Impurities Forum
Identification, Risk Assessment and Control of Impurities in Drug Products, Drug Substances and Excipients

Speakers from Authority & United States Pharmacopeia

Dr Ulrich Rose
EDQM, France

Dr Kahkashan Zaidi
USP, USA

Industry Speakers

Dr Gerd Jilge
Boehringer Ingelheim Pharma, Germany

Dr Samuel Powell
Pfizer, UK

Dr Xaver Schratt
LPU GmbH, Germany

Dr Andrew Teasdale
AstraZeneca, UK

Dr Lise Vanderkelen
Toxicon Europe, Belgium

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

Part I:

■ General Strategies
  27 June 2017, Copenhagen, Denmark

Part II:

■ Elemental Impurities
  28 June 2017, Copenhagen, Denmark

Post-Conference Workshop* on 29 June 2017:
"The Elemental Impurities Database for Excipients"

(*Free of charge for those who participate in at least one part of the Impurities Forum!)
PART I: GENERAL STRATEGIES

Objectives

Part I of The Impurities Forum will provide an opportunity to reinforce and expand your knowledge of the general area of impurities in chemical entities from initial development to the market with emphasis on:

- Detection, profiling and control of impurities in drug substances, intermediates and drug products
- Practical aspects of method validation for impurities determination
- Analytical techniques used for detecting and qualifying impurities
- Extractables and Leachables as a source of impurities
- Stress stability testing as a tool to determine degradation pathways

During this event you will get to know the relevant aspects of impurities analysis, characterisation and control in drug substances and drug products and their recording and reporting.

Background

Setting specifications for impurities are one of the most critical topics in the development of new drug products. Impurities analysis in drug substances and drug products and their recording and reporting is quite often a challenge for the scientific experts in routine production and quality control. This challenge is even bigger when profiles of unknown impurities in complex matrices have to be established.

Target Audience

This workshop addresses all personnel involved in development of drug substances and drug products from scientific staff to laboratory heads involved in R&D. The needs of Laboratory Managers, Supervisors and Analysts in pharmaceutical quality assurance and quality control departments will also be covered. This event will also address regulatory requirements and hence is applicable to people working in the regulatory affairs area.

Programme

**Impurities analysis and qualification in Drug Substances and Drug Products – general overview**

- Impurity profiling in synthetic drug substances
- Qualification of impurities
- Degradation studies
- Identification of chiral impurities, polymorphic phases and new impurities
- Residual solvents
- Impurities in starting materials and intermediates
- Pharmacopoeial tests and acceptance criteria
- Drug product specifications and parametric release
- Inorganic impurities

**Control of organic impurities in the European Pharmacopoeia**

- Ph. Eur. analytical techniques used for impurity control
- Impurity control in general chapters and monographs
  - General monograph 2034
  - General chapter 5.10 - control of impurities
  - General chapter 2.2.46 - chromatographic separation techniques
- Qualitative and quantitative control
  - System suitability tests
  - Methods of quantification
  - Limit test vs quantitative test
- Response and correction factors

**Practical aspects of method validation for impurity determination**

- Important ICH and FDA guidelines
- Quantitation of impurities
- How to define an impurity profile (stress tests)
- Reference substances
- Validation of methods at various development stages
- Statistical approaches to method validation (LOD & LOQ)

**Presentation and Workshop: Analytical techniques for determination and qualification of impurities in Starting Materials and Intermediates**

- Purity analysis by HPLC, impurity profile
- Residual solvents by GC
- Inorganic impurities (heavy metals, sulphated ash)
- For chiral compounds in addition: enantiomeric purity and proof of the absolute configuration
In the Workshop the participants will learn which activities are necessary to characterise drug substances taking into account the following aspects:

- analytical procedures are necessary for the characterisation
- experiments necessary to check the downstream impurities in order to justify acceptance criteria for the respective impurities
- other impurities have to be taken into account
- experiments to be performed in order to get a stability-indicating analytical procedure

**Leachables and extractables**

- Why should Extractables & Leachables be assessed?
- Regulatory requirements in the EU and US
- Compendial requirements and industry standards
- Safety qualification of Leachables and Extractables

**Stress stability testing during development**

- Elucidation of impurities of the drug substance
- Identification of possible degradation products
- Check of the degradation pathways
- Typical experiments
- Test parameter
- Storage conditions
- Stress tests of multi-use products
- Impact on excipients and packaging materials

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**PART II: ELEMENTAL IMPURITIES**

**Objectives**

In Part II of the Impurities Forum the key principles of the ICH Q3D Guideline on elemental impurities will be highlighted. You will get to know the essential aspects and approaches of how to determine and control elemental impurities in drug substances, drug products and excipients. You will learn

- what has to be considered with respect to the drug substance monographs of the European Pharmacopoeia
- how to perform a risk assessment in order to establish a control strategy for elemental impurities,
- how the route of administration and the duration of exposure affect the limits of elemental impurities
- which analytical methods are suitable to determine elemental impurities and what you have to consider when you apply them,

**Background**

In November 2014 the ICH Q3D Guideline for Elemental Impurities was published as Step 4 document. This document outlines

- the evaluation of the toxicity data for potential elemental impurities
- the PDEs for each element of toxicological concern
- the basis for an EI risk assessment and the key factors for evaluation.
- the development of controls designed to limit the inclusion of elemental impurities in drug products to levels at or below the PDE

In the European Pharmacopoeia the test for heavy metals (2.4.8) from approx. 760 individual monographs on substances for pharmaceutical use (except substances for veterinary use only) were deleted. The revised versions of the general monographs on Substances for pharmaceutical use (2034) and Pharmaceutical preparations (2619), of the general chapters on Elemental Impurities (5.20) and on Determination of elemental impurities (2.4.20) have been adopted and will become effective on 1 January 2018.

In March 2015 USP announced a revision to General Notices section 5.60.30 Elemental Impurities in USP Drug Products and Dietary Supplements, establishing 1 January 2018 as the new date of applicability of General Chapters <232> Elemental Impurities-Limits and <2232> Elemental Contaminants in Dietary Supplements.
The conference addresses all personnel involved in development of drug substances and drug products from scientific staff to laboratory heads involved in R&D. The needs of Laboratory Managers, Supervisors and Analysts in pharmaceutical quality assurance and quality control departments will also be covered.

### Programme

**EDQM’s implementation strategy of ICH Q3D in the European Pharmacopoeia – an update**
- History of heavy metals tests
- Implementation strategy of ICH Q3D in Ph. Eur.
- Modifications of general chapters and general monographs
- Specific metal tests in individual monographs

**ICH Q3D on elemental impurities – requirements and implementation status in the USP general chapters and monographs**
- An update on USP chapter <232> and its harmonization with ICH-Q3D
- Fate of USP chapter <231>
- Impact of <232> on other USP chapters and how it will be addressed.
- Elemental impurities implementation plans
- Where we are with the harmonization of USP chapter <233> Elemental Impurities- Procedures through PDG

**Analytical methods to determine elemental impurities**
- Principles and characteristics of the most common spectrometric techniques AAS, ICP-OES, ICP-MS
- Compound methods (sample preparation plus spectrometric detection and quantification)
- Special considerations for trace-elemental analysis
- Application-based approach for choice of methodology
- Analytical process (method development, validation strategy, routine testing)

**Control Strategies for Elemental Impurities in final dosage forms – Case studies**
- Utilisation of Data as part of an Integrated EI Risk Assessment Process
- Potential Sources of Elemental Impurities in the Finished Product
  - API
  - Equipment
  - Container closure system
  - Excipients
- Conclusions

**Workshop: Conducting a risk assessment**
In this Workshop the participants will work on several case studies and perform a risk assessment for different scenarios taking into account e.g. manufacturing equipment, dosage form of the drug product etc.

**POST CONFERENCE WORKSHOP ON 29 JUNE 2017**

**THE ELEMENTAL IMPURITIES DATABASE FOR EXCIPIENTS**

The Elemental Impurities database is an initiative of a pharma consortium and aims to collect and share data from pharmaceutical excipients.

In this workshop the following points will be discussed:
- How to contribute to/send data to the database: What is the procedure?
- How to get information out of the database: What are the prerequisites and requirements?
- What about confidentiality regarding the submission to or reception of information from the database?

As part of this workshop the importance of data in a step wise integrated risk based approach and potential sources of these data will also be examined.

*Only for those who participate in at least one part of the Impurities Forum*
DR Gerd Jilge, Boehringer Ingelheim Pharma GmbH & Co. KG, Germany
In 1991 Dr Gerd Jilge came to Boehringer Ingelheim working in product development where he was responsible for method development and validation for the application of analytical procedures. In 2000 Dr Jilge took a position in Drug Regulatory Affairs of Boehringer Ingelheim GmbH with the focus on CMC documentation for the submission of new and registered drug products. Since July 2007 he is working in Quality Management on method development for new drug substances.

DR Samuel Powell, Pfizer, United Kingdom
Dr Sam Powell graduated in medicinal and biological chemistry. He started his career at Invitrogen and joined Pfizer Discovery Biology in 2007. In 2008 he moved into pharmaceutical science as an analytical chemist and has held since then many positions within the organisation from vaccines and devices. He first started using ICP to assay gold particles from a needleless delivery device, moving this to assay gold and DNA in combination.

DR Ulrich Rose, EDQM, France
Dr Rose works since 1991 at the EDQM in Strasbourg. Until 2011 he was responsible for establishment and monitoring of the Ph. Eur. reference standards. Moreover he was involved in the elaboration and revision of monographs of the European Pharmacopoeia. After that he became coordinator and auditor for EDQM’s Mutual Joint Audit Program. Within this function he had to audit the Official Medicines Control Laboratories (OMCLs) in Europe. Since 2014 he is head of division A and deputy head of the European Pharmacopoeia Department where he is overseeing the monograph work on chemicals, excipients, herbals and general chapters of Ph. Eur. and is involved in the international harmonisation of pharmacopoeias.

DR Xaver Schratt, LPU Labor für Pharma- und Umweltanalytik GmbH, Germany
Dr Schratt studied Chemistry at the University of Bayreuth, where he specialized in HPLC and HPLC/MS. In 2005 he joined LPU (formerly LAT) and since 2006 he is head of department R & D 2. In charge of national and international pharmaceutical companies he manages all analytical aspects of projects from preclinical stage up to phase III and post market approval. As an expert for chromatography and mass spectrometry he mainly focuses on method development, validation and qualification of reference substances.

DR Andrew Teasdale, AstraZeneca, United Kingdom
Andrew Teasdale PhD has over 20 years’ experience in the pharmaceutical industry as an analytical chemist and within quality assurance and regulatory roles. He has led a number of industry expert groups; these include both safety and quality groups within Pharmaceutical Research and Manufacturers of America (PhRMA), European Federation of Pharmaceutical Industries and Associations (EFPIA), Product Quality Research Institute (PQRI) and the Extractables and Leachables safety Information exchange (ELSIE) for which he is the chair of the materials working group. Dr Teasdale is also currently the chairman of the Joint Pharmaceutical Analytical Group (JPAG) in the UK.

DR Lise Vanderkelen, Toxikon Europe, Belgium
Lise Vanderkelen received her Ph.D. from the Faculty of Bioscience Engineering at the University of Leuven (Belgium) in 2012. She started at Toxikon Europe in 2013 as study director at the Extractables & Leachables Department, focusing on Injectables and Parenterals and in 2014 she became responsible for the chemical characterization testing for the medical device industry. Today, she is Department Head Pharma Services at Toxikon Europe. The main focus of this department is identifying organic impurities in drug products.

DR Kahkashan Zaidi, USP, USA
Dr Kahkashan Zaidi is a Principal Scientific Liaison in the General Chapters group of the Science Division at the United States Pharmacopeia. She is a liaison to the USP Expert Committees on Dosage Forms, Chemical Analysis, and Expert Committee on Physical Analysis. Kahkashan joined USP in May 1999. Prior to that, she worked in the Pharmaceutical industry as a Research Scientist. She has published articles and lectured internationally on topics related to impurities and USP, and the standards development process. She represented USP on the ICH–Q3D (Elemental Impurities) working group and the ICH-Q3D Implementation working group. She is also the USP lead on this topic.

Social Event
In the evening of the first conference day, 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.
Dates
Part I: General Strategies
Tuesday, 27 June 2017, 09.00 – 18.00 h
(Registration and coffee 08.30 – 09.00 h)

Part II: Elemental Impurities
Wednesday, 28 June 2017, 09.00 – 17.45 h
(Registration and coffee 08.30 – 09.00 h)

Post-Conference Workshop:
The Elemental Impurities Database for Excipients
Thursday, 29 June 2017, 09.00 – 12.00 h
(Registration and coffee 08.30 – 09.00 h)

Venue
Radisson BLU Scandinavia Hotel
Amager Boulevard 70
2300 Copenhagen S, Denmark
Phone +45 33 96 50 00
Fax +45 33 96 55 00

FEES (per delegate plus VAT)
Part I: General Strategies
ECA Members € 790
APIC Members € 890
Non-ECA Members € 990
EU GMP Inspectorates € 495

Part II: Elemental Impurities
ECA Members € 790
APIC Members € 890
Non-ECA Members € 990
EU GMP Inspectorates € 495

Part I and II
ECA Members € 1,390
APIC Members € 1,490
Non-ECA Members € 1,590
EU GMP Inspectorates € 795

Post-Conference Workshop Non-ECA Members € 390
APIC Members € 290
EU GMP Inspectorates € 195

The Post-Conference Workshop is free of charge only for those who participate in at least one part of the Impurities Forum!

The conference fee is payable in advance after receipt of invoice and includes conference documentation, dinner on 27 June, lunch on 27 and 28 June and all refreshments. VAT is reclaimable.

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

Reservation Form (Please complete in full)

IMPURITIES FORUM, 27-28 June 2017, Copenhagen, Denmark

☐ Part I: 27 June 2017 ☐ Part I and II: 27-28 June 2017
☐ Part II: 28 June 2017 ☐ Post-Conference Workshop on 29 June 2017

☐ Mr ☐ Ms

Title, first name, surname

Company

Department

Important: Please indicate your company’s VAT ID Number

Street / P.O. Box

City Zip Code

Country

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E-Mail (Please fill in)

Reservaton Form: CONCEPT HEIDELBERG
P.O. Box 10 17 64
69007 Heidelberg, Germany

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. Reservation should be made directly with the hotel. Early reservation is recommended.

Organisation and Contact
ECA has entrusted Concept Heidelberg with the organisation of this event.

CONCEPT HEIDELBERG
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For questions regarding content:
Dr Gerhard Becker (Operations Director) at +49(0)6221 / 84 44 65, or per e-mail at becker@concept-heidelberg.de.

For questions regarding reservation, hotel, organisation etc.:
Mr Ronny Strohwald (Organisation Manager) at +49(0)6221 / 84 44 51 or per e-mail at strohwald@concept-heidelberg.de.

Questions regarding the cancellation of events
We are happy to welcome a substitute colleague at any time.

1. We are happy to welcome a substitute colleague at any time.
2. If you have to cancel entirely we must charge only for those who participate in at least one part of the Impurities Forum!

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

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69007 Heidelberg
Germany

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 only for those who participate in at least one part of the Impurities Forum!

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.

In case you do not appear at the event without informing us, you are entitled to participate in the conference receipt of payment will not be reclaimed.

If you have to inform us in writing.

In case you do not appear at the event without informing us, you are entitled to participate in the conference receipt of payment will not be reclaimed.

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.

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 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).

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.