicable

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Date

Venue

Analytical Methods for Cleaning Validation, 03/04 June 2020, Heidelberg, Germany

Fee (per delegate, plus VAT)

ECA Members € 1,590
APIC Members € 1,690
Non-ECA Members € 1,790
EU GMP Inspectors € 895

The conference fee is payable in advance after receipt of invoice and includes conference documentation, dinner on the first day and all refreshments. VAT is reclaimable.

Registration

The official conference language will be English.

Registration is via the attached reservation form, by e-mail or by fax message. Or you register online at www.gmp-compliance.org.

Accommodation

CONCEPT HEIDELBERG has reserved limited number of rooms in the conference hotel. You will receive a room reservation form/POG when you have registered for the course. Reservation should be made directly with the hotel. Early reservation is recommended.

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Venue

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