ACA
PHARMA CONCEPT GMBH

PGS **TOXIKOLOGIE UND UMWELTSCHUTZ**

TOXNETZ
Portal für Toxikologie
UNIVERSITÄT LEIPZIG

SEMINAR

Evaluation & qualification of impurities in small molecule drug substances and products, cleaning validation, extractables and leachables

05.-06.02.2020
BIOCITY LEIPZIG, DEUTSCHER PLATZ 5, 04103 LEIPZIG, GERMANY

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EVALUATION & QUALIFICATION OF IMPURITIES IN SMALL MOLECULE DRUG SUBSTANCES AND PRODUCTS, CLEANING VALIDATION, EXTRACTABLES AND LEACHABLES

Ladies and Gentlemen,

As you know: An impurity is designated as any component of a drug substance that is not the drug substance itself and in addition, for a medicinal product or a medical device, any component that is not a formulation ingredient. Impurities in active substances or drug products can arise due to synthetic/manufacturing processes or storage and may depend also on excipients and packaging materials. An impurity may simply derive from degradation of active substance, or from interaction products of active substance-excipient, excipient-excipient, or active substance-residual impurities existing in excipients. In addition, an impurity may result from cross contamination by using shared manufacturing facilities, or may leach out of the packaging material during storage. Hence, from a regulatory point of view, impurities may affect the quality of a medicinal product/ medical device and ultimately may affect the safety of the patient. Accordingly, a comprehensive quality management and control system has to be established that should assure the control of impurities at those levels that rule out a significant toxicological concern.

Recently, the contamination of valsartan with nitrosamines has raised a discussion whether control of impurities in drug products is strictly enough regulated. In this context the FDA estimated that if 8,000 people took the highest valsartan dose (320 mg) containing N-nitroso-dimethylamine (NDMA) from the recalled batches daily for four years, there may be one additional case of cancer over the lifetimes of those people.

It is a pleasure to invite you and your colleagues to our English language seminar on the evaluation and qualification of impurities in small molecule drug substances and products, cleaning validation, extractables and leachables.

The seminar will be held over 2 days on 5th and 6th February 2020 at the BioCity in Leipzig, Germany.

The seminar is led by renown experts and speakers who will help you to gain a better understanding of a variety of issues surrounding impurities, as well as on cleaning validation, extractables and leachables. In addition to that, you will be updated on the latest regulatory developments and regulatory requirements concerning impurities, the analytical approaches for impurity detection and identification, and to gain insight in the principles of toxicological qualification and risk assessment.

You will also have the chance to mingle with the speakers and other participants in an informal environment during breaks and during an evening event on the 5th to discuss issues that are of concern to you and to your company.

Please find enclosed the event details with information how to participate. Please feel free to contact us if you do have any questions. You can reserve your space at the seminar by visiting our website, where you can book online. Early booking is highly recommended as the number of participants is restricted.

Should you require immediate assistance, please email us with your inquiry separately.

We look forward to seeing you in Leipzig in February 2020.

Yours,

Prof. Dr. Clemens Allgaier
Managing Director
ACA-pharma concept GmbH
- Regulatory and Scientific Expert Services -

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TOPICS

Day 1 - Small molecule impurities

- Overview on relevant guidelines (ICH Q3A-D, Q6A, QWP/199250/2009corr)
- Analytical approaches of identification/ quantification (HPLC, HPLC-MS/MS, UHPLC-QTOF-MS, GC-MS, NMR (HSQC/HMPC), LCNMR)
- Control of impurities (organic/inorganic impurities, residual solvents) in drug development
- Toxicological qualification of impurities/adoption of specification limits in marketed drug products
- Testing strategies for genotoxic impurities (testing battery: in vitro, in vivo, in silico)
- Non-animal strategies for non genotoxic impurities (TTC, QSAR, read across, in vitro testing)

Day 2 - Elemental impurities

- ICH Q3D/Q10
- PDE derivation
- Element classification
- Elemental impurities
- Risk assessment
- Control strategies
- ICP-MS
- Product-specific validation

Day 2 - Cleaning validation

- PDE derivation of (herbal) active ingredients
- DNEL of cleaning agents
- Calculation of MACO
- Braketting and worst-case rating
- SWP/169430/2012

Day 2 - Extractables & Leachables (E&L)

- Regulatory background in EU and US (QWP/4359/03, BPOG‘s, USP<1663>)
- Analytical concepts and study design
- Extraction media and conditions
- Analytical approaches/analytical evaluation threshold (GC-MS, HPLC-UV-MS, ICP-MS)
- Risk assessment/tolerable exposure (SCT, TTC Concept, Cramer classification), EN-ISO 10993-17: 2009-08

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PROGRAMME

Evaluation & qualification of impurities in small molecule drug substances and products, cleaning validation, extractables and leachables

Day 1: Small molecule impurities

5 FEBRUARY 2020: 9:30 AM – 4:15 PM

BIOCITY LEIPZIG, DEUTSCHER PLATZ 5, D-04103 LEIPZIG

09:30—10:00 am	**Registration and Come-together**
10:00—11:00 am	**Overview on the regulatory framework concerning impurities** *Dr. Roland Frötschl, Bonn (angefragt)*
11:00—11:45 am	**Identification and quantification of small molecule impurities** *Dr. Ralph Nussbaum, SYNLAB Analytics & Services Germany GmbH, Aachen*
11:45—12:30 pm	Lunch break
12:30—01:15 pm	**Rationale and control of impurities in drug substances and drug products** *Dr. Roland Frötschl, Bonn (angefragt)*
01:15—02:15 pm	**Toxicological qualification of impurities and justification of specification limits in products that are already on the market** *Prof. Dr. Clemens Allgaier, ACA-pharma concept GmbH, Leipzig*
02:15—02:30 pm	Coffee break/Networking
02:30—03:30 pm	**Genotoxic impurities and testing strategies for the assessment of genotoxicity** *Dr. Roland Frötschl, Bonn (angefragt)*
03:30—04:15 pm	**Non-animal strategies on the qualification of non-genotoxic impurities** *Prof. Dr. Clemens Allgaier*
06:30 pm	**Dinner** *Following the official program, we invite all participants and speakers for dinner in a traditional Saxon restaurant. This will be the perfect time to relax and let day's events settle in and to enjoy traditional local food and beverages; the perfect atmosphere to mingle with speakers and other participants alike, to exchange ideas and to create valuable contacts within your business.*

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Evaluation & qualification of impurities in small molecule drug substances and products, cleaning validation, extractables and leachables

Day 2: Elemental impurities, Cleaning validation and Extractables & Leachables (E&L)

6 FEBRUARY 2020: 8:30 AM – 4:15 PM

BIOCITY LEIPZIG, DEUTSCHER PLATZ 5, D-04103 LEIPZIG

ELEMENTAL IMPURITIES

08:30—10:00	**Elemental impurities (ICH Q3D): experiences, developments and strategies** *Dr. Roland Frötschl, Bonn (angefragt)*
10:00—10:15	Coffee break
10:15—11:30	**Application of ICH Q3D in quality control of drug substances and drug products** *Dr. Dirk Freitag-Stechl, CUP LABORATORIEN DR. FREITAG GMBH, Dresden*
11:30—12:30	Lunch break

CLEANING VALIDATION

12:30—01:45 pm	**PDE and DNEL as threshold values for cross contamination in cleaning validation** *Prof. Dr. Clemens Allgaier*
01:45—02:15 pm	**MACO calculation in cleaning validation** *Prof. Dr. Clemens Allgaier*
02:15—02:30 pm	Coffee break

EXTRACTABLES & LEACHABLES (E&L)

02:30—03:00 pm	**Strategies on testing of E&L in drug products and medical devices** *Tim Averbeck, SYNLAB Analytics & Services Germany GmbH, Aachen*
03:00—04:15 pm	**Strategies on toxicological evaluation of Leachables and exposure based risk assessment** *Prof. Dr. Clemens Allgaier*
04:15 pm	Final coffee and farewell

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SPEAKERS

Clemens Allgaier (ACA-pharma concept GmbH) PhD. Professor at Rudolf-Böhm-Institute for Pharmacology and Toxicology, University of Leipzig; Responsible person at Module „Regulatory Affairs and Risk Assessment“ of postgraduate study „Toxicology and Environment“. Managing Director. Main focus: Toxicological qualification of impurities and leachables in medicinal products and medical devices; risk and exposure assessment; preclinical testing strategies and product development; preparation of toxicological and biocompatablity reports.

Tim Averbeck (SYNLAB Analytics & Services Germany GmbH, Aachen) Chemical engineer. Head of development. Main focus on identification of impurities using various methodological approaches (HPLC-UV-MS, GC-MS, NMR, preparative HPLC).

Roland Frötschl (BfArM, Bonn) PhD, biologist. Focus on risk assessment of drug products in particular concerning mutagenicity and cancerogenicity. Research on biomarkers and forecast of genotoxic potential of chemical substances. Lecturer at University Vienna, Medical Department and Deutsche Gesellschaft für experimentelle und klinische Pharmakologie und Toxikologie e.V. (DGPT).

Ralph Nussbaum (SYNLAB Analytics & Services Germany GmbH, Aachen) PhD, chemist. Founder and Managing Director of Analytical Services in Aachen; since July 2017 Site & Key Account manager. Focus on identification of impurities and extractables and leachables.

Dirk Freitag-Stechl (CUP LABORATORIEN DR. FREITAG GMBH in Radeberg/Sachsen) PhD, chemist. Since 2008 Managing Director of CUP LABORATORIEN with focus on determination of elemental impurities and residual solvents in medicinal products;

Target audience

Employees of the pharmaceutical and the medical device industry, from regulatory affairs, R&D, quality assurance, from competent authorities and consultants; in particular those responsible for authorisation, analytics (laboratory), manufactoring.

Registration*

Please find the registration form on our website: www.aca-pharma.de

Registration Fee**

1,150.00€ for both days, 690.00€ for the participation on one day of the seminar. For participiants and alumni of the postgraduate study programme (PGS) „Toxicology and Environmental protection“ the fee is 890.00€ for both days and 540.00€ for one seminar day. Payment after receipt of invoice. All prices are net prices, excluding VAT (where applicable).

The registration fee includes lunch and beverages during the seminar as well as dinner on evening of day 1. All participants receive a printed version of the presentations.

BIO CITY LEIPZIG

Biotechnologisch-Biomedizinisches Zentrum

Organiser

ACA-pharma concept GmbH, BioCity Leipzig, Deutscher Platz 5, Leipzig in connection with the postgraduate study programme (PGS) „Toxicology and Environmental protection“ of Universität Leipzig (TOXNETZ).

Contact

Ms Bianca Leubner
Phone: +49 (0) 341 33 73 33 60
Fax: +49 (0) 341 33 73 33 67
E-Mail: aca-campus@aca-pharma.eu

Accommodation

Hotels with special rates: Please refer to the individual key words when booking your hotel room.

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ACA-pharma concept GmbH, BioCity Leipzig,Deutscher Platz 5, D-04103 Leipzig
Phone: +49 341 33 73 33 60, Fax: +49 341 33 73 33 69, Email: aca24@aca-pharma.de

* Cancellation policy: Please be aware that we have to charge a processing fee of 10% of the registration fee up to 4 weeks before the event. If canceled until 1 week before the event, 70% of the participation fee will be charged; within 1 week before f the event, 100% of the participation fee will be charged. In case of a cancellation by the organiser, you will receive back the fees already paid.

** Discount is granted for employees of the same company: 10% for second and each following person.