ECA
European Compliance Academy

Image: CARBOGEN-AMCIS

Manufacture of highly potent APIs

Avoiding Cross-Contamination – Complying with occupational safety requirements

17-18 April 2012, Barcelona, Spain

SPEAKERS

DR TOM BUGGY
DSM Sinochem Pharmaceuticals, The Netherlands
APIC Representative of Quality Working Group

PROF GERNOD DITTEL
Dittel Engineering, Germany

DR ANDREAS FLÜCKIGER
F. Hoffmann-La Roche, Switzerland

DR FILIPE GASPAR
Hovione, Portugal

DR FRIEDERIKE HERMANN
Lonza, Switzerland

DR PETER MÜLLER
CARBOGEN AMCIS, Switzerland

DR RAINER NICOLAI
F. Hoffmann-La Roche, Switzerland

DR HARALD STAHL
GEA Pharma Systems, Germany

MAARTEN PRAUSE
CARBOGEN AMCIS, Switzerland

HIGHLIGHTS:

- Determination of the right level of containment based on toxicological and pharmacological data
- Possibilities for closed product handling: transfer, sampling and analytics
- Usage of flexible containment solutions
- Design of a containment facility
- Contamination prevention in dedicated and multipurpose facilities
- Update on regulatory requirements for dedicated facilities
- Cleaning of equipment and cleaning limits
- Case Studies
  - Hovione: Spray drying of HP APIs
  - Lonza: Production plant for cytotoxic APIs
  - F. Hoffmann-La Roche: Multi purpose plant
- Containment measurements

This conference is recognised for the ECA GMP Certification Programme „Certified API Production Manager“. Please find details at www.gmp-certification.eu

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Objectives

This event aims at examining the state of the art in the currently widely discussed field of containment in the manufacture of APIs. 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 toxic ingredients and due to the toxicity of the product itself the manufacture of 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 European Medicines Agency (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.

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 to 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.

During the conference the following questions represent some of the issues discussed and presented in case studies:

- 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?
- Where are the regulatory requirements going to?
- How is the right level of containment proven/measured?
- What has to be considered for the cleaning of equipment?
- What can a lab environment look like for highly potent materials?

Target Audience

Managers and technical experts from production, development and occupational health & safety, responsible for the manufacture and handling of highly potent APIs. Also engineers who design, install and qualify containment facilities and systems.

Moderator

Dr Harald Stahl

Social Event

On 17 April, 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.

Programme

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 (cf. Risk-MaPP, ADEs).

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

CASE STUDY F. HOFFMAN-LA ROCHE:
Usage of flexible containment technologies for high potent APIs
FIBC System for Wet-Cake Transfer

- Safety versus GMP versus Containment
- Operational Experience

Contamination prevention in Manufacturing Sites with both dedicated and multipurpose facilities – a risk-based approach

- Sources of contamination
- Dedicated facilities
- Multipurpose facilities and equipment
- Risk based process proposal
  - Product types and level of protection
  - Contamination prevention for open product processing and handling
  - Contamination risk reduction
  - Responsibilities
- Importance of contamination control on "other" sources

Engineering of a containment facility for APIs

- Layout & Zone concepts
- HVAC and filters
- Possibilities for protecting product and / or employees
- Handling of exhaust air and waste water
- Cost comparison for different technical solutions

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

Proof of Performance: Containment Measurements

- Where, how and what to measure
- Measurement of substitute vs product (SMEPAC)
- Analytics and filters
- Sampling Locations
- Interpretation of the results

Programme

CASE STUDY F. HOFFMANN-LA ROCHE:
API HIGH CONTAINMENT MULTIPURPOSE DEVELOPMENT PLANT

- Containment Concept
- Process Equipment
- Operational Experience

CASE STUDY HOVIONE:
SPRAY DRYING OF POTENT APIS

- Spray Drying working principles and applications in pharma industry
- Assessing potent processes and risk analysis
- Building, equipment, and the powder handling requirements

CASE STUDY LONZA AG:
ESTABLISHEMENT OF A PRODUCTION PLANT FOR THE MANUFACTURE OF CYTOTOXIC HAPIS

The project in Visp, Switzerland covered the remodelling of an existing plant as well as the new setup of premises for the biotechnological and chemical manufacture of high potent APIs.

- Planning according to GMP and safety aspects
- Technical aspects of facility and equipment
- Remodelling aspects
- Risk Management: general approach and examples
- Cleaning and waste management

Speakers

DR TOM BUGGY, ***DSM Sinochem Pharmaceuticals, The Netherlands - APIC Representative of Quality Working Group***

Dr Buggy is the International GMP Compliance Adviser for DSM DSM Sinochem Pharmaceuticals (former DSM Anti-Infectives). based in Delft. He is responsible for the international Quality procedures, Internal Auditing of the manufacturing sites and generally supporting the DSM sites on Quality related topics. He has 27 years experience of working in the Pharmaceutical Industry specializing on the Research, Development, Manufacture and Quality Assurance of APIs. He represents DSM in the CEFIC/APIC Quality Working Group and is the Leader of the APIC Third Party Audit Programme.

PROF GERNOD DITTEL, ***Dittel Engineering GmbH & Co. KG, Germany***

Prof Gernod Dittel has a degree in mechanical engineering. He founded DITTEL Cleanroom Engineering Bavaria in 1993, where he now takes the position of CEO for the whole company. DITTEL Engineering designs supervises and qualifies cleanroom production facilities in turn-key, especially in pharmaceutics, cosmetics, medical engineering. Professor Dittel lectures on cleanroom technology at Carinthia Villach, Austria. He also holds a professorship for "Cleanroom Technologies" at the Xian Jiaotong Technical University in China. Prof. Dittel is vice president of the German Expert Committee in Cleanroom Technology managed by VDI, the German Mirror Committee which is managed by DIN and the Institute of Cleanroom Technology of Germany.

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

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 (ECETOC).

DR FILIPE GASPAR, ***Hovione, Portugal***

Filipe Gaspar gained profound knowledge in the use of supercritical fluids technologies in both pharmaceutical and nutraceutical industries. In 2003, Dr Gaspar joined Hovione, first as Production Engineer and later in R&D as a Senior Engineer. He is now the Director of the Discipline of Particle Design and the focus of his work is in the application of particle engineering technologies, such as spray drying, to active ingredients and pre-formulated products.

DR FRIEDERIKE HERMANN, ***Lonza AG, Switzerland***

Dr Friederike Hermann is chemist and occupational hygienist. Following graduation, she obtained a doctorate in the field of analytical chemistry with an emphasis on element speciation. Since 2001, Dr. Hermann has been employed at Lonza AG initially in the environmental department, now in the area of occupational hygiene. She graduated from the ETH Zurich and the University of Lausanne, with a Master's degree in advances studies on work and health. She is member of the steering committee of COP Containment ISPE Affiliate D/A/CH.

Speakers

DR PETER MÜLLER, *CARBOGEN AMCIS AG, Switzerland*
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 RAINER NICOLAI, *F. Hoffmann-La Roche, Switzerland*
After finishing his Ph.D. thesis in process engineering Rainer worked as a senior researcher at the Swiss Federal Institute of Technology (ETHZ) in the field of processing of fine solids. In 1998 he joint 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.

DR HARALD STAHL, *GEA Pharma Systems, Germany*
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.

MAARTEN PRAUSE, *CARBOGEN AMCIS AG, Switzerland*
Maarten Prause has a broad experience in industrial hygiene within the chemical and pharmaceutical industry and he holds a Master's degree in Environmental Sciences. Previous to his role with CARBOGEN AMCIS, Maarten was based in the Netherlands working for a consultancy in industrial hygiene. He has now been working for 4 years in this field with CARBOGEN AMCIS where he leads the company's compound categorisation team. Maarten plays a pivotal role in defining and optimising the concepts of working safely with highly potent compounds within CARBOGEN AMCIS.

Conference Exhibition

The European Compliance Academy offers you the opportunity to present your company, your products and services to your target group almost without any scattering losses. The costs for an exhibition space at this event are € 1,490,-. You will find details and a registration form on our website www.gmp-compliance.org. Just follow the link „Conferences“ on the homepage.

GMP Certification Programme

This seminar is recognised within the GMP Certification Programme Modules "Pharmaceutical API Production Manager" and "Technical Operations Manager". By attending selected seminars, the participant can acquire an additional certificate. We offer the following certification modules:

- ECA Validation Manager
- ECA QA Manager
- ECA API Production Manager
- ECA Quality Control Manager
- ECA Technical Operations Manager
- ECA Computer Validation Manager
- ECA Regulatory Affairs Manager
- ECA Microbiological Laboratory Manager
- ECA Sterile Production Manager
- ECA Biotech Manager
- ECA Pharmaceutical Development Manager

On the internet at www.gmp-compliance.org you will find a text explaining which seminars are recognised for which certificates. Or you send an e-mail to info@gmp-compliance.org or a fax to +49-6221-84 44 64 with the request for information about the GMP Certification Programme. We will then send you our brochure on the topic.

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We look forward to welcoming at one of our next events – and we already wish you a pleasant flight!

*Please note: You may have to enable pop-ups on the Mobility Partner Program website – otherwise the booking platform window will not open.

Easy Registration

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69007 Heidelberg
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Reservation Form:
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e-mail:
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Internet:
www.gmp-compliance.org

Date
Tuesday, 17 April 2012, 10.00 –17.45 h
(Registration and coffee 09.30 – 10.00 h)
Wednesday, 18 April 2012, 08.30 – 16.15 h

Venue
NH Constanza
Deu i mata, 69-99
08029 Barcelona, Spain
Phone +34 93 281 1500
Fax +34 93 281 15 25

Fees
ECA Members: € 1.490,- per delegate + VAT.
APIC Members: € 1.590,- per delegate + VAT
EU GMP Inspectorates: € 845,- per delegate + VAT.
Non-ECA Members: € 1.690,- per delegate + VAT.
The conference fee is payable in advance after receipt of invoice and includes conference documentation, dinner on the first day, lunch on all two days and all refreshments. VAT is reclaimable.

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 or be sure to mention "ECA7279 17-18April2012" to receive the specially negotiated rate (single room € 143,- per night, incl. breakfast + 8% tax) for the duration of your stay. Reservation should be made directly with the hotel not later than 19 March 2012. 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.

Organisation and Contact
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