ECA Academy
Your GMP/GDP Information Source

GMP Certification Programme
Certified Quality Control Manager

Speakers

Dr Christopher Burgess
Burgess Analytical Consultancy, UK

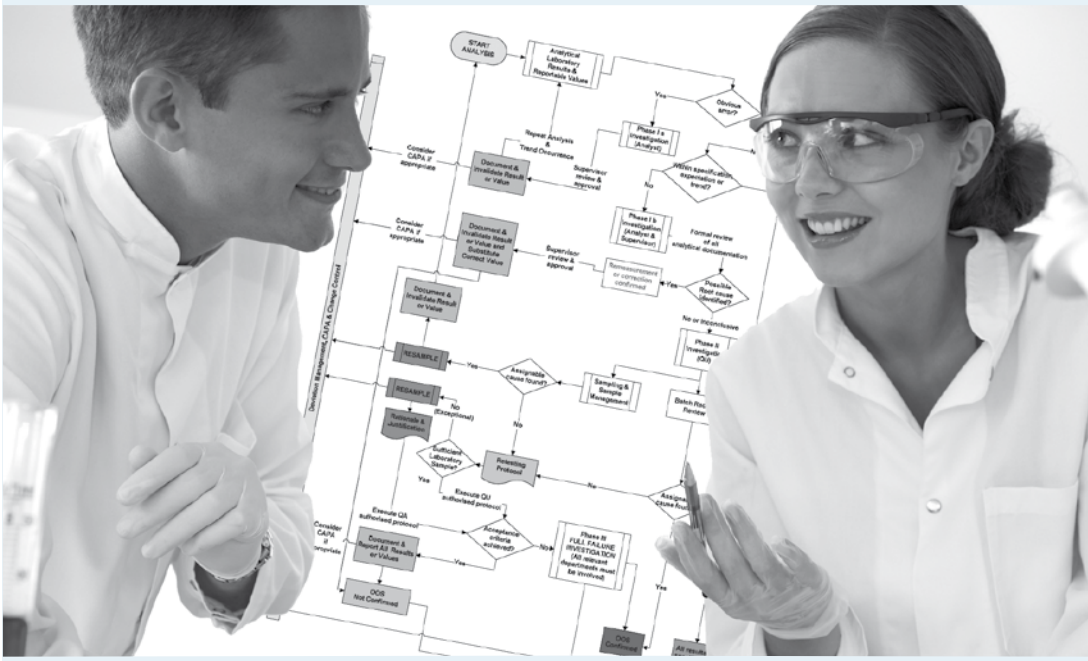
Dr Lori McCaig
Seagen, Inc, USA

Dr Bernd Renger
Bernd Renger Consulting, Germany

Dr Lance Smallshaw
UCB Biopharma sprl, Belgium

Handling OOE and OOT Results

20/21 April 2021 | Berlin, Germany



Every participant will get free access to the current version of ECA's Laboratory Data Management Guidance on OOE and OOT Results!

Highlights

- Practical Advice on how to Identify OOE and OOT Results
- Laboratory Data Management Guidance Out of Expectation (OOE) and Out of Trend (OOT) Results compiled by
- ECA's Analytical Quality Control Group
- Methods and Approaches for Detecting
  - Out of Expectation (OOE) Data
  - Out of Trend (OOT) Data, where no Trend is expected
  - Out of Trend (OOT) Data, where a Trend is expected,
  - Trending for Stability Testing

With 4 interactive workshops and an optional Post-Conference OOS Workshop on 22 April

Objective

At this ECA OOE/OOT Training Course participants will get practical advice on how to identify OOE and OOT Results. You will get to know how to use the statistical tool box for detecting OOT data and what FDA and European guidelines tell us about handling OOS Results. You will also learn what both FDA and European Regulators expect regarding the handling of OOT and OOS results. During the training the following aspects will be discussed:

- Regulatory Importance of Trend Analysis under the EU GMPs
- The statistical tool box to discover trends
- Process stability versus process capability
- Recommendations on Out of Expectation Results (OOE)
- Recommendations for Process Control of Variables
- Trending for Process Control of Attributes
- Trending for Stability Data

In the ECA OOS Workshop the following topics will be discussed:

- OOS: US/FDA Guidelines and European Regulatory Expectations
- OOS Results in R&D Laboratories
- Strategies not to generate OOS results

The current version of the OOE/OOT Laboratory Data Management Guidance will be presented and participants will have the opportunity to review and discuss the contents and technical aspects of the guidance document as well as looking at the scope and application of the proposed methods within industry.

Background

Laboratory tests are performed on active pharmaceutical ingredients, excipients and other components, inprocess materials, and finished drug product. In these tests a trend can occur and a trend analysis has to be performed by applying techniques for detecting an underlying pattern of behaviour in a time or batch sequence which would otherwise be partly or nearly completely hidden by noise.

There are two distinct types of trend situations:

- No trend is expected, for example for production or analytical process data which are known or assumed to be under statistical control.
- A trend is expected, for example in stability testing.

There is a fundamental difference between these two situations in that the variance increases with time in the second situation. Trend analysis is of regulatory relevance and a key aspect in both in EU guidelines (e.g. Annex 15, EU GMP-Guide) and FDA Guidances (e.g. Guidance for Industry, Process Validation: General Principles and Practices).

Since the often cited Barr ruling (Wolin Judgement) of February 1993 pharmaceutical companies all around the world have implemented procedures and strategies on how to deal with results that do not comply with their predetermined specifications. Although 27(!) years have passed since that judgement and although in the meantime FDA and MHRA have published guidances about OOSs, the investigation of OOS results continues to be a hot topic in FDA inspections. The incorrect handling and investigation of OOS results is still frequently cited in Warning Letters.

The **ECA Working Group on Analytical Quality Control** decided to address these aspects and developed a harmonised **guideline SOP** on managing analytical deviations within the laboratory including OOS, OOE and OOT results. It encourages the application of a consistent and scientifically sound approach to trend analysis as part of a QMS. The current Version 2 is available for all ECA members on the ECA members area.

Target Audience

This training is recommended for all levels of technical staff and managerial personnel dealing with out-of-trend results and out-of-specification results, including analytical laboratories, contract laboratories, and Quality Assurance/Quality Control personnel.

Moderator

Dr Christopher Burgess, Burgess Analytical Consultancy Ltd, UK, Chairman of the Analytical QC Group

Programme

Introduction to ECA's Analytical QC Working Group and the OOT Process

- Overview of ECA's Analytical QC Working Group
- Data quality management in the Laboratory
- Structure of the OOT/OOE guideline generation process
- Importance of a Technical Glossary
- Overview of the contents of the OOT/OOE Guideline
- Aims and objectives for this Forum

Regulatory Importance of Trend Analysis under the EU GMPs

- Regulatory concern for the control of processes
- Overview of the cited regulatory references
- Challenges for implementation and inspection
  - within the industry
  - for the inspectorate

The Statistical Tool Box; Basis for Selection

- What is a trend?
- What is a control chart?
- Data types
- Data distributions
- Statistical control
  - Common cause variation
  - Special cause variation
- Process stability versus process capability

Recommendations on Out of Expectation Results (OOE)

- Definitions for OOE
- Unexpected variation in replicate determinations
- Unexpected results in a Single Test or a Small Set of Tests
- What level of investigation is necessary and appropriate for OOE results?

Example Applications for Variables I - SPC

- Importance of individuals and means
- Example of SPC for continuous individual data; a Moving Range (MR) Shewhart Chart
- Setting the control limits
- Example of SPC for continuous data for subgroups; Xbar and R
- Process Capability
- What if data are not normally distributed?

Recommendations for Process Control of Variables

- Overview of the control of Continuous Data Monitoring for manufactured batches and for analytical test samples
- The basis for Statistical Process Control (SPC)
- Control Charts for Individuals
- Control Charts for Subgroups
- Control Charts for post mortem investigations

Example Applications for Variables II - Cusum for Investigations

- Theory and application of Cusum analysis
- Cusum versus EWMA charts
- Example of a post mortem Cusum investigation

Recommended Methods: Trending for Process Control of Attributes

- Basic differences between attributes and variables
- Control charts for attributes
- Applications for attribute data

Examples for Trending for Process Control of Attributes

- Theory and application of n and np charts
- Theory and application of C and U charts
- Example of np charting

Trending for Stability Data I: A Simplified Linear Regression Approach

- Challenges for trending stability data
- Simplified linear regression approach
  - Assumptions and limitations
  - Minimum data requirements
  - Theory and calculation of prediction intervals
- Worked example illustrated using Excel
- Comparison with SAS JMP; why aren't the numbers exactly the same?

Trending for Stability Data II: Random Coefficients Regression and other more Advanced Models

- Why is it sometimes necessary?
- Basics of the RCR model
- Advantages and disadvantages over the simplified linear regression approach
- Evaluation of stability data
- Examples of its application using statistical packages

INTERACTIVE WORKSHOPS

Workshop – Part I – OOE
Based on real life examples, the delegates will learn a step-by-step approach to determine whether suspect results are really out of expectation or must be accepted as given variability of the method.
Dr Bernd Renger

Workshop – Part II – Variables
Creating Control Charts in JMP
This workshop will include construction of variables control charts in SAS JMP
Dr Lance Smallshaw

Workshop – Part III – Attributes
This workshop will include construction of Attribute control charts in Minitab
Dr Chris Burgess

Workshop – Part IV – Stability
Dr Lori A. McCaig

OOS Workshop on 22 April 2021

Directly after the OOE/OOT Education Course the ECA **OOS Workshop** will take place.
The following topics will be discussed:

- OOS: US/FDA and European Regulatory Expectations
- OOS Results in R&D Laboratories – Specific Cases of OOS Results
- WORKSHOP I:
  ECA Analytical Quality Control Working Group - OOS SOP Version 02
- Strategies not to generate OOS results
- WORKSHOP II:
  Laboratory OOS results scenarios in QC and Development will be presented and evaluated in workshop groups

Speakers:
Dr Christopher Burgess, Dr Bernd Renger

Speakers

Dr Christopher Burgess
Burgess Analytical Consultancy, UK

Dr Burgess is a Chartered Chemist and has more than 40 years' experience in the pharmaceutical industry initially with Glaxo in Quality Assurance and Analytical R&D and then in international consultancy. He is a "Qualified Person" in the European Union and a member of the European QP Association advisory board. He was appointed to the United States Pharmacopoeia's Council of Experts 2010 to 2015 and re-elected 2015 to 2020 for and is a visiting professor of the University of Strathclyde's School of Pharmacy and Biomedical Sciences (SIPBS). In addition, he is the chairman of the ECA Analytical Quality Control Group and a member of the Executive committee of European Compliance Academy. He is also a member of the USP Expert Panel on Validation and Verification entrusted to revise General Chapters <1224>, <1225> and <1226>.

Dr Lori McCaig
Seagen, Inc, USA
Director, Stability Program Strategy

Lori McCaig, Ph.D., is the Director, Stability Program Strategy at Seagen, Inc. and is responsible for strategy, governance, and innovation in stability program design, data evaluation, and knowledge management from development through registration and product lifecycle. Before joining Seagen she has held stability program management leadership positions at Genentech/F. Hoffmann-La Roche Ltd, Connetics Corporation and Stiefel Laboratories, GlaxoSmithKline. Lori is a member of the USP Biologics Stability Expert Panel and enjoys working with stability colleagues across industry.

Dr Bernd Renger
Bernd Renger Consulting, Germany

Dr Bernd Renger started at Hoechst AG. Since then, he has held several quality management positions at Mundipharma, Byk Gulden (now Takeda) and Baxter BioScience in Vienna and Vetter Pharma-Fertigung. He was a member of the European Compliance Academy (ECA) Advisory Board and is Immediate Past Chair of the European QP Association.

Dr Lance Smallshaw
UCB Biopharma sprl, Belgium

Lance Smallshaw is Global Director of Analytical Strategy for NBEs at UCB Biopharma sprl in Belgium. Before that he was Senior Scientist at Eli Lilly and Company, having many years experience in Analytical Development and QC Laboratories. He is a member of the Executive Board of ECA and member of the EQPA training team.

Date

Handling OOE and OOT Results
Tuesday, 20 April 2021, 09.00 – 18.00 h
(Registration and coffee 08.30 – 09.00 h)
Wednesday, 21 April 2021, 09.00 – 17.00 h

OOS Workshop
Thursday, 22 April 2021, 08.30 – 16.00 h
(Registration and coffee 08.00 – 08.30 h)

Venue

Steigenberger Hotel Berlin
Los-Angeles-Platz 1
10789 Berlin, Germany
Phone +49 (0)30 212 7 - 0
Email berlin@steigenberger.de

Fees (per delegate, plus VAT)

Handling OOE and OOT Results
ECA Members € 1,590
APIC Members € 1,690
Non-ECA Members € 1,790
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.

Post-Conference OOS Workshop
ECA Members € 790
APIC Members € 840
Non-ECA Members € 890
EU GMP Inspectorates € 445
The conference fee is payable in advance after receipt of invoice and includes conference documentation, lunch and all refreshments. VAT is reclaimable.

Handling OOE and OOT Results & Post-Conference OOS Workshop
ECA Members € 2,190
APIC Members € 2,290
Non-ECA Members € 2,390
EU GMP Inspectorates € 1,340
The conference fee is payable in advance after receipt of invoice and includes conference documentation, dinner on the first day, lunch on all 3 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/POG when you have registered for the conference. 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.

Social Event

In the evening of 20 April 2021, 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.

Conference language

The official conference language will be English.

Organisation and Contact

ECA has entrusted Concept Heidelberg with the organisation of this event.
CONCEPT HEIDELBERG
P.O.Box 10 17 64
69007 Heidelberg, Germany
Phone +49(0)62 21/84 44-0
Fax +49(0)62 21/84 44 34
info@concept-heidelberg.de
www.concept-heidelberg.de

For questions regarding content please contact:
Dr Gerhard Becker (Operations Director) at
+49(0)62 21/84 44 65, or at
becker@concept-heidelberg.de.

For questions regarding reservation, hotel, organisation etc. please contact:
Ms Julia Grimmer (Organisation Manager) at
+49(0)62 21/84 44 44, or per e-mail at
grimmer@concept-heidelberg.de.

Every participant will get free access to the current version of the ECA Laboratory Data Management Guidance Document for the handling of Out of Expectation (OOE) and Out of Trend (OOT) Results.
The Appendices of this document contain a Technical Glossary and worked examples illustrating the main statistical tools and regression methods for setting stability trend limits.

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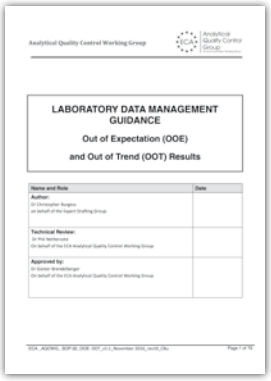

Your Benefit: Internationally Acknowledged Certificate from ECA Academy

The EU GMP Guide requires: „... All personnel should be aware of the principles of Good Manufacturing Practice that affect them and receive initial and continuing training,...". This is why you receive an acknowledged participant certificate, which lists the contents of the seminar in detail and with which you document your training.

WA/06112020

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CONCEPT HEIDELBERG
P.O. Box 101764
Fax +49 (0) 62 21/84 44 34

D-69007 Heidelberg
GERMANY

Reservation Form (Please complete in full)

☐ Handling OOE and OOT Results, 20/21 April 2021, Berlin, Germany
☐ Post-Conference OOS Workshop, 22 April 2021, Berlin, Germany

Title, first name, surname

Department Company

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

City ZIP Code Country

Phone / Fax

E-Mail (Please fill in)

General terms and conditions
If you cannot attend the conference you have two options:
1. We are happy to welcome a substitute colleague at any time.
2. If you have to cancel entirely we must charge the following processing fees:
- Cancellation until 2 weeks prior to the conference 10 %,
- Cancellation until 1 weeks prior to the conference 50 %
- Cancellation within 1 week prior to the conference 100 %.

CONCEPT HEIDELBERG reserves the right to change the materials, instructors, or speakers without notice or to cancel an event.
If the event must be cancelled, registrants will be notified as soon as possible and will receive a full refund of fees paid. CONCEPT HEIDELBERGwill not be responsible for discount airfare penalties or other costs incurred due to a cancellation.
Terms of payment: Payable without deductions within 10 days after receipt of invoice.
Important: This is a binding registration and above fees are due in case of cancellation or non-appearance. If you cannot take part, you have to inform us in writing. The cancellation fee will then be calculated according to the point of time at which we receive your message.
In case you do not appear at the event without having informed us, you will have to pay the full registration fee, even if you have not made the payment yet. Only after we have received your payment, you are entitled to participate in the conference (receipt of payment will not be confirmed)! (As of January 2012).
German law shall apply. Court of jurisdiction is Heidelberg.

Privacy Policy: By registering for this event, I accept the processing of my Personal Data. Concept Heidelberg will use my data for the processing of this order, for which I hereby declare to agree that my personal data is stored and processed. Concept Heidelberg will only send me information in relation with this order or similar ones. My personal data will not be disclosed to third parties (see also the privacy policy at http://www.gmp-compliance.org/eca_privacy.html). I note that I can ask for the modification, correction or deletion of my data at any time via the contact form on this website.