Speakers:

Dr Christopher Burgess
Chairman of the Analytical QC Working Group, UK

Dr Milan Crnogorac
Roche, Switzerland

Dr Lori McCaig
Genentech/Roche, USA

Dr Peter Rauenbuehler
Genentech/Roche, USA

Dr Bernd Renger
Member of the Analytical QC Working Group, Germany

Dr Lance Smallshaw
UCB Biopharma, Belgium

Dr Bianca Teodorescu
UCB Biopharma, Belgium

Stephen Young
Head of Analytical Science Inspection, Enforcement and Standards Division, MHRA, UK

Every participant will receive Version 01 of ECA's SOP on OOE and OOT Results!

ECA ACADEMY

International Conference

OOT Forum 2015

SOP Out of Expectation (OOE) and Out of Trend (OOT) Results
Compiled by ECA's Analytical Quality Control Working Group

2-3 December 2015, Barcelona, Spain

Highlights

- 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
- All participants will have the opportunity to provide input to the contents of this guidance document during the interactive 'critique of the proposals' sessions for each of these topics

With Post-Conference **OOS Workshop** on 4 December 2015

Objective

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 is already 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 guideline was developed by an international team to provide a harmonised approach to trending.

At this ECA OOT Forum in Barcelona version 1 of our guideline 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 QC Working 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 Group

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.

Forum Moderator

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

Social Event

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

INTRODUCTION / REGULATORY SESSION

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

Dr Christopher Burgess

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

Stephen Young

The Statistical Tool Box; Basics of 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

Dr Christopher Burgess

SESSION 2 — TRENDING FOR PROCESS CONTROL OF VARIABLES (OOT 1)

Recommendations for Process Control of Variables (OOT1)

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

Lance Smallshaw

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?

Dr Bianca Teodorescu

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

Dr Bianca Teodorescu

SESSION 3 — TRENDING FOR PROCESS CONTROL OF ATTRIBUTES (OOT 2)

Recommended methods: Trending for Process Control of Attributes (OOT 2)

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

Dr Christopher Burgess

Examples for Trending for Process Control of Attributes (OOT 2)

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

Dr Milan Crnogorac

SESSION 4 — TRENDING FOR STABILITY DATA (OOT 3)

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?

Dr Peter Rauenbuehler

Trending for Stability Data II; a more advanced Random Coefficients Regression Model

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

Dr Lori A. McCaig

SESSION 5 — OUT OF EXPECTATION RESULTS (OOE)

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?

Dr Bernd Renger

SESSION 6 — SCOPE AND APPLICATION OF THE TOOLS

WORKSHOP: Next Steps; Implementation Strategy

- Review output from the 6th GMP Conference Workshop on OOT & OOE, Heidelberg, June 2015
- Detailed review of the sections of Analysis & Testing and S tability Testing
- Mapping the tools to the identified tasks
- Inputs to version 2 of the OOT/OOE Guideline SOP

Dr Christopher Burgess

ECA Post Conference OOS Workshop
on 4 December 2015, 08.30 - 16.00 h
Barceló Sants Hotel, Barcelona

Directly after the OOT Forum on Friday, 4 December 2015 there will be the ECA **OOS Workshop** with these topics:

- OOS: US/FDA 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

Organisation / Contact
CONCEPT HEIDELBERG
P.O. Box 10 17 64 | D-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:
Dr Günter Brendelberger (Operations Director)
at +49-62 21 / 84 44 40, brendelberger@concept-heidelberg.de.
For questions regarding reservation, hotel, organisation etc:
Ms Katja Kramer (Organisation Manager)
at +49 (0) 62 21 / 84 44 16, kramer@concept-heidelberg.de.

Speakers

Dr Christopher Burgess, Burgess Analytical Consultancy Limited, Barnard Castle, UK
Chairman of the Analytical QC Working Group
Dr Burgess is a "Qualified Person" 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 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 Milan Crnogorac, Roche, Switzerland
Milan Crnogorac, Ph.D., is a Senior Quality Leader within External Quality at Roche. He oversees Quality System and Quality Issues, as well as Product Release, Risk Management, and Technology Transfer processes.

Dr Lori McCaig, Roche/Genentech, USA
Lori McCaig, Ph.D., is the Head of Stability Program Management within Global Biologics Quality Control at Genentech/F. Hoffmann-La Roche Ltd. She is responsible for the strategic direction, oversight, and management of Stability across the Biologics OU including the design, implementation, compliance readiness, and governance of stability programs starting at the transition from development to approval and through the commercial life-cycle, and the interpretation, use, and management of stability information.

Dr Peter Rauenbuehler, Roche/Genentech , USA
Peter Rauenbuehler, Ph.D., is a Senior Principal Technical Advisor, within Global Quality System & Processes at Genentech. He is responsible for the design, development, implementation support and governance for GMP laboratory related policies under the Quality System.

Dr Bernd Renger, Bernd Renger Consulting, Germany
Member of the Analytical QC Working Group
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 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.

Dr Bianca Teodorescu, UCB Biopharma sprl, Belgium
Bianca Teodorescu is Associate Director Non Clinical Statistics in the Technical Operations department at UCB Biopharma sprl in charge of the non-clinical statistical team supporting the development department for biological and chemical entities (analytical, process, pharma), as well as the QC and manufacturing department.

Stephen Young, Head of Analytical Science Inspection, Enforcement and Standards Division, MHRA, UK
Stephen Young worked for ten years in the UK Pharmaceutical Industry, in various roles including analytical development, product stability and manufacturing technical support. He joined the Inspection, Enforcement and Standards division of MHRA in 2003 and currently provides leadership to the Agencies physico-chemical laboratories, which include the Pharmacopoeia and Regulatory Laboratory functions.

Special Offer with Lufthansa – Discounted Travel for OOT Forum 2015 Attendees
As an ECA course or conference attendee, you will receive up to 20% discounted travel fares (according to availability). And this is how it works: Once you registered for a course or conference you will receive a link together with your registration confirmation. Opening that link will take you to the Mobility Partner Program website where you can enter a code in the "Access to Event Booking" area you will also receive. This will take you into an online booking platform* that will automatically calculate the discount offered or provide you with an even better offer if another promotional fare is available. We look forward to welcoming at one of our next events – and we already wish you a pleasant flight!

*Please note that you may have to enable pop-ups on this site – otherwise the booking platform window will not open.

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Date
OOT Forum
Wednesday, 2 December 2015, 09.00 – 18.30 h
(Registration and coffee 08.30 – 09.00 h)
Thursday, 3 December 2015, 08.30 -16.30 h

OOS Workshop
Friday, 4 December 2015, 08.30 – 16.00 h
(Registration and coffee 08.00 – 08.30 h)

Venue
Barceló Sants
Placa dels Paisos Catalans, s/n
Estació de Sants
08014 Barcelona, Spain
Phone +34 93 503 53 00
Fax +34 93 490 60 45

Conference Fees (per delegate plus VAT)
OOT Forum
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.

OOT Forum **and** OOS Post Conference Workshop
ECA Members € 2,090
APIC Members € 2,190
Non-ECA Members € 2,290
EU GMP Inspectorates € 1,145
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 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 to info@concept-heidelberg.de by fax to +49 6221 / 84 44 34 . Or you register online at www.gmp-compliance.org

Conference Language
The official conference language will be English.

If the bill-to-address deviates from the specification to the right, please fill out here:

CONCEPT HEIDELBERG
Postfach 10 17 64
Fax 06221/84 44 34

D-69007 Heidelberg

Reservation Form (Please complete in full)

+ 49 6221 84 44 34

☐ **OOT Forum 2015**
2-3 December 2015, Barcelona, Spain

☐ Yes, I also want to participate in the ECA Post Conference **OOS Workshop** on 4 December 2015, Barcelona, Spain

☐ Mr ☐ Ms

Title, first name, surname

Company Department

Important: Please indicate your company's VAT ID Number **P.O. Number (if applicable)**

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