

**Speakers:**

**Dr Tony Bennett**  
GSK, UK

**Dr Christopher Burgess**  
Chairman of the Analytical Quality Control Group

**Margarida Mesquita Carvalho**  
Bluepharma Industria Farmaceutica S.A., Portugal

**Trevor Duguid Farrant**  
Reading Scientific Services Limited (KraftFoods), UK

**Dr Matthias Heuermann**  
European GMP Inspector,  
NRW Centre for Health (LZG.NRW), Germany

**Dr Elin Jensen**  
Novo Nordisk, Denmark

**Dr Olaf Kunze**  
CSL Behring GmbH, Germany

**Di Morris**  
MHRA, UK

**Dr Peter Rauenbuehler**  
Roche, USA

**Dr Bernd Renger**  
European QP Association, Germany

**Dr Ulrich Rose**  
EDQM, France

**Dr Dawn Toronto**  
CMC & Analytical Consultant, Germany



EUROPEAN COMPLIANCE  
ACADEMY

in cooperation with



# Invitation

to the

# OOS Forum 2012

Prague, Czech Republic

19-20 June 2012

## International Launch Conference

SOP "Out of expectation (OOE), Out of Trend (OOT) and Out of Specification (OOS) Results"

Compiled by ECA's Analytical Quality Control Working Group



Demystifying the secrets of proper handling  
of OOS results



## Part I - REGULATORY SESSION

### OOS: US / FDA Expectations

- Background to the FDA Final Guidance 2006
- Long standing FDA Principles
- Key points from the Final Guidance
  - Scope
  - Investigation Processes
  - Roles and Responsibilities
  - Analysis and reporting of results
  - Outlier testing
  - Cautions

Dr Christopher Burgess, Chairman of the Analytical QC Group

### OOS Results – European Requirements and Expectations of a European GMP Inspector

- The OOS SOP
  - Definition of in-spec and out-spec Results
  - OOS Investigation phases
  - Batch disposition
  - Surveillance of the release decision
  - Comparison ECA OOS SOP and MHRA approach
- Dr Matthias Heuermann, European GMP Inspector, NRW Centre for Health (LZG.NRW), Germany

### Fundamentals of Analytical Variability

- Sources and types of variables
  - Measures of variables
  - Process Capability
  - Replications and reportable values
- Dr Christopher Burgess, Chairman of the Analytical QC Group

## Part II - LABORATORY DATA MANAGEMENT; OOE, OOT, and OOS Results

### ECA Analytical Quality Control Working Group SOP

- Background
  - Scope and limitations
  - Process
  - Key elements and process flow
- Dr Christopher Burgess, Chairman of the Analytical QC Group

## Alternative Approaches

Members of ECA's OOS Review Team who helped to develop the ECA OOS SOP will present their comments and alternative approaches (15 min each):

**Margarida Mesquita Carvalho**, Bluepharma Industria Farmaceutica S.A., Portugal

**Dr Dawn Toronto**, CMC & Analytical Consultant, Germany

**Dr Tony Bennett**, GSK, Global Manufacturing Supply, UK

**Dr Peter Rauenbuehler**, Roche, USA

**Dr Elin Jensen**, Novo Nordisk, Denmark

These ECA OOS Review Team Members will discuss their company's actual and/or established OOS processes with focusing on differences to the ECA SOP with emphasis on these individual options, including e.g.

- When to start an OOS investigation
- QA involvement already in early stages?
- Scope and limitations of Phase II investigation
- Retesting - assessment and acceptance criteria
- Reporting

These inputs could form the basis for a revised and updated version 2 of ECA's OOS SOP.

## Part III - CRITICAL ASPECTS OF OOS INVESTIGATIONS

### Terms Used in Out of Specification Investigations

- FDA Guidance for Industry terms - many terms for the same subject, e.g. for sample – sample, lot, resample, new sample, homogenous sample, portion of a batch, etc.
  - Further relevant ASTM terms
  - GSK's attempts to weld the FDA and ASTM terms together
  - How these terms direct an OOS/atypical result investigation at GSK
- Dr Tony Bennett, GSK, UK

### Identification, Isolation and Evaluation of Outliers

- Consequences of inconclusive Investigations
- Isolation approaches; How to show that the OOS result is highly unlikely to be representative of the sample population
  - z scores
  - Rosner's test
  - Dixon's tests (and why not to use them!)
  - Hampel's rule
- How many retests do I need to achieve 'isolation'?

- Calculation approaches that take into account the outlier
  - 95% confidence interval comparison with specification (Current SOP approach)
  - Robust procedure H15 proposal for v2 of the SOP

Dr Christopher Burgess, Chairman of the Analytical QC Groupy, UK and Trevor Duguid Farrant, Reading Scientific Services Ltd., UK

### Out-of-Trend Results

- Roche's current perspective on detecting out of trend results
- Investigation of out of trend results

Dr Peter Rauenbuehler, Roche, USA

## Part IV - APPLICATION-SPECIFIC CONSIDERATIONS

### Pharmacopoeial Compliance

- Mandatory requirements for monograph compliance
- OOS and monograph compliance
- Identification tests and monograph compliance
- Impurity tests and monograph compliance
- Compliance with specifications given in the assay - possible approaches

Dr Ulrich Rose, EDQM

### OOS Results in R&D Laboratories

- Drug development & analytical life cycle
- Aberrant analytical data in R&D
- OOE results in preclinical development & investigation medicinal products
- OOE in bioassay samples
- OOE and OOT results in stability studies

Dr Bernd Renger, European QP Association, Germany

### OOS in Biologics

- Biological Assays
- Intermediates
- Real time equipment or system adjustments
- OOE
- Stability OOS

Dr Olaf Kunze, CSL Behring, Germany

### OOS in Microbiology

- The microbiological OOS procedure
- Planning investigations
- The investigation process
- Take away messages

Di Morris, MHRA, UK

## Speakers

Dr Tony Bennett, GSK, UK

Tony Bennett is an Analytical Leader within GSK's central quality functions for Global Manufacturing and Supply.

Dr Christopher Burgess, Burgess Analytical Consultancy Ltd, UK

Dr Burgess is a "Qualified Person" and a member of the European QP Association advisory board. In addition, he is the chairman of the ECA Analytical Quality Control Group and a member of the Executive committee of European Compliance Academy.

Margarida Mesquita Carvalho, Bluepharma Industria Farmaceutica S.A., Portugal

Margarida Mesquita Carvalho, PharmaD, is a senior QA officer at Bluepharma and was a member of the Review Team that provided the industry feedback.

Trevor Duguid Farrant, Reading Scientific Services Limited (Kraft-Foods), United Kingdom

Trevor is the statistics leader; during his career he has developed new methodologies and applications for Gillette, P&G, Cadbury & KraftFoods.

Dr Matthias Heuermann, European GMP Inspector, NRW Centre for Health (LZG.NRW), Germany

Since 2004 Dr Heuermann is employed as head of the Official Medicines Control Laboratory (OMCL), today within the NRW Centre for Health of the federal state Nordrhein-Westfalen in Münster.

Dr Elin Jensen, Novo Nordisk, Denmark

Dr Jensen has worked as manager of quality control laboratories for many years. Currently she is working cross-organisationally with harmonisation of laboratory processes in Novo Nordisk, among these also OOS investigations.

---

**Dr Olaf Kunze, CSL Behring GmbH, Germany**

Dr Kunze is Director Quality Control Chemistry with CSL Behring in Marburg, Germany. He was member of the Review Team that provided the industry feedback.

**Di Morris, MHRA, UK**

GMP Inspector for Medicines and Healthcare products, Regulatory Agency (MHRA) UK

**Dr Peter Rauenbuehler, Roche, USA**

Peter Rauenbuehler, Ph.D., is a Senior Principal Technical Advisor, within Global Quality Systems & Processes at Genentech focused on laboratory policies.

**Dr Bernd Renger, European QP Association, Germany**

Dr Bernd Renger is a member of the ECA Advisory Board and Chairman of the European QP Association.

**Dr Ulrich Rose, EDQM, France**

Dr Ulrich Rose is Scientific Officer at the European Directorate for the Quality of Medicines & Health Care (EDQM) in Strasbourg. Dr. Rose is also member of the "Analytical Quality Control Group" of ECA.

**Dr Dawn Toronto, CMC & Analytical Consultant, Germany**

Dawn Toronto, PhD is a CMC consultant located in Munich, Germany and specializing in Regulatory Affairs, Analytical Development & Outsourcing Management.

## Conference Language

The official conference language will be English.

## 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,  
or per e-mail at [brendelberger@concept-heidelberg.de](mailto:brendelberger@concept-heidelberg.de).

For questions regarding reservation, hotel, organisation etc:

Mr Ronny Strohwalde (Organisation Manager) at +49 (0) 62 21 / 84 44 51,  
or per e-mail at [strohwalde@concept-heidelberg.de](mailto:strohwalde@concept-heidelberg.de).



### Special Offer with Lufthansa – Discounted Travel for OOS Forum 2012 Attendees

As an ECA course or conference attendee, you will receive **up to 20% discounted travel fares** (according to availability). And as Lufthansa German Airlines offers a comprehensive global route network linking major cities around the world you will most likely be able to benefit from these special prices and conditions. 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.

## About the European QP Association

The European Qualified Person (QP) Association was founded on 7 July 2006 by the European Compliance Academy's (ECA) Advisory Board Members. With this unique association the ECA wants to provide QPs in Europe with a platform allowing them to exchange their experience, discuss the latest regulatory requirements, to identify and address difficulties and challenges and to support a harmonised European approach. More information about the QP Association and a membership application form are available at [www.qp-association.eu](http://www.qp-association.eu).

## About CONCEPT HEIDELBERG

Founded in 1978, CONCEPT HEIDELBERG is the leading organiser of seminars on pharmaceutical production, quality control, quality assurance and GMP in Europe. This year more than 240 events will be organised by CONCEPT HEIDELBERG. The European QP Association has entrusted CONCEPT HEIDELBERG with the organisation of its events.

ECA Conference

### Compliance Update: EP, USP, and JP

- Update on New Monographs
  - Dealing with Divergent Compendial Methods
- 21 – 22 June 2012, Prague, Czech Republic

Directly following the OOS Forum - 21 – 22 June 2012 -, there will be the ECA Conference Compliance Update: EP, USP, and JP with these topics:

- Analytical Instrument Qualification and Computerised System Validation: Extension of USP <1058>
- Elemental Impurities
- Revision of USP Chapters for Analytical Procedures:
  - <1224> Transfer
  - <1225> Validation
  - <1226> Verification
- New USP Chapters for Spectroscopic Methods
- Dissolution Testing: USP Chapter <711> versus FDA Mechanical Calibration Approaches
- Analytical Testing according to JP
- How to Deal with Divergent Compendial Method Requirements (EP, USP, JP)
- WORKSHOP Multicompendial and Alternative Testing

Further information about this course can be received at [www.gmp-compliance.org](http://www.gmp-compliance.org).

Register simultaneously for both courses and receive a 350 € discount (not valid for EU GMP Inspectorates).

## Date

Tuesday, 19 June 2012, 09.00 – 18.30 h  
(Registration and coffee 08.30 – 09.00 h)  
Wednesday, 20 June 2012, 08.30-16.00 h

## Venue

Corinthia Hotel Prague  
Kongresova 1  
14069 Prague 4, Czech Republic  
Phone + 420 261 191 111  
Fax + 420 261 225 011

## Conference Fees

ECA Members EUR 1,490,-\*  
QPA Members EUR 1,490,-\*  
APIC Members EUR 1,590,-\*  
Non-ECA Members EUR 1,690,-\*  
EU GMP Inspectorates EUR 845,-\*  
\* per delegate plus VAT

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.

## Would you like to safe money?

If you register for the ECA Education Course "Compliance Update: EP, USP, and JP" from 21-22 June 2012 at the same time, you will receive a € 350 discount. This is not valid for EU GMP Inspectorates.

## 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 or be sure to mention

"XCON180612" to receive the specially negotiated rate (single room € 137,50 per night, incl. breakfast) for the duration of your stay. Reservation should be made directly with the hotel not later than 21 May 2012. 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.oos-forum.org

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

- OOS Forum**, 19 - 20 June 2012, Prague, Czech Republic
- Yes, I also want to participate in the ECA Conference "Compliance Update: EP, USP, and JP" on 21 - 22 June 2012, Prague, Czech Republic
- Mr       Ms

\_\_\_\_\_  
Title, first name, surname

\_\_\_\_\_  
Company

\_\_\_\_\_  
Department

**Important: Please indicate your company's VAT ID Number**

**P.O. Number (if applicable)**

\_\_\_\_\_  
Street / P.O. Box

\_\_\_\_\_  
City

\_\_\_\_\_  
Zip Code

\_\_\_\_\_  
Country

\_\_\_\_\_  
Phone / Fax

\_\_\_\_\_  
E-mail ( Please fill in)

## General Terms of Business

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 % of the registration fee.
  - until 1 week prior to the conference 50 % of the registration fee.
  - within 1 week prior to the conference 100 % of the registration fee.

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 HEIDELBERG will 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. You are not entitled to participate in the conference until we have received your payment (receipt of payment will not be confirmed) (As of January 2012)