



EUROPEAN COMPLIANCE
ACADEMY

SPEAKERS

DR ABRAM BECKER

Becker & Associates, France

DR ANDREAS FLÜCKIGER

F. Hoffmann-La Roche,
Switzerland

DR RUDOLF HEIMERL

Delta Vertriebs GmbH,
Germany

DR CHRISTIAN KÖCHER

CARBOGEN AMCIS,
Switzerland

DR JEAN-DENIS MALLET

Formerly Head of the French
Pharmaceutical Inspection
Department

DR PETER MÜLLER

CARBOGEN AMCIS,
Switzerland

DR GÜNTER NYKAMP

Haupt Pharma Münster,
Germany

EMMANUEL PAQUES

NextPharma, Belgium

FRANCK PAVAN

Pierre FABRE Medicament
Production, France

JOLANDE SCHOEMAKER

Schoemaker Consultancy,
The Netherlands

DR HARALD STAHL

GEA Pharma Systems,
Germany

MARCO WEIMER

Sanofi-Aventis, Germany



With guided tour at
!booked up!
CARBOGEN AMCIS

Handling of highly potent Compounds

Containment Solutions for the Pharmaceutical Industry

Basle, Switzerland
18 – 19 May 2010

HIGHLIGHTS:

- Determination of the right level of Containment based on toxicological and pharmacological Data
- Coalescence of Containment and GMP
- Possibilities for closed Product Handling: transfer, sampling, analytics
- Cleaning of Equipment
- Safety in the analytical Lab for highly potent Materials
- Possibilities and Limitations for the use of personal protective Equipment
- Combination of biological and chemical Entities: HP-Conjugates
- Future Trends and Developments of highly potent Materials
- Case Studies: Sanofi-Aventis, Haupt Pharma, CARBOGEN AMCIS

Objectives

This event aims at examining the state of the art in the currently widely discussed field of containment. It will deal with the calculation of limits, the possibilities offered by containment technology and the connections of cGMPs with safety aspects.

Background

Due to the increasing number of very potent and toxic ingredients the manufacture of pharmaceutical products and APIs is more and more becoming a challenge. In addition to the already well known GMP requirements relative to product protection manufacturers now also have to adhere to employee protection requirements. However, can GMP and job safety requirements be combined? It is safe to say that the meaning of cross-contamination prevention during the handling of highly potent materials gained a complete new dimension.

Another issue has been raised by EMA and is still under discussion: the decision whether or not dedicated facilities will be made mandatory for certain substances. From the industry's perspective this decision should only be based on a scientific risk analysis.



Image: Haupt Pharma



Image: CARBOGEN AMCIS

During this conference the following questions represent some of the issues discussed:

- How are iOEL Limits calculated?
- How much containment do I need?
- What are the different technical solutions?
- What should a risk analysis contain?
- Which kind of zone and layout concepts are reasonable?
- How are exposition measurements carried out?
- What has to be considered for the cleaning of equipment?
- What can a lab environment look like for highly potent materials?
- How will the field of highly active materials develop in the future?

Well established examples for layout concepts, equipment for closed product handling and analytics are demonstrated through case studies with different pharmaceutical applications in primary, secondary and R&D facilities.

Target Audience

Managers and technical experts from production, development and occupational health & safety responsible for the handling of highly- potent APIs, intermediates and drugs.

Further target groups are engineers who design, install and qualify containment systems.

Moderator

Dr Harald Stahl, *GEA Pharma Systems, Germany*

Social Event

On 18 May 2010 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.

Principles of Assessing and Managing Occupational Health Risks in Potent Compound Handling

- Legal requirements regarding worker safety
- Assessing the hazard: potency and toxicity of the compounds. Occupational exposure limits and health hazard categories
- Ensuring the right level of process containment: Design exposure limits as drivers for equipment selection. The illusion of “closed processes”.
- Dedicated facilities or risk-based acceptance of multi-purpose manufacturing?

Exposures to pharmaceuticals at the workplace must be controlled to below acceptable limits. For most APIs, the manufacturer himself needs to develop these limits and compliance with them must be documented. Protection of the workers from overexposure must be achieved primarily by technical means and not by means of personal protective equipment. Equipment must have adequate containment so that the required exposure control is ensured at least in all routine situations. Existing facilities must be upgraded accordingly. The toxicological and pharmacological basis of assessing APIs with the objective of worker protection is the same as the one justifying GMP cleaning validation criteria and acceptance of multi-product use of a facility.

GMP Aspects of Containment

- Historical GMP requirements on containment
- Current situation and possible approaches. The Q9-Q10 contribution
- Is cross-contamination the only issue ? What about the biological risks ?
- How GMP is affected in case of defective containment ?
- Case study : techniques used to manufacture betalactam and non-betalactam products in the same building

Review of technical requirements for contained product handling

- Product transfer- review of current possibilities
- Sampling 1 - Review of possibilities for contained sampling
- Sampling 2 - Examples for in-line measurements allowing to drop sampling
- Cleaning- Examples of automatic cleaning

Personal Protective Equipment in API Environment: Possibilities and Limitations

- From Respiratory Protection up to Individual Containment
- Requirements on Construction and Building Services
- Regulatory Affairs
- Occupational Health Requirements
- Cost Comparison of different Personal Protective Equipment
- Performance Comparison of Commonly Used PPE
- Protecting Operator and Product: A new Approach
- Brief Practical Demonstration of an Individual Containment

Highly Potent APIs: Focus on Analytics and Cleaning of Equipment

- Analyzing different types of highly potent APIs (daily doses per determination)
- Safety in the analytical lab for highly potent APIs
- Exposure and the special case of women of childbearing age
- Partially dedicated production equipment: Importance of and approaches to cleaning
- Cleaning validation and analytical requirements
- Controlling carry-over and analytical requirements
- Conclusion: Safety of patients and workers

The future of high-potent APIs

- Introduction
- Sources of B&A data
- Classification
- Overview & statistic of launched HP-APIs
- Overview, statistic & examples of clinical Low dosage/toxic HP-APIs
- Key drivers to move towards high-potent drugs
- Potential therapeutic areas for HP-APIs
- Conclusion

Case Study Haupt Pharma: Innovative Containment Production Design for the Manufacture of Highly Potent Solid Dosage Forms

- Pilot- and commercial-scale production of highly potent oral solid dosage forms applying state of the art containment technologies at Haupt Pharma Münster
- "Customized to the needs"-concepts for rooms and equipment
- Utilization of appropriate containment technologies like isolators, V-processors, high containment tablet presses and closed containment equipment during the production chain

Case Study Sanofi-Aventis: A multipurpose R&D area for highly potent drugs: design, construction, commissioning.

- Layout
- Handling systems
- RABS and isolator
- Material and personnel flow
- Proofing a safe environment: SMEPAC

New generation isolators for freeze dried products with ATEX compliance approach

- 1991 to 2000: first generation of isolators: technical characteristics
- After 2000: second generation of isolators: different objectives – technical difference
- Nowadays: new generation of isolators: ATEX standard

Manufacturing of highly potent drugs for clinical trials : a practical approach

- Analysis of the toxicity of the APIs
- Evaluation of the Exposure Potential
- Determination of the Protection levels for the operators.

Case Study: A Biosafety Level 3 Pilot Containment Facility for Biologicals

- Facility design
- Segregation of live and inactivated organisms
- Handling personnel flow
- Handling multiple products in the same facility
- Containment and prevention of cross-contamination as a quality system

Manufacture of HP-Conjugates (Drug Substance): Considerations on Process Development and Scale-up"

- HP Conjugates: Particular considerations for HP compounds attached to biologics and polymers
- Issues to be considered upon process development (HP conjugates) and regarding infrastructure
- Implementation of a large-scale HP plant in India

Guided Tour on 20 March 2010
CARBOGEN AMCIS
Haupt Pharma
Bubendorf, Switzerland

booked up

Bubendorf facility was opened in 1987 and has seen a number of additions in its more than 20-year history. The manufacturing building was commissioned in 1996 and the lab, administration and containment facilities were opened in 2005. The site now supports 180 employees, who focus on process optimization and supply of late-phase and commercial Active Pharmaceutical Ingredients (API) supplies. In addition to four process research and development laboratories our state-of-the-art infrastructure in Bubendorf includes manufacturing capabilities for small batch sizes of up to 10-15 kg.

The specialized laboratories and kilo-scale manufacturing equipment are designed based on a containment concept utilizing the "split-butterfly valve" and barrier isolation technology as well as a strict zone concept with pressure cascades, airlocks and access controls. This allows the safe handling of highly-potent compounds of all categories including cytostatics / and category IV compounds (OEL < 1 µg/m³), the highest category in the CARBOGEN AMCIS categorization system.

During the tour you will see the highly active production area, the analytical laboratories for high actives, flexible containment solutions and you will get insight to Containment in India.

****Please understand that due to a competitive situation some delegates may not be granted access to the site.****

Speakers

DR ABRAM BECKER, *Becker & Associates*

D.Sc. College de France, Scientific director (pharmaceutical companies.) Author & Editor of Future generics -the life science encyclopedia. Director of Becker & Associates.

DR ANDREAS FLÜCKIGER, *F. Hoffmann-La Roche AG*

An occupational physician by training, Andreas Flückiger has been the head of the occupational health services of the Roche Group for 20 years. He is active in leading roles in numerous national and international associations such as the International Association for Occupational and Environmental Health in the Chemical Industry (Medichem), in the Scientific Committee of the European Council for Ecotoxicology and Toxicology of Chemicals (ECE-TOC).

DR RUDOLF HEIMERL, *Delta Vertrieb GmbH*

Dr Heimerl studied biology and holds a doctoral degree in virology from the Ludwig-Maximilians-University of Munich. He is working for Delta Vertrieb GmbH since 1994 in various managing positions. He is now head of the research and development department.

DR CHRISTIAN KÖCHER, *CARBOGEN AMCIS AG*

Christian Köcher holds a PhD in chemistry and an Executive MBA degree from the University of Zürich. He worked for a manufacturer of generic APIs before joining CARBOGEN AMCIS. He has worked on early- and late-phase projects as a PR&D Chemist, Group Leader, Manager PR&D and currently as Project Manager. He is focused on projects dealing with hp compounds and process validation.

DR JEAN-DENIS MALLET, *International Committee Red Cross*

Jean-Denis Mallet is a doctor pharmacist, graduated in technological pharmacy and management. He is currently a GMP auditor within the International Committee of the Red Cross. He was previously the Head of the Pharmaceutical Inspection Department at the French Health Products Regulatory Agency (AFSSAPS). He also used to work in or with the pharmaceutical industry at various positions including QA, Production, Engineering and GMP Consulting.

DR PETER MÜLLER, *CARBOGEN AMCIS AG*

Peter M. Mueller did his PhD-thesis at ETHZ and worked for 2 years at MIT, for 10 years in Roche Basel's medicinal chemistry and CNS-pharmacology research, and for 10 years as head of R+D of Roche's fragrances, flavors and cosmetics division. He left Roche in 1995 and soon was C.O.O. of AMCIS AG Bubendorf. Today, he is consultant and one of CARBOGEN AMCIS' key experts regarding containment and highly potent APIs.

DR GÜNTER NYKAMP, *Haupt Pharma Münster GmbH*

Dr Nykamp is a pharmacist and holds master and doctoral degrees in pharmaceuticals and pharmaceutical technology resp.. He is in charge of the manufacturing and formulation development departments at Haupt Pharma Muenster.

EMMANUEL PAQUES, *NextPharma*

Mr Paques is Development Director, working in the Sterile Products Development Center at NextPharma, Braine-l'Alleud, Belgium. He is Industrial Pharmacist by training with a degree in pharmaceutical technology and industrial production. He is working in the sterile production for more than 30 years and has a large experience in cytostatic production and lyophilisation.

FRANCK PAVAN, *Pierre FABRE Medicament Production*

Franck Pavan is an engineer in Biochemistry. After working as plant manager in sterile manufacturing, he is now working for Pierre Fabre Medicament Production in France. First as an Industrial Development Manager and Cytotoxic Production Manager and also Project leader for the Taxotere Project, today in the position as Outsourcing Business Development Manager.

JOLANDE SCHOEMAKER, *Schoemaker Consultancy*

Jolande Schoemaker works as a consultant to the pharmaceutical industry. Previous she was the Director Quality Affairs at Crucell. Jolande gained a wide field of experience in many aspects of the pharmaceutical and biotechnology industry, including formulation of drugs, manufacturing of sterile pharmaceutical products, clinical trials, Regulatory Affairs, Quality Control and Quality Assurance. Furthermore, she was involved in many regulatory inspections.

DR HARALD STAHL, *GEA Pharma Systems*

Harald Stahl worked for the Pharmaceutical Development of Schering AG in Germany. Since 1995 he served within GEA Process Technology in various positions. Presently he owns the position of a Senior Pharmaceutical Technologist of GEA Pharma Systems. He has published more than 20 papers on various aspects of pharmaceutical production.


MARCO WEIMER, *Sanofi-Aventis Deutschland GmbH*

Marco Weimer is currently Head of Pharmaceutical Engineering in the Pharmaceutical Sciences Department at Sanofi-Aventis in Frankfurt. He holds degrees in Pharmaceutical engineering and Process engineering.

Easy Registration

 **Reservation Form:**
CONCEPT HEIDELBERG
P.O. Box 10 17 64
69007 Heidelberg
Germany

 **Reservation Form:**
+ 49 6221 84 44 34

 **e-mail:**
info@concept-heidelberg.de

 **Internet:**
www.gmp-compliance.org

Date

Tuesday, 18 May 2010, 09.00 – 18.30 h
(Registration and coffee 08.30 – 09.00 h)
Wednesday, 19 May 2010, 08.30 – 17.45 h

The **guided tour** at the CARBOCAT MCIS site will take place on Thursday, 20 May 2010. A transfer from the hotel to CARBOCAT will be provided. Return to the hotel after the tour. The Bus will arrive at approx. 13.30 h at the hotel.

Venue

Ramada Plaza Basel
Messeplatz 12
4058 Basle, Switzerland
Tel. +41 (0)61 560 4000
Fax +41 (0)61 560 55 55

Reduced Fees - Conference only, without guided tour at Carbogen

Non-ECA Members EUR 1,690.- per delegate plus VAT
ECA Members EUR 1,521.- per delegate plus VAT
APIC Members EUR 1,606.- per delegate plus VAT
(does not include ECA Membership)
EU GMP Inspectorates EUR 845.- per delegate plus VAT
The conference fee is payable in advance after receipt of invoice and includes conference documentation, dinner on the first day, lunch on both days and all refreshments. VAT is reclaimable.

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 conference. Please use this form for your room reservation or be sure to mention "VA 6377 ECA Event" to receive the specially negotiated rate for the duration of your stay. Reservation should be made directly with the hotel not later than 19 April 2010. Early reservation is recommended.

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
69007 Heidelberg, GERMANY
Phone +49 (0) 62 21/84 44-0
Fax +49 (0) 62 21/84 44 34
E-mail: info@concept-heidelberg.de
www.concept-heidelberg.de

For questions regarding content:


Dr Robert Eicher (Operations Director) at +49-62 21/84 44 12 or per e-mail at eicher@concept-heidelberg.de.

For questions regarding reservation, hotel, organisation etc.:

Ms Marion Weidemaier (Organisation Manager) at +49-62 21/84 44 46 or per e-mail at weidemaier@concept-heidelberg.de.

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

Reservation Form (Please complete in full)

 +49 6221 84 44 34

Handling of highly potent Compounds (only Conference)

Basle, Switzerland, 18–19 May 2010

Mr Ms

Title, first name, surname

Company

Department

Important: Please indicate your company's VAT ID Number

Please indicate the Purchase Order Number, if applicable

Street / P.O. Box

City

Zip Code

Country

Phone / Fax

E-Mail (Please fill in)

CONCEPT HEIDELBERG
P.O. Box 10 17 64
Fax +49 (0) 6221/84 44 34

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 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 %.

CONCEPT HEIDELBERG reserves the right to change the materials, instructors, or speakers without notice or to cancel an event. 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.

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. 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)!