QP ASSOCIATION

APIC active pharmaceutical ingredients committee

a sector group of cefic

2nd Compliance Meeting 2020

Nitrosamine Impurities

1 Day | Frankfurt/Main, Germany | 19 March 2020

How to effectively identify, communicate and mitigate risks related to nitrosamine contamination

Speakers

Dr Mark Harrison
Astra Zeneca, United Kingdom

Dr Hiltrud Horn
Horn Pharmaceutical Consulting, Germany

Dr Ulrich Kissel
European QP Association, KisselPharmaConsulting, Germany

Dr Corina Nachtsheim
Quality Assessor, Germany

Dr Lance Smallshaw
UCB, Belgium

Dr Andrew Teasdale
Astra Zeneca, United Kingdom

Dr Christian Trendelenburg
Novartis, Switzerland

Highlights

- Nitrosamine Impurities and the Sartan Cases
- Root causes for Nitrosamine Contamination
- Practical Approaches to Risk Assessments
- Analytical Methods for Nitrosamine Testing
- Safety Aspects of Nitrosamine Impurities in Drug Products
- Communication of Risks to Regulatory Authorities
- Nitrosamine Impurities and Supplier Qualification
- Cooperation between MAHs, finished Product Manufacturers and API Manufacturers
- Regulatory Action to be taken in Case of Nitrosamine Contamination

ECA Academy
Your GMP/GDP Information Source

Objectives

During this conference the relevant aspects of risk mitigation with respect to potential Nitrosamine contamination in drug substan-ces 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,
- how suppliers for raw materials, solvents and packaging materials should be qualified,
- what to take into account when risks have to be assessed and communicated to regulatory authorities,
- which safety aspects need to be considered regarding Nitrosamine Impurities in drug products,
- how supply chain quality oversight can mitigate risks of Nitrosamine contamination,
- which regulatory actions are to be taken in case of Nitrosamine impurities.

You will get advice from industry experts on how to cope with the challenge of performing risk assessments within short timelines.

Background

In June 2018 EU authorities were notified that a Chinese API manufacturer had detected the presence of N-nitrosodimethylamine, NDMA, in batches of Valsartan. NDMA is a genotoxic and carcinogenic agent in animals and is classified as a Class 2A carcinogen to humans. After a referral under Article 31 of Directive 2001/83/EC triggered by the European Commission the CHMP assessed the impact of the presence of this impurity on the benefit – risk balance of valsartan-containing drug products and issued a recommendation whether the concerning marketing authorisations can still be maintained or should be suspended.

Meanwhile different Nitrosamines (NDMA, NDEA and others) were detected in almost every drug product which contains a Sartan derivative as an API. In an EMA Questions & Answers Document various potential sources of Nitrosamine contaminations are described. In September 2019 EMA published a press release where pharmaceutical companies were advised on steps to be taken to avoid nitrosamines in human medicines. In another document which appeared at about the same time Marketing Authorisation Holders are requested to evaluate the risk of the presence of Nitrosamine impurities in human medicinal products containing chemically synthesised APIs and to submit these assessments not later than end of March 2020.

Target Audience

This conference is of interest to all personnel involved in risk assessments of drug substances and drug products regarding potential Nitrosamine contamination. Scientific staff, Laboratory Managers, Supervisors and Analysts in pharmaceutical quality assurance and quality control departments are addressed. During this event regulatory requirements will be discussed, and hence the event also is applicable to people working in the regulatory affairs area.

Programme

Nitrosamine Impurities and the Sartan cases - Background

- Initial cause of Valsartan contamination
- Other causes and their implications
- Article 31 and its implications
- Reflection on alignment with ICH M7

Root Causes for Nitrosamine 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

Confirmatory Testing: Analytical Methods for Determination of Nitrosamines

- Current status of methodology
- Analytical challenges
  - Sensitivity
  - Specificity – risk of false positives

Safety Aspects of Nitrosamine Impurities in Drug Products

- Mutagenic and carcinogenic potential
- Safety threshold, application of ICH M7 principles
- Human carcinogenic risk assessment in drug substances

Nitrosamine Impurities and Supplier Qualification

- Supplier Qualification: Points to consider
- API Manufacturers and Nitrosamines
- Responsibilities of the API Manufacturer
- Potential Sources of Nitrosamines
- Responsibilities of the MAH
- Reporting
- Practical Example: Risk Assessment

Assessment and Communication of Risks – what Regulatory Authorities want to see

Ensuring Supply Chain Quality Oversight: How MAHs, finished Product Manufacturers and API Manufacturers should cooperate

- Communication between the parties involved
- Who needs to know what
- How to cope with the complexity of supply chains
- Activities to be shared between the parties involved
- The role of the Qualified Person

Regulatory Consequences in Case of a Contamination

- Mitigation of risk
- Filing a variation/change
- Is a global approach possible?

Questions, Answers, Discussion

Moderator

Dr Lance Smallshaw, UCB, Belgium

Speakers

Dr Mark Harrison
Astra Zeneca, United Kingdom

Dr Mark Harrison works for AstraZeneca UK in drug development and research since 18 years. He is an MS specialist with a responsibility for trace analysis strategy within Pharmaceutical Technology and Development at AstraZeneca and has been involved in the fields of E&L and PMI analysis and risk assessment. Previously he worked in the NHS as a Clinical Biochemist, primarily involved with research and the routine toxicology service.

Dr Hiltrud Horn
Horn Pharmaceutical Consulting, Germany

Dr Hiltrud Horn is managing director of HORN Pharmaceutical Consulting with focus on CMC, GMP and Regulatory Affairs. She started in pharma industry in 1990 and held several managerial positions within Hoffmann-La Roche in Basel and Knoll (Abbott) with global responsibility within QC / QA / Regulatory Affairs / Project Management / Medical Writing.

Dr Ulrich Kissel
European QP Association, KisselPharmaConsulting, Germany

Dr Ulrich Kissel is Qualified Person and Member of the Board of Directors of the European Qualified Person Association (EQPA). He works as a GMP consultant and contract QP to the Pharmaceutical Industry. Previous to his current role he held leadership positions in Quality and Supply Chain and served for many years as QP for Roche.

Dr Corina Nachtsheim
Quality Assessor, Germany

Dr Corina Nachtsheim studied chemistry at the University of Cologne and received a Ph.D. (Dr. rer. nat.) in pharmaceutical chemistry at the University of Bonn. She is working as a quality assessor at the German Federal Institute for Drugs and Medical Devices since Jan. 2001. Since Nov. 2007, she is an external expert in the framework of the certification procedure of the EDQM in Strasbourg. She became a member of the chemical Technical Advisory Board (EDQM) in Nov. 2011 and is currently chairperson.

Dr Lance Smallshaw
UCB, Belgium

Dr Lance Smallshaw is Global Analytical Expert (Global Pharmacopoeias Leader) within the Regulatory Intelligence Network (RIN) in the UCB Site Quality Operations Team. He is also Co-Chair of the Executive Board of ECA and Associate Director and European CMC Strategy Committee member for CaSSS Biopharm

Dr Andrew Teasdale
Astra Zeneca, United Kingdom

Dr Andrew Teasdale is an analytical chemist and held several positions 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.

Dr Christian Trendelenburg
Novartis, Switzerland

Dr Christian Trendelenburg is a senior toxicologist in Preclinical Safety (PCS) at the Novartis Institutes for Biomedical Research (NIBR) in Basel/ Switzerland. He is a scientific expert for the safety evaluation of impurities, extractables/leachables and excipients, with major expertise in the safety evaluation of pharmaceutical products for children. He represents PCS in global project teams to support drug development by summarizing, evaluating, and interpreting nonclinical safety aspects. He is a EUROTOX-certified toxicologist and member of the German and Swiss toxicological societies (DGPT & SST).

Important Information

You will receive a USB memo stick when you register in Frankfurt.

Note: there will be no print-outs available during the conference.

Date
Thursday, 19 March 2020, 09.00 – 18.00 h
(Registration and coffee 08.30 – 09.00 h)

Venue
Scandic Frankfurt Museumsufer
Wilhelm-Leuschner-Straße 44
60329 Frankfurt, Germany
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Email museumsufer@scandichotels.com

Fees (per delegate plus VAT)
ECA Members € 990
APIC Members € 1,090
Non-ECA Members € 1,190
EU GMP Inspectorates € 595
The conference fee is payable in advance after receipt of invoice and includes conference documentation (on USB memo stick), lunch and all refreshments. VAT is reclaimable.

Accommodation
CONCEPT HEIDELBERG has reserved a limited number of rooms in the conference hotel. You will receive a booking link when you have registered for the event. 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.

Certificate of Participation
Shortly after the event, you will receive your certificate of participation by email.

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

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Germany

Reservation Form (Please complete in full)

Nitrosamine Impurities
19 March 2020, Frankfurt/Main, Germany

☐ Mr ☐ Ms

Title, first name, surname

Company Department

Important: Please indicate your company's VAT ID Number **Purchase Order No. if applicable**

Street / P.O. Box

City Zip Code

Country

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E-Mail (Please fill in)

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 %,
- until 1 weeks prior to the conference 50 %
- within 1 week prior to the conference 100 %.

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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. 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).

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