

## SPEAKERS



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



**DR GAVIN SCHMID**  
CARBOGEN AMCIS



**FRANK GENEROTZKY**  
Baxter Oncology



**DR FRIEDERIKE  
HERMANN**  
Lonza



**DR RAINER NICOLAI**  
F. Hoffmann-La Roche



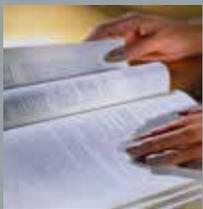
**DAVID O'CONNELL**  
Penn Pharma



**DR HARALD STAHL**  
GEA Pharma Systems



**DR CLEMENS STIEF**  
Pfizer



Each participant receives an industrial guidance document on the derivation of ADE/PDE values

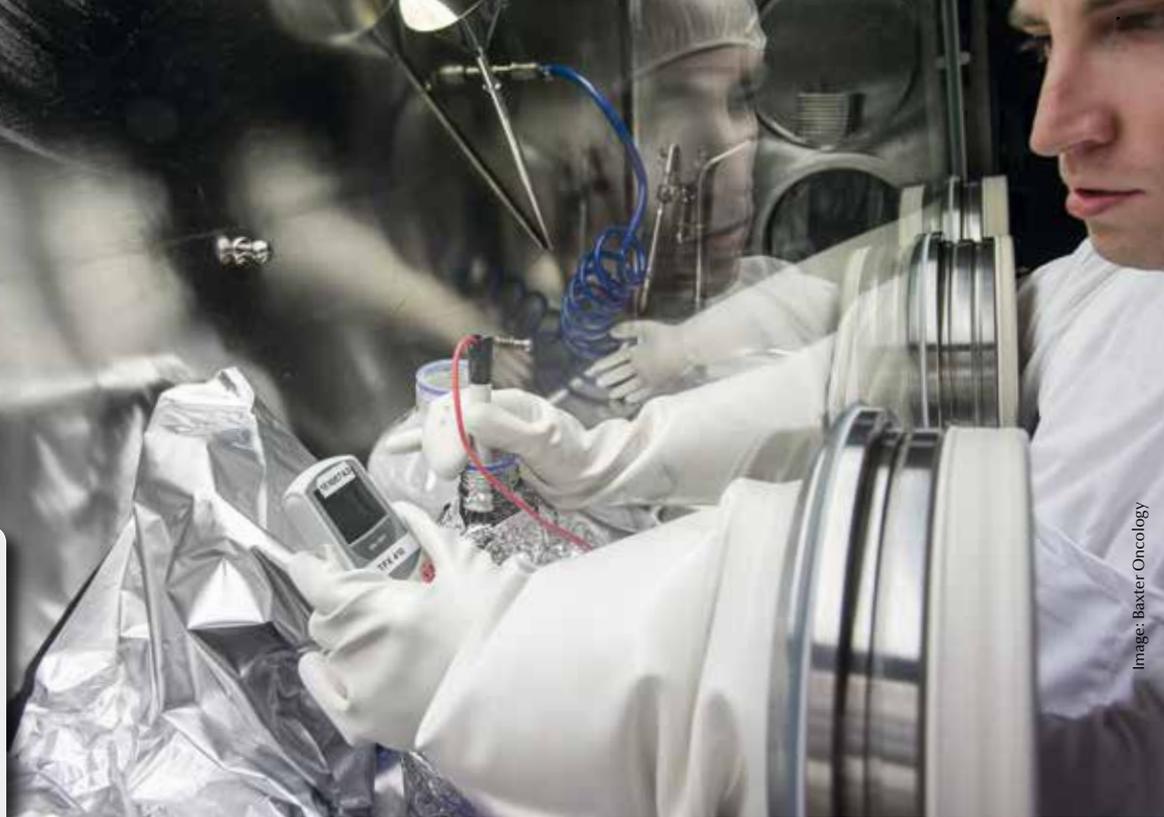


Image: Baxter Oncology

# Manufacture of highly potent compounds

## Avoiding cross contamination & minimizing exposure

5-6 May 2015, Barcelona, Spain

### HIGHLIGHTS:

- Determination of the right level of containment based on toxicological and pharmacological data
- Risk-Analysis: GMP and EH&S aspects
- Possibilities for closed product handling: transfer, sampling and analytics
- Determination of cleaning limits: how much cross contamination is allowed?
- Proof of concept: Containment measurements

### Case Studies

- **F. Hoffmann-La Roche:** Recent developments in hp-API production
- **Carbogen Amcis:** Cleaning of equipment in API production
- **Lonza:** Single-Use-Containment solutions
- **Pfizer:** Manufacture of highly potent oral solid dosage forms
- **Baxter Oncology:** Manufacture of highly potent sterile dosage forms
- **Penn Pharma:** Contract development of highly active substances

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# Manufacture of highly potent Compounds

5-6 May 2015, Barcelona, Spain

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- Objectives** Main focus of this conference is on the connection of cGMPs with safety aspects, especially on avoiding cross contamination and minimizing exposure.  
It will also deal with the calculation of exposure limits, limits for cleaning validation and the possibilities offered by containment technology, shown by real life examples from pharmaceutical industry ranging from the manufacture of APIs, to oral solid dosage forms and sterile medicinal preparations.
- Background** Many manufactures have to deal with the situation how to implement a new and potent product in an existing facility. Is it possible? Only by complying with regulatory demands with regards to the prevention of cross contamination and using risk management tools based on ICH Q9, a safe and cost effective solution can be found. Furthermore the Safety Working Group of the European Medicines Agency (EMA) has released a draft Guideline on setting health based exposure limits. This corresponds to updates of chapters 3.6 and 5.18/19 of the EU GMP-Guide.  
This will have an impact on the handling of highly potent materials within the pharmaceutical industry and the way, risks have to be evaluated. This will have to be done in much more scientific way, based on toxicological and pharmacological data.
- During this conference the following questions represent some of the issues discussed:
- Which highly active substances can be handled in the same building/facility/plan?
  - How are OEL Limits and ADIs calculated?
  - How much containment do I need?
  - What are the different technical solutions?
  - What should a risk analysis contain?
  - How are exposure measurements carried out?
  - What has to be considered for the cleaning of equipment?
- Well established examples for layout concepts, equipment for closed product handling and analytics are demonstrated through case studies with different pharmaceutical applications in primary and secondary facilities.
- Target Audience** Managers and technical experts from production, development and occupational health & safety, responsible for the manufacture and handling of highly potent materials. Also engineers who design, install and qualify containment facilities and systems.
- Moderator** Dr Harald Stahl

## Programme

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### 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.

### 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

### **A risk-based approach to define the containment strategy**

- Stepwise evaluation of single processing steps
- Risks for employees
- GMP Risks versus SHE Risks
- Systematic evaluation of risks
- Definition of appropriate actions: equipment, organisation, process changes,...
- Usage of formal tools: GAP-Analysis, FMEA, ..

## **Case Study Hoffmann-La Roche**

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### **Chemical Production of Highly Active APIs - Recent Developments at F. Hoffmann-La Roche**

Most of the newly developed APIs are "highly active" resulting in increased requirements on the plant installation to ensure workplace protection by technical means, rather than PPE. Some recent developments will be shown, starting from general concepts going into technical details.

- hygienic design piping class for chemicals
- special reactor design
- isolator technologies

## **Case Study Carbogen Amcis**

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### **Cleaning of Equipment in the HiPo Production Plant**

- What is worker protection before cleaning vessels
- How much do we clean before opening for visual inspection
- How do we clean
- What PPE for visual inspection
- How much cleaning follows after visual inspection
- To what limit
- How do we clean the room around the vessels
- Clothing rules for all people including visitors



Image: Carbogen Amcis

### **Toxicological evaluation to set science-based [cleaning] limits**

- How much carry-over is allowed?
- Controlling cross contamination
- Old and new approach for determination of cleaning validation limits
- The PDE / RiskMaPP principle in the cleaning of pharmaceutical equipment
- Concrete examples

## **Case Study Pfizer**

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### **Design of a facility for the manufacture of oral solid dosage forms and its operation**

In this case study a Pfizer high potent development plant will be presented used for the manufacture of oral solid dosage forms for clinical trials as well as for marketed product support.

#### **Design: Determination of the right level of containment**

- Layout
- Environmental protection
- HVAC and pressure concept
- Personal Protection Equipment

#### **Operation: Minimising exposure and cross contamination**

- Start up of a high containment plant considering new processes
- How to introduce a new product/compound
- Process evaluation
- Usage of industrial hygiene data for GMP argumentations
- Cleaning of equipment and premises
- Waste handling (solids, liquids, air, used equipment)

## **Case Study Baxter**

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### **Facility and Equipment Design for High Potent Sterile Drugs produced by Aseptic Processing**

- Process development
- Process design (Airflow concept, monitoring, decontamination).
- Process equipment: Isolator vs. cRABS
- Risk analysis and qualification
- Routine aseptic processing steps in an highly active environment
- Industrial hygiene

## Case Study Lonza

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### Single-Use Technology/Flexible Isolators & Containment Measurements

- Manufacture of highly active APIs at Lonza
- Pros & cons for flexible containment technology
- Proof of performance with containment measurements

## Case Study Penn Pharma

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### Contract Development of highly active substances

- How to handle substance with little knowledge on toxicity
- Designing of High Potent Development and Clinical Manufacturing facility
- How Develop and scale-up a high potent drug product.

## Speakers



### **DR ANDREAS FLÜCKIGER, F. HOFFMANN-LA ROCHE**

An occupational physician by training, Andreas Flückiger has been the head of the occupational health services of the Roche Group for almost 30 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 (ECETOC) and ISPE.



### **DR GAVIN SCHMID, CARBOGEN AMCIS AG**

Dr Schmid has a Master's degree in chemistry and received his PhD at the ETH Zürich. He has been working for CARBOGEN AMCIS since 2002 in different positions, amongst others as Senior Chemist in Process Research & Development and API Synthesis. In 2007 he became a member of the categorization team, responsible for the toxicological and pharmacological assessment of active substances. Since 2011 he is Head of ESH (Environment, Safety & Health) for all Swiss sites and in this position has developed the current cleaning limit concept at CARBOGEN AMCIS.



### **FRANK GENEROTZKY, BAXTER ONCOLOGY GMBH**

Frank Generotzky has been in the pharmaceutical industry for more than 15 years and has held leadership roles in process engineering, qualification, manufacturing and project management. During the last 15 years Frank and his teams have designed, installed and ramped up several new production facilities in conventional Cleanroom Technology as well as in Isolator Technology according to customer and market requirements. He is Director Technology & Engineering and responsible for Project Management and Strategic Development of the Pharmaceutical Technology, as well as Facility Management for high potent sterile forms at Baxter's facility in Halle.



### **DR FRIEDERIKE HERMANN, LONZA AG**

Dr Friederike Hermann is chemist and occupational hygienist. She graduated from the ETH Zurich and the University of Lausanne, with a Master's degree in advanced studies on work and health. Since 2001, Dr Hermann has been employed at Lonza AG initially in the environmental department, now in the area of occupational hygiene. She is member of the steering committee of COP Containment ISPE Affiliate D/A/CH.



### **DR RAINER NICOLAI, F. HOFFMANN-LA ROCHE**

After finishing his Ph.D. thesis in process engineering Rainer Nicolai worked as a senior researcher at the Swiss Federal Institute of Technology (ETHZ) in the field of processing of fine solids. In 1998 he joined Roche as an engineering project manager. Between 2000 and 2007 he worked for Evonik Industries (formerly Degussa) as process manager for the production of ultra high pure raw materials and later as head of production and technology for this business unit. Since 2007 he works for Roche again as project manager with the focus on handling highly active substances.



### **DAVID O'CONNELL, PENN PHARMA**

David O'Connell has been in the Contract Development and Manufacturing Pharmaceutical area for over 12 years. David joined Penn Pharma as the Head of Formulation Development 2009 from Aptuit's clinical development group. David was part of the design team that built a high containment development and manufacturing facility at Penn and currently leads the formulation development group in formulating potent and non-potent drug product as a client service.



### **DR HARALD STAHL, GEA PHARMA SYSTEMS**

Dr Harald Stahl worked for 3 years in the Pharmaceutical Development of Schering AG in Germany. At that time his main interest was the aseptic production of pellets. 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.



### **DR CLEMENS STIEF, PFIZER MANUFACTURING DEUTSCHLAND GMBH**

Dr Stief studied Pharmacy and gained his PhD in Pharmaceutical Technology in 1994. After several management positions at Gödecke / Parke-Davis Dr Stief became Team Leader Operations of the Product and Process Development at Pfizer Manufacturing Deutschland GmbH in Freiburg. He is the qualified person manufacturing for IMP and commercial products and responsible for the manufacture of solid dosage forms in a high containment area.



### **SOCIAL EVENT**

At the end of the first day of the event you are invited to take part in an evening program where you can discuss with speakers and colleagues in a relaxed atmosphere.

### **WHAT ARE THE ECA FOUNDATION AND THE ECA ACADEMY?**

The European Compliance Academy Foundation (ECA Foundation) is an independent professional organisation chaired by a Scientific Advisory Board with members from the pharmaceutical industry and regulatory authorities. The ECA Foundation's goal is to support to the Pharmaceutical Industry and Regulators to promote the move towards a harmonised set of GMP and regulatory guidelines by providing information and interpretation of new or updated guidances. The ECA Academy offers professional basic and advanced education (training) programmes. All services offered by the ECA Academy and with regard to ECA Academy Memberships are solely managed by Concept Heidelberg (a leading European training and information services provider). The ECA Foundation is conceptual sponsor of the ECA Academy.

### **HOW DO YOU BECOME A MEMBER OF ECA?**

By participating in one of the ECA Academy Conferences or Courses you will automatically become a ECA Academy Individual Member for two years - free of charge. More information about ECA Academy can be obtained on the Website <http://www.gmp-compliance.org>



### **WHAT ARE THE BENEFITS OF ECA?**

During the membership, you enjoy a EUR 200,- discount on the regular participation fee of any European Conference or Course presented by the ECA Academy. In addition you will receive the GMP Guideline Manager Software with a large number of guidelines, e.g. EC Directives, FDA Guidelines, ICH Guidelines.

### **USE THE GMP APP AT NO COSTS!**

The ECA Foundation has developed a GMP App which offers a comprehensive GMP Guideline database with more than 1,400 GMP Guidelines and ten thousands of pages. Check relevant Guidelines (full text versions) during internal audits, regulatory inspections or GMP compliance meetings – simply on your smartphone or tablet PC. In addition to this wealth of guideline information the GMP App also comprises features like GMP News, a comprehensive GMP Search Engine. To open the app just enter [app.gmp-compliance.org](http://app.gmp-compliance.org) in your browser and the WebApp opens immediately.



## 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, 5 May 2015, 09.00 to approx. 18.00 h  
(Registration and coffee 08.30 – 09.00 h)  
Wednesday, 6 May 2015, 08.30 to approx. 15.30 h

### Venue

Barceló Sants  
Placa dels Paisos Catalans, s/n  
Estació de Sants  
08014 Barcelona, Spain  
Phone +34 93 503 53 00  
Fax +34 93 490 60 45

### Fees (per delegate plus VAT)

ECA Members: € 1,490  
APIC Members: € 1,590  
Non-ECA Members: € 1,690  
EU GMP Inspectorates: € 845  
The conference fee is payable in advance after receipt of invoice and includes conference documentation, lunch on both days and dinner on the first day and all refreshments. VAT is reclaimable.

### Conference language

The official conference language will be English.

### Accommodation

CONCEPT has reserved a limited number of rooms in the conference hotel. You will receive a room reservation form when you have registered for the course. Please use this form for your room reservation to receive the specially negotiated rate for the duration of your stay. Reservation should be made directly with the hotel. Early reservation is recommended.

### 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, 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.:

Mr Ronny Strohwalde (Organisation Manager) at +49-62 21/84 44 51, or per e-mail at strohwalde@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

### Manufacture of highly potent Compounds

5-6 May 2015, Barcelona, Spain

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 week 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)! (As of January 2012).

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