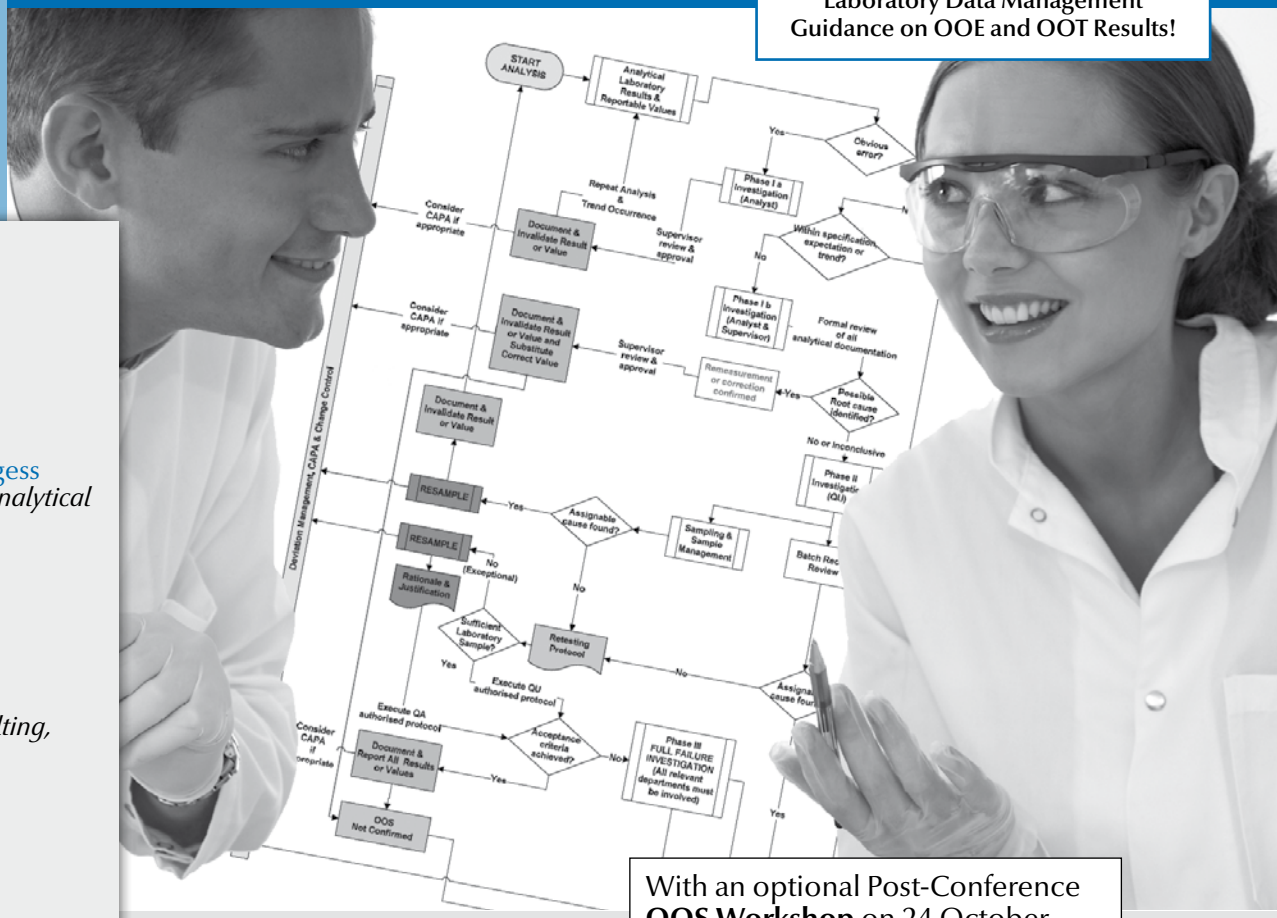
20 YEARS ECA Academy Your GMP/GDP Information Source

Handling OOE and OOT Results

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



With an optional Post-Conference **OOS Workshop** on 24 October

SPEAKERS:

Dr Christopher Burgess
Chairman of ECA's Analytical QC Group

Dr Bernd Renger
Bernd Renger Consulting, Germany

Lance Smallshaw
UCB Biopharma sprl, Belgium

Dr Lori McCaig
Roche/Genentech, USA

22 - 23 October 2019, Vienna, Austria

PROGRAMME:

- 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 (70 pages)
- 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, e.g. for Stability Testing

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

Handling OOE and OOT Results

22 - 23 October 2019, Vienna, Austria

Objectives

The ECA Working Group on Analytical Quality Control was founded in 2010 in order to generate a harmonised SOP on managing analytical deviations within the laboratory including OOS, OOE and OOT results.

Version 2 of the ECA OOS SOP has already been available for all ECA members since 2013.

Given the complexity of the topic, it was decided that the handling of OOT and OOE results should be addressed in a separate guideline SOP, since there is both a lack of knowledge in the industry and a lack of guidance for trend analysis from the regulators in spite of increased regulatory interest in this area.

In 2013 the ECA's QC Working Group decided to address these issues by developing a new guideline aimed at QC and other quality groups to encourage the application of a consistent and scientifically sound approach to trend analysis as part of a QMS for assuring data integrity.

There were initially three core components:

1. Recommended approaches for detecting out of expectation (OOE) data within an analytical sequence which are based on the known process capability of the analytical procedure used.
2. Recommended approaches to detecting out of trend (OOT) data between analytical sequences where no trend is expected. These are based on standard Statistical Process Control methodology and
3. Recommended approaches for detecting out of trend (OOT) data between analytical sequences where a trend is expected as is the case for Stability Testing.

From this foundation the current OOE/OOT Laboratory Data Management Guidance was developed by an international team to provide a harmonised approach to trending.

At this ECA OOE/OOT Training Course version 01 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.

The ECA Analytical QC Group's goal is to have a basic global framework for OOT/OOE within R&D, production and QC laboratories which is acceptable to the authorities and adaptable for individual companies.

Target Audience

This conference is intended for technical and managerial personnel dealing with out-of-trend or out-of expectation results, including R&D, production, analytical laboratories, contract laboratories, and Quality Assurance/ Quality Control personnel.

Moderator

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

Programme

Introduction to ECA's Analytical QC 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?

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 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?

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

Workshop – Part II – Attributes
This workshop will include a live construction of Attribute control charts in Minitab v18
Dr Chris Burgess

Workshop – Part III – Stability
Dr Lori A. McCaig

Workshop – Part IV – 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

Post-Conference OOS Workshop
24 October 2019, Vienna, Austria

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

- OOS: US/FDA and MHRA Guidelines and European Regulatory Expectations
- OOS Results in R&D Laboratories
- 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 Limited, UK
Chairman of the Analytical QC Group
Dr Burgess is a "Qualified Person" and was 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 for the 2015 to 2020 cycle. In addition, he is the chairman of the ECA Analytical Quality Control Group and a member of the Executive committee of European Compliance Academy.

Dr Lori McCaig

Roche/Genentech, USA
Lori McCaig, Ph.D., is the Head of Stability Program Management within Global Quality Control at Genentech/F. Hoffmann-La Roche Ltd. She is responsible for the strategy, oversight, and governance of commercial Stability programs starting during the registration phase and supporting the product lifecycle, and the control and use of stability related information for small molecules and biologics. She is a member of the USP Biologics Stability Expert Panel.

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.

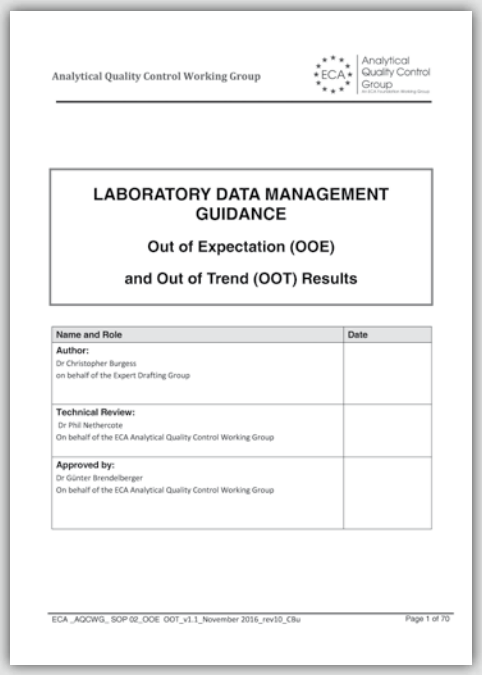
Lance Smallshaw

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 nearly 34 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 for the past 8 years.

Every participant will receive 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.** This 70 page Guidance Document covers the following topics:

- Scope and application
- Regulatory references
- Overview of the data management in the laboratory and the analytical process
- Responsibilities of QC and QA
- Overview and purpose of trend analysis
- The concept of control charts
- Detection and managing of OOE results
- Statistical Process Control (SPC) of continuous and discrete data
- Techniques for the retrospective investigation of historical data
- Trend analysis in stability testing

The document also has 7 Appendices; a Technical Glossary and worked examples illustrating the main statistical tools and regression methods for setting stability trend limits.


Analytical Quality Control Working Group

ECA Analytical Quality Control Group

LABORATORY DATA MANAGEMENT GUIDANCE

Out of Expectation (OOE)

and Out of Trend (OOT) Results

Name and Role	Date
Author: Dr Christopher Burgess on behalf of the Expert Drafting Group	
Technical Review: Dr Phil Nethercote On behalf of the ECA Analytical Quality Control Working Group	
Approved by: Dr Günter Brendelberger On behalf of the ECA Analytical Quality Control Working Group	

ECA_AQCWG_SOP 02_OOE OOT_v1.1_November 2016_rev10_CBu Page 1 of 70

Social Event

In the evening of the first course day, all participants are invited to a guided sight-seeing tour of Vienna and a dinner. This is an excellent opportunity to share your experiences with colleagues from other companies in a relaxed atmosphere.

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.

Conference language

The official conference language will be English.

Organisation and Contact

CONCEPT HEIDELBERG
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Fax +49 (0) 62 21/84 44 34
E-mail: info@concept-heidelberg.de
www.concept-heidelberg.de

For questions regarding content please contact:
Dr Günter Brendelberger (Operations Director) at +49-62 21 / 84 44 40, or per e-mail at brendelberger@concept-heidelberg.de.

For questions regarding reservation, hotel, organisation etc. please contact:
Mr Rouwen Schopka (Organisation Manager) at +49-62 21 / 84 44 13, or per e-mail at schopka@concept-heidelberg.de.

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☐ **Handling OOE and OOT Results**, 22 - 23 October 2019, Vienna, Austria
☐ **Post-Conference OOS Workshop**, 24 October 2019, Vienna, Austria

☐ Mr. ☐ Ms.

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Company Department

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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 %,
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Date

Handling OOE and OOT Results
Tuesday, 22 October 2019, 09.00 – 18.00 h
(Registration and coffee 08.30 – 09.00 h)
Wednesday, 23 October 2019, 08.30 -16.30 h

OOS Workshop
Thursday, 24 October 2019, 08.30 – 16.00 h
(Registration and coffee 08.00 – 08.30 h)

Venue of both events

Radisson Blu
Park Royal Palace Hotel, Vienna
Schlossallee 8
1140 Vienna, Austria
Phone +43/1/89110 9 200
info.parkroyalpalace.vienna@radissonblu.com

Conference 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.