Environmental Monitoring
Data Management
From collecting to trending

SPEAKERS:

Dr Raphael Bar
BR Consulting

Michael Schiffer
Novartis Pharma Stein, Switzerland

This education course is recognised for the ECA GMP Certification Programme „Certified Microbiological Laboratory Manager“. Please find details at www.gmp-certification.eu

PROGRAMME:

- Regulations and Infra Structure
- Charting, Trending and approaches for Interpretation
- Data Variability
- Control Charts
- Contamination Recovery Rates (New USP <1116> approach)
- Risk assessment in investigation
- Strategy and Tools for detecting Trends

15 - 16 November 2017, Barcelona, Spain
Objectives

This practical course will first present the basic methodology of evaluating the Environmental Monitoring (EM) data using elementary Statistical Process Control (SPC) tools as well as empirical approaches to set microbial control limits for clean rooms. This course will address the following issues:

- Overview of controlled rooms classifications, elements of an EM program and present EU and FDA regulations including the recent ISO 14664 changes.
- How to organize and present an abundant amount of microbial data in meaningful graphs
- How to draw useful Control Charts with this data, using the software program Minitab®17
- To understand how action and alert control limits are set
- How to demonstrate that the environmental microbial monitoring process is under a state of control
- How to calculate and plot the newly proposed Contamination Recovery Rates in USP Chapter <1116>
- To detect a trend in the environmental microbial monitoring process
- How to apply risk assessment in investigations

All above issues will be demonstrated on examples and case studies of microbial counts generated in controlled rooms of manufacturing facilities of sterile products.

PLEASE NOTE that a laptop with Excel© is needed for the practical exercises. Also, the “Minitab” software must be installed on this computer to solve exercises and generate control charts. You can download a 30 days trial version of this software here: https://www.minitab.com/en-us/products/minitab/

Background

Regulatory agencies require from manufacturing companies of pharmaceuticals and biopharmaceuticals, particularly of sterile drug products, to maintain an environmental monitoring program, whereby particulates as well as microorganisms in either air samples (active and passive sampling) or in surfaces (contact plates) are routinely tested and monitored.

Thus, a multitude of environmental microbial data is generated on a routine basis and it is recorded in a manner permitting trend evaluation. But collecting EM data is only the first challenge. The following challenge for the responsible person in quality is charting, analyzing data, setting action and alert limits, interpreting the overall monitoring process behavior, detecting a trend or shift in contamination levels, monitoring excursion rates and contamination recovery rates, while conducting an ongoing risk analysis. Therefore, this course is aimed at providing empirical tools for charting and trending EM data.

Target Audience

- Environmental Monitoring personnel in facilities of pharmaceuticals, biopharmaceuticals and medical devices
- Microbiologists
- Quality Assurance personnel
- Regulatory Affairs personnel
- Production Managers
- QC Managers

Programme

Introduction to charting and trending
- QbD and trending
- Run Chart vs. Shewhart Control Charts
- Control charts of grouped data versus of individual data
- Examples of microbial charts: grouped vs individual counts
- Variables versus attributes charts
- Poisson and Binomial control chart
- Common cause variation vs. Special Cause (Assignable) variation
- State of control

Overview of Environmental Monitoring: regulations and infra structures
- Overview of current regulations:
- Practical aspects of Environmental Monitoring
- How to set up an structured EM program and gain strong data
- Risk-based approach
- Handling of big data amounts
- EM program examples from Industrial clean rooms

Variability of data
- Standard deviation of a sample and of population
- Histogram
- Standard deviations of the mean range
- Relation between standard deviation and range
- Short-term variation versus global variation
- Separating the signal from noise

Exercise: Calculation of within-group and global standard deviations

Control Charts of grouped data
- Plotting Run chart and control chart (Process Behavior Chart)
- Computation of three-sigma Control limits
- Control charts of average, range and standard deviation

Brief acquaintance with Minitab 17
- Basic structure of Minitab software
- Drawing a Control Chart
Control Charts of individual microbial counts
- Moving range (mR)
- Control charts of individual data (XmR)
- Calculation of control limits
- The three-way chart
- Examples of three-way charts

Exercises: Building control charts of microbial counts from passive and active air sampling with Minitab

Contamination Recovery Rates
- Contamination recovery rates (USP approach <1116>)
- Plotting recovery rates and excursion rates
- Limits of rates versus actual values
- Calculations of contamination recovery rates per USP <1116>

Distribution-free approach
- Disadvantages of the distribution-based approach
- Non-parametric percentile as control limit
- Tolerance intervals limits
- Shewhart approach for setting control limits

Exercises of percentile determination, plotting of Laney’s charts, Calculations of contamination recovery rates per USP <1116>

Trending Tool applications
- Trending tool examples from industries
- Data collection tools
- Reaction and measures on negative trends
- Responsibilities

General approach to microbial monitoring
- Overall strategy for microbial monitoring
- Plotting Contamination recovery rates
- Laney’s charts

Exercises: Control charts of microbial counts of active air samples in area Grade B and contact plates in area Grade C; Determining Alert Limits with the methods of percentile and confidence intervals

Investigation and Risk Assessment
- Case studies of evaluation of EM Data
- Use of supportive data

Strategy for detecting a trend and for Continuous Improvement
- Phase 1 and Phase 2 in process monitoring
- Statistical Control of a process: Is your EM process predictable?
- Nelson rules
- Trending and continued process verification
- Trending for Annual Product Review document

Example of detecting a shift in microbial counts

Speakers

Dr Raphael Bar, BR Consulting, Israel
Raphael Bar is presently a pharmaceutical consultant for the Pharma and bio-Pharma industries. He is consulting various companies and provides development and analytical support to investigational, generic, new drugs as well as combination device-drug products and CMC project management. With a doctorate in Chemistry (1984), Dr Bar joined (1995) Teva Pharmaceuticals and headed for three years the Analytical R&D Laboratory. He was involved in preparation of ANDA files. He then joined Pharmos where he managed the quality control and R&D laboratory till 2007. As Senior Director of Analytical Development he was actively involved in preparation of CMC packages for clinical trial studies

Michael Schiffer, Process Expert, Novartis Pharma, Stein, Switzerland
Michael studied Applied and Molecular Biotechnology at the RWTH Aachen. After his Master Thesis at Novartis, he joined Novartis 2013 as QA Specialist. 2016 he became Senior QA Specialist and Process Expert. Assistant production manager for state-of-the-art fill/finish Sterile Manufacturing of a biotech brand for w/o supply. Professional focus on compounding, filling and packaging of Prefilled Syringes. Furthermore responsible for an Autoinjector assembly line. Further activities: Process improvements, launch projects, inspections and audits (incl. FDA, RHI, 3rd Party), deviations & complaints, SOPs.

Moderators
Raphael Bar and Axel Schroeder

Social Event
In the evening of the first day, you are cordially invited to a social event (city tour and dinner). This is an excellent opportunity to share your experiences with colleagues from other companies in a relaxed atmosphere.
### Reservation Form

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**Date**

- Wednesday 15 November 2017, 08.30 to 18.00 h (Registration and coffee 08.00 - 08.30 h)
- Thursday, 16 November 2017, 08.30 to 17.00 h

**Venue**

Barcelo Sants Hotel  
Pl. Països Catalans, s/n  
08014 Barcelona, Spain

Phone +34 93 503 53 00  
Fax +34 93 490 60 45

**E-Mail**
sants@barcelo.com

**Fees (per delegate plus VAT)**

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

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

**Accommodation**

CONCEPT HEIDELBERG has reserved a limited number of rooms in the conference hotel. You will receive a room reservation form when you have registered for the event. Please use this form for your room reservation to receive the specially negotiated rate for the duration of your stay. Reservation should be made directly with the hotel. Early reservation is recommended.

**Registration**

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

**Conference language**

The official conference language will be English.

**Organisation and Contact**

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For questions regarding content:  
Mr. Axel Schroeder (Operations Director) at +49(0)6221 / 84 44 10, or per e-mail at schroeder@concept-heidelberg.de.

For questions regarding reservation, hotel, organisation etc.:  
Mr. Niklaus Thiel (Organisation Manager) at +49(0)6221/84 44 43, or per e-mail at thiel@concept-heidelberg.de

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