ECA Academy
Your GMP/GDP Information Source

Speakers

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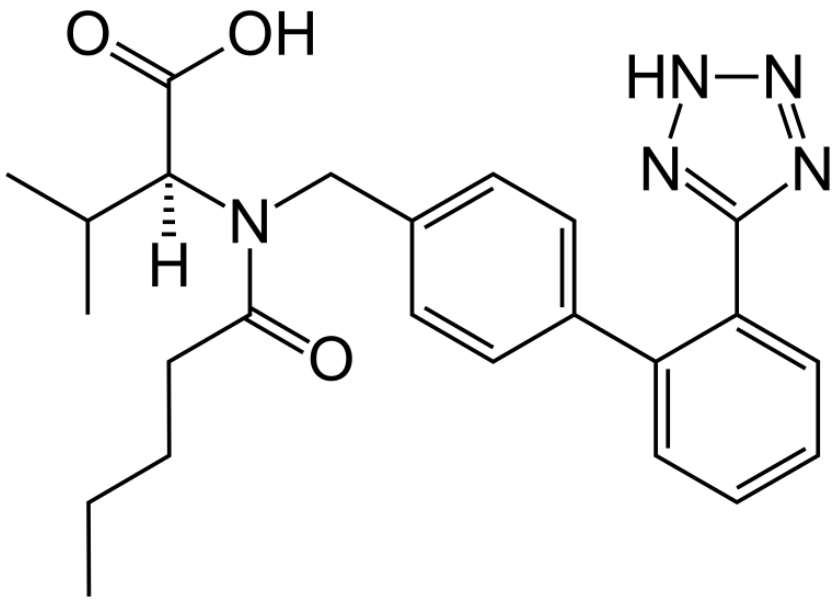
Nitrosamine Impurities – an Update

Live Online Training on 10 June 2021



Current requirements for Marketing Authorisation Holders and Manufacturers of APIs/Finished Products

Highlights

- Control of Nitrosamine Impurities – Latest European Pharmacopoeia Activities
- Assessment of Risks and Communication to the Authorities
- Quality and Safety Aspects related to Nitrosamine Impurities
- Practical Approach to Conduct an actual Risk Assessment

Actual Challenges:
- Conducting a Risk Assessment
- Establishing an adequate control strategy
- Meeting the deadlines

Objective

It is the aim of this Live Online Training to provide the latest information on requirements Marketing Authorisation Holders have to meet with respect to Nitrosamine Impurities. Important points to be considered by Quality Assurance and Quality Control departments from manufacturers of APIs and finished products will also be discussed. You will get to know

- what regulatory authorities want to see regarding assessment of risks
- which European Pharmacopoeia monographs of sartans
- how to conduct a significant and comprehensive risk assessment
- which quality and safety aspects have to be taken into account for a risk assessment
- how to choose a suitable analytical method for determination of Nitrosamines

Background

In June 2018 EU authorities were notified that a Chinese API manufacturer has 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 sartan-containing drug products and issued a recommendation whether the concerning marketing authorisations can still be maintained or should be suspended.

Building on this Article 31 referral EMA together with the EU Network and international partners was continuing the review to identify whether there are any consequences for medicinal products apart from the class of sartans. As a result of this the CHMP issued a document entitled **"Nitrosamine impurities in human medicinal products"** as part of the procedure under Article 5(3) of Regulation EC (No) 726/2004. This assessment report contains comprehensive recommendations on how to detect and mitigate the risk of Nitrosamine Impurities in human medicinal products containing chemically synthesised APIs as well as biological medicinal products.

In a subsequent assignment the CHMP was requested by the European Commission to assess the impact of the outcome of the Article 5(3) assessment on Nitrosamines regarding angiotensin-II-receptor antagonists (sartans) which resulted in a **final assessment report** with respect to Candesartan, Irbesartan, Losartan, Olmesartan and Valsartan. This assessment report contains **changes to the current conditions to the Marketing Authorisations for sartans such as limits for Nitrosamine Impurities to be implemented for the finished products and deadlines to be met.**

As a consequence the five European Pharmacopoeia monographs on sartans with a tetrazole ring, namely Valsartan, Losartan Potassium, Irbesartan, Candesartan ciletexil and Olmesartan medoxomil have been revised to align them with the above mentioned final assessment report. The implementation date of these monographs is 1 April 2021.

Target Audience

This Training 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. On this event regulatory requirements will be discussed and hence it is applicable to people working in the regulatory affairs area.

Programme

Latest European Pharmacopoeia Activities on Control of Nitrosamine Impurities

- General principles of control DNA reactive (genotoxic) impurities in the European Pharmacopoeia
- Update on revisions of monographs on Sartans – Nitrosamine impurities
- Update on revisions of general monographs

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

- Regulatory basis
- Requirements for Nitrosamines
- Limits and deadlines
- Scenarios for implementation
- Sartans and Non-Sartans

Management of Nitrosamines – Key Quality and Safety Challenges

- How are Nitrosamines formed and under what conditions
  - Synthetically – API manufacture
  - Within the drug product + other routes
  - How to place risks into context
- Analysis of Nitrosamines
  - Sensitivity challenges
  - Interference / false positives
- Safety of Nitrosamines – are all of concern?
  - Factors that impact potency
  - Can Less than lifetime approaches be taken?
  - How to assess – utility of the Ames test – factors for consideration

Nitrosamine Impurities – How to Conduct an Actual Risk Assessment

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

Analytical Methods for Determination of Nitrosamines used for Confirmatory Testing

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

Your Benefit

Internationally Acknowledged Certificate from ECA Academy

The EU GMP Guide requires: „... All personnel should be aware of the principles of Good Manufacturing Practice that affect them and receive initial and continuing training,...". This is why you receive an acknowledged participant certificate, which lists the contents of the seminar in detail and with which you document your training.


CERTIFICATE

Mr John Doe

ECA - Lab Data Integrity - Meeting FDA & EU Concerns
Part 2: Self Inspections and Audits to Confirm Effective Data Integrity Controls

Contents of the course:

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 Corina Nachtsheim
Quality Assessor, Germany

Dr Corina Nachtsheim has 20 years of work experience as a quality assessor at the German Federal Institute for Drugs and Medical Devices (BfArM). She is also an external expert in the framework of the certification procedure of the EDQM in Strasbourg since 2007 and has been an active member of the chemical Technical Advisory Board (EDQM) for 9 years, which she chaired from 2013 to 2019.

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 Ph. Eur.. After that he became coordinator and auditor for EDQM's Mutual Joint Audit Program. Since 2014 he is head of division A and deputy head of the Ph. Eur. Department where he is overlooking the monograph work on chemically defined APIs, finished products, herbals and general chapters of Ph. Eur. and is involved in the international harmonisation of pharmacopoeias.

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.

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Reservation Form (Please complete in full)

Nitrosamine Impurities – an update, Live Online Training on 10 June 2021

Title, first name, surname

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Important: Please indicate your company's VAT ID Number | Purchase Order Number, if applicable

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Date of the Live Online Training

Thursday, 10 June 2021, 09.00 to approx 16.30 h CEST

Technical Requirements

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At http://www.webex.com/test-meeting.html you can check if your system meets the necessary requirements for the participation at a WebEx meeting and at the same time install the necessary plug-in. Please just enter your name and email address for the test.
If the installation is not possible because of your rights for the computer system, please contact your IT department. WebEx is a standard nowadays and the necessary installation is fast and easy.

Fees (per delegate, plus VAT)

ECA Members € 890
APIC Members € 950
Non-ECA Members € 990
EU GMP Inspectorates € 495
The fee is payable in advance after receipt of invoice.

Registration

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

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.

Conference language

The official conference language will be English.

Ordering a Recording

Independent from the Live Online Training, you can also order a recording of this training at the same conditions. This recording will be provided on our media server. All you need to watch it is an Internet browser – no additional software. You can order the recording of the Live Online Training at the earliest 10 days after the live performance at https://www.gmp-compliance.org/gmp-webinars/recorded-gmp-webinars.

Organisation and Contact

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

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