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GMP Certification Programme
Certified Quality Control Manager

Speakers

Dr Karel Haesevoets
Nelson Labs, Belgium

Dr Gerd Jilge
Formerly Boehringer Ingelheim, Germany

Dr Cornelia Nopitsch-Mai
Quality Assessor, Germany

Dr Ulrich Rose
Former Deputy Head of the European Pharmacopoeia Department, EDQM, France

Dr Xaver Schratt
GBA Pharma GmbH, Germany

Dr Reinhard Stidl
Safetree Consulting, Austria

Dr Andrew Teasdale
Astra Zeneca, UK

The Impurities Forum

Practical Approaches for Assessing the Risks of Impurities

Live Online Training on 09/10 November 2023

Save up to € 490 by booking both parts!

Part I:

Identification and Control of Impurities in Drug Substances and Drug Products
Live Online Training on 09 November 2023

Part II:

Nitrosamines and other Mutagenic Impurities
Live Online Training on 10 November 2023

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
- Important monographs and chapters in Ph. Eur. for control of impurities
- Practical aspects of method validation for impurities determination
- Analytical techniques used for detecting and qualifying impurities
- Extractables and Leachables as a source of impurities
- Approaches for investigation and determination of unexpected impurities

This Live Online Training is designed to provide a comprehensive review of impurities analysis and characterisation 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. The **Valsartan case** made clear the importance of a thorough process understanding.

Target Audience

This Live Online Training 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 of Impurities 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

Control of Impurities in Ph.Eur.

- Which impurities are controlled?
- General texts/monographs/ICH guidelines
- Organic impurities in Ph. Eur.
- Specification setting
- Validation
- Elemental impurities

Analytical Method Validation for Impurities Determination at Various Development Stages

- Quantification 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

Applying an example of an API synthesis the participants will learn in the Workshop which activities are necessary to characterize drug substances taking into account the following aspects:

- Analytical procedures are necessary for the characterization
- 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

Extractables and Leachables – What is Expected from Packaging Materials for Drug Products?

- Why should Extractables & Leachables be assessed?
- Regulatory requirements and guidelines in the EU and US and pitfalls
- General flow and critical aspects of Extractables & Leachables studies
- Safety qualification of Extractables and Leachables

How to Avoid Unexpected Impurities: Approaches to Establish a Holistic Understanding of Impurity Risks

- Is there such a thing as ‘unexpected impurities” or is there a lack of process understanding?
- Valsartan – overview of events
- Source of contamination
- Mechanistic understanding
- Examination of risk within other Sartans – overview of how to conduct a risk assessment and to identify key factors
- Are there other mutagenic impurities related risks?

Objectives

In Part II of the Impurities Forum the relevant aspects of root cause analysis and risk assessment with respect to potential Nitrosamine contamination in drug substances and drug products will be discussed. You will hear what you need to know about the required risk assessments for medicinal products containing chemically synthesized APIs. In particular you will learn

- which root causes for Nitrosamine Impurities should be considered,
- which practical approaches can be applied to assess the risks related to potential Nitrosamine contamination,
- which safety aspects need to be considered regarding Nitrosamine Impurities in drug products,
- which regulatory actions are to be taken in case of Nitrosamine Impurities and what authorities expect in these cases.

You will get advice from industry experts on how to cope with the challenge of performing risk assessments. Furthermore, you will be informed you about the European Pharmacopoeia activities on Nitrosamines and other mutagenic impurities.

Background

Mutagenic substances as impurities in drug substances or drug products are of big concern as they have the potential to alter or damage human DNA. Among these species Nitrosamines and elemental impurities have triggered various regulatory activities and initiatives. Since September 2019, Marketing Authorisation Holders are requested to evaluate the risk of the presence of Nitrosamine impurities in human medicinal products containing chemically synthesised APIs. In case of a contamination with Nitrosamines MAHs are requested to file a variation application. The deadline for submission of variations has been extended once again and needs to be filed within 2023.The ICH Q3D Guideline for Elemental Impurities was published as Step 4 document and has meanwhile been revised twice, regarding Cadmium Inhalation PDE and cutaneous and transdermal products.

Target Audience

The Live Online Training 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 Live Online Training will also address regulatory requirements and hence is applicable to people working in the Regulatory Affairs area.

Programme

European Pharmacopoeia Activities on Nitrosamines and other Mutagenic Impurities

- Ph. Eur. General policy on DNA reactive impurities
- Control of Nitrosamines in Ph. Eur.
- Changes in individual and general monographs following the Sartan case
- New general chapter on control of nitrosamines

Root Causes for Nitrosamine Impurities and other Mutagenic Impurities – Practical Approaches to Assess the Risks

- Development of a systematic risk-based approach
- Key factors and the development of a decision tree
  - API
  - Drug product
  - Packaging

Safety Qualification of Impurities - Current Principles and Methods

- General approaches and regulatory framework for impurity qualification by safety threshold derivation
- Generic and substance specific safety thresholds
- Threshold of Toxicological Concern (TTC) - different scenarios
- Derivation of Permitted Daily Exposure (PDE) limits
- Acceptable exposure calculations based on TD50 and their limitations
- Approaches for data poor substances: (Q)SARs and read-across
- Route-to-route considerations for safety thresholds

Nitrosamines and Other Genotoxic Impurities – Authorities Expectations and Dossier Requirements

- The assessor's approach: principles of toxicological assessment
- Structural alerts
- Limits and Permitted Daily Exposure
- The ALARP principle
- Examples of low daily dose drug substances
- Impurities derived from alkylating agents (mesilate, besilate, tosilate, diisothionate); examples
- Nitrosamines – the Valsartan case
- Potential mutagenic residual solvents
- Impurities derived from metal catalysts

Workshop: Conducting a Nitrosamine 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.

Dr Karel Haesevoets
Nelson Labs, Belgium

Dr Haesevoets is Study Director Extractables & Leachables at Nelson Labs. His key technical expertise is analytical chemistry which forms the backbone of his case-by-case study designs for the E&L analysis of variable drug packaging systems and technical advice to pharmaceutical and manufacturing companies. As study director he's on the interface between the sponsor's requests and the analytical laboratory.

Dr Gerd Jilge
Formerly Boehringer Ingelheim, Germany

In 1991, Dr Jilge came to Boehringer Ingelheim working in drug product development, where he was responsible for method development and validation for the application of analytical procedures. In 2000, he 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. From July 2007 to January 2022, he was working in Quality Control in the method development group for drug substances.

Dr Cornelia Nopitsch-Mai
Quality Assessor, Germany

Dr Nopitsch-Mai is scientist at the Federal Institute for Drugs and Medical Devices in the assessment of the quality part of the dossier since 1991. Since 2000 she is assessor for the Certification Procedure (EDQM) in Strasbourg. She was member of the Technical Advisory Board (EDQM) from 2001 until 2010; in that time, she was chairperson from 2005 until 2010. From 2007 until 2011 she was a member of the EMA Quality Working Party.

Dr Ulrich Rose
Former Deputy Head of the European Pharmacopoeia Department, EDQM, France

Dr Rose was Deputy Head of the European Pharmacopoeia Department at the EDQM in Strasbourg and in this context responsible for the preparation of monographs on chemical defined APIs, finished products, herbal drugs & preparations, and general chapters. He was also involved in the harmonization of international pharmacopoeias. Previously, he was responsible for the establishment and control of Ph. Eur. Reference Standards, and later served as coordinator and auditor for EDQM's Mutual Joint Audit Program, which audits Official Medicines Control Laboratories in Europe (OMCLs).

Dr Xaver Schratt
GBA Pharma GmbH, Germany

Dr Schratt is head of department R&D 2 and an expert for chromatography and mass spectrometry. 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 with focus on method development, validation and qualification of reference standards.

Dr Reinhard Stidl
Safetree Consulting e.U., Austria

Dr Stidl has more than 15 years of experience as Toxicological Risk Assessor in the pharmaceutical context and is Senior Toxicologist at and founder of Safetree Consulting e.U. (since 2018). He holds a Master and PhD in Chemistry (University of Vienna), a Master of Advanced Studies Toxicology (Medical University of Vienna), is Certified European Risk Assessor (TRISK) and EUROTOX registered toxicologist (ERT). Dr Stidl started his career as Toxicological Risk Assessor and team leader at Baxter, later Baxalta and Shire, where his last assignment was Associate Director Toxicological Risk Assessments. He is specialized in chemical safety assessment, with focus on impurities (including extractables and leachables), active ingredients (carry-over PDEs, OELs) and excipients. Today, Dr Stidl provides his expertise to pharmaceutical companies around the world, assisting to assure pharmaceutical and medical product safety for patients.

Dr Andrew Teasdale
Astra Zeneca, United Kingdom

Dr 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 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). He is also currently the chairman of the Joint Pharmaceutical Analytical Group (JPAG) in the UK.

GMP/GDP Certification Scheme

Building on your education the ECA GMP/GDP certification programmes provide you with the appropri-ate supplement to acquire this qualification. Simply choose any three courses within the programme according to your professional interest. Your certificate is then valid for two years. To renew it, you can pick any training from the ECA courses and conferences list within that two-years period – allowing you to broaden your knowledge in GMP and GDP compliance.

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

D-69007 Heidelberg
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Reservation Form (Please complete in full)

The Impurities Forum, Live Online Training

☐ *Part I: 09 November 2023*
☐ *Part II: 10 November 2023*
☐ *Part I and Part II: 09/10 November 2023*

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)

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If you cannot attend the conference you have two options:
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- Cancellation until 3 weeks prior to the conference 25 %,
- Cancellation until 2 weeks prior to the conference 50 %,
- Cancellation within 2 weeks prior to the conference 100 %.

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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.

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Date of the Live Online Training

The Impurities Forum Part I: Identification and Control of Impurities in Drug Substances and Drug Products
Thursday, 09 November 2023, 08.30 – 17.00 h CET

The Impurities Forum Part II: Nitrosamines and other Mutagenic Impurities
Friday, 10 November 2023, 08.30 – 15.45 h CET

Technical Requirements

We use WebEx for our live online training courses and webinars.
At https://www.gmp-compliance.org/training/online-training-technical-information you will find all the information you need to participate in our trainings and you can check if your system meets the necessary requirements to participate. If the installation of browser extensions is not possible due to your rights in the IT system, please contact your IT department. WebEx is a standard nowadays and the necessary installation is fast and easy.

Fees (per delegate, plus VAT)

The Impurities Forum Part I
ECA Members € 990 | APIC Members € 1,090
Non-ECA Members € 1,190 | EU GMP Inspectorates € 595

The Impurities Forum Part II
ECA Members € 990 | APIC Members € 1,090
Non-ECA Members € 1,190 | EU GMP Inspectorates € 595

Save up to € 490 by booking both parts:
The Impurities Forum Part I and Part II
ECA Members € 1,690 | APIC Members € 1,790
Non-ECA Members € 1,890 | EU GMP Inspectorates € 945

Presentations/Certificate

The presentations will be made available to you prior to the Live Online Training as PDF files. After the event, you will automatically receive your certificate of participation.

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

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

CONCEPT HEIDELBERG
P.O. Box 10 17 64 | D-69007 Heidelberg
Phone +49(0) 62 21/84 44-0 | Fax +49(0) 62 21/84 44 34
info@concept-heidelberg.de | www.concept-heidelberg.com

For questions regarding content please contact:
Ms Anne Günster (Operations Director) at
+49(0) 62 21/84 44 50, or at
guenster@concept-heidelberg.de.

For questions regarding organisation please contact:
Mr Ronny Strohwald (Organisation Manager) at
+49(0) 62 21/84 44 51, or per at
strohwald@concept-heidelberg.de