ECA
European Compliance Academy

Visit the Dissolution Laboratories at Bayer HealthCare Pharmaceuticals in Berlin

Image: Bayer Schering Pharma

SPEAKERS

DR CHRISTOPHER BURGESS
Burgess Analytical Consultancy, UK

DR THOMAS FÜRST
Boehringer Ingelheim

DR KERSTIN PAULI
Bayer HealthCare Pharmaceuticals

DR JOCHEN SCHER
Boehringer Ingelheim

Dissolution Testing

Development / Quality Control and *in vivo* Relevance

17 – 19 October 2012, Berlin, Germany

HIGHLIGHTS:

- *In vivo* Relevant Dissolution Testing
- Regulatory Requirements (Pharmacopoeias, Required Data for the Application of a Marketing Authorisation)
- Mechanical Qualification versus Performance Verification Testing (PVT)
- Development of Dissolution Methods
  - How to Set Specifications?
  - Analytical Validation
  - Practical Recommendations
- OOS Results in Dissolution Testing
- The Importance of Biowaiving in Drug Product Development
- Dissolution Profile Comparison
- Automation of Dissolution Methods
- Country-specific Challenges: Japan, Korea, Taiwan, etc.

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

Objectives

This conference on Dissolution Testing aims at providing delegates with a sound understanding of the principles and best practices in dissolution testing. As dissolution testing has become increasingly important as a tool for predicting *in vivo* performance and for assessing drug product quality, this topic will be extensively discussed.

Background

The dissolution test is a key performance indicator for solid and semi-solid dosage forms in both drug development and quality control. In these fields it is used to assure batch-to-batch quality as well as providing process control information as part of the new approach to Process Validation.
Dissolution testing is usually connected to *in vivo* performance because the API must be released from the formulation in the gastro intestinal tract (GIT) before *in vivo* absorption can occur. Therefore dissolution testing is generally employed during drug product development and optimization. Where dissolution testing data can be shown to be correlated to *in vivo* performance, clinical trials may be avoided by *in vitro* dissolution studies under certain circumstances, thereby reducing development time and costs.

There are a great diversity of dissolution testing guidances and associated guidelines (e.g. FDA, EMA and the Pharmacopoeias) dealing with Scale-up and Post-Approval Changes, Bioequivalence studies, Waiver of *in vivo* Bioavailability and Bioequivalence Studies. Additionally there are some country-specific dissolution requirements which are very challenging for global pharmaceutical companies.

This conference will therefore cover the following topics:

- physicochemical and biopharmaceutical foundations
- dissolution method development
- validation of the dissolution methodology
- approaches for setting specifications
- OOS Results in dissolution testing
- statistical methods for comparing dissolution profiles
- approaches for substitution of BE-studies (biowaiver) and
- approaches to establish *in vitro in vivo* correlations (IVIVC)
- country-specific dissolution requirements and challenges

In addition, the expectations of the European Medicines Agency (EMA) and of the pharmacopoeias (Ph.Eur. 2.9.3 and USP Chapters <711> and <1092>) including USP Reference Standard Tablets and Mechanical calibration for the dissolution apparatus qualification will be discussed.

The objective of this event is to cover all aspects of dissolution testing with a focus on practical examples. Workshops are an essential part of the conference in order to encourage the exchange of experience and to allow interactive and in depth discussions of the subject.

Target Audience

This conference is dedicated to scientists and managers in the pharmaceutical industry working in:
- Quality control
- Quality assurance
- Analytical development
- Research and development
- Regulatory Affairs

The conference is also intended for participants from contract laboratories, regulatory authorities, and inspectorates.

Moderator

DR CHRISTOPHER BURGESS, *Burgess Analytical Consultancy Ltd., UK*

Programme

Fundamentals of Dissolution Testing: From Physicochemistry to Bioavailability
- Mechanism and theories of solid dissolution (e.g. diffusion layer model)
- Intrinsic dissolution rate
- Sink conditions
- Kinetics of drug release
- Relationship between dissolution and bioavailability
- Quality control dissolution testing and in vivo predictive dissolution testing
- Biopharmaceutics Classification System
- Hurdles and limitations of dissolution testing

DR JOCHEN SCHER, *Boehringer Ingelheim*

Programme (cont'd)

In vivo Relevant Dissolution Testing
- What is Biorelevance? Meaning and Misconceptions
- How to establish a link between dissolution and bioavailability
- The role of IVIVC
- Setting biorelevant dissolution specifications

DR THOMAS FÜRST, *Boehringer Ingelheim*

Dissolution Testing and Qualification from a Pharmacopoeial Perspective
- Requirements of the USP & EP
- Qualification and calibration
- Harmonisation of methods
- Key differences between the USP and EP
- FDA and ASTM activities
- Related methodologies: disintegration and friability

DR CHRISTOPHER BURGESS, *Burgess Analytical Consultancy*

WORKSHOP I
Analytical Instrument Qualification

Part 1: Mechanical Qualification
- Real-time demonstration

Moderator: **Jan Wolff, SOTAX, Switzerland**

Part 2: Performance Verification Testing (PVT)
Moderator: **Dr Christopher Burgess, Burgess Analytical Consultancy, UK**

Setting Specifications for Dissolution Methods
- How to set adequate dissolution specifications for various types of formulations
- Requirements of different Pharmacopoeias and Guidelines
- Specifics and exceptions

DR KERSTIN PAULI, *Bayer HealthCare Pharmaceuticals*

WORKSHOP II
How to Set Specifications: Sharing Information of the Learned Theories
- Presentation of Case Studies and discussion of potential results
- Q&A Session

Moderator: **Dr Kerstin Pauli, Bayer HealthCare Pharmaceuticals**

OOS Results in Dissolution Testing
- When is a result OOS and when is it not?
- Performance verification issues
- Failure investigations in dissolution testing.
- Are statistical outlier tests useful as part of dissolution test failure investigations?
- Documenting the outcome of the failure investigation

DR CHRISTOPHER BURGESS, *Burgess Analytical Consultancy, UK*

Development of Dissolution Methods with regard to Quality Control
- Method development for Immediate Release, Extended Release and Delayed Release Formulations
- Regulatory recommendations concerning method development
- Dissolution apparatus and medium selection
- Use of surfactants
- Adequate discriminatory capability
- Variability of dissolution results (stage/level testing)
- Dissolution methods for developing an IVIVC
- Case studies

DR JOCHEN SCHER, *Boehringer Ingelheim*

Automation in Dissolution Testing
- Why and when is automation valuable?
- Various types of dissolution systems
- New products on the market

DR KERSTIN PAULI, *Bayer HealthCare Pharmaceuticals*

Programme (cont'd)

Analytical Validation of Dissolution Testing Methods

- Pharmacopoeial and Regulatory Recommendations (e.g. ICH Q2 (R1) and USP <1092>)
- Validation characteristics:
  - Specificity, Linearity, Precision, Accuracy and Robustness
  - Furthermore:
    - filter validation
    - selecting the right deaeration method
    - validation of automated methods
- Some practical recommendations for performing the validation and recommended acceptance criteria
- Dissolution method transfer

DR JOCHEN SCHER, *Boehringer Ingelheim*

WORKSHOP III
Analytical Validation of Dissolution Methods

- Putting theory to work (case studies):
- Develop validation protocol for validation of dissolution methods for different solid oral dosage forms
- Pitfalls in performing the experiments

Moderator: **Dr Jochen Scher, Boehringer Ingelheim**

The Likelihood of Success: Statistical Properties of the Dissolution Test

- Basic statistics and dissolution testing
- Simulation studies
- Practical rules of thumb

DR THOMAS FÜRST, *Boehringer Ingelheim, Germany*

The Importance of Biowaiving in Drug Product Development

- The BCS system
- BCS based biowaivers
- Waivers based on proportional similarity
- Country specific regulatory differences
- Case studies

DR THOMAS FÜRST, *Boehringer Ingelheim, Germany*

Dissolution Profile Comparison; Approaches and Issues

- Dissolution processes and data variability
- What are we trying to compare?
- What do the agencies specify?
- Model independent approaches
- Examples of approaches

DR CHRISTOPHER BURGESS, *Burgess Analytical Consultancy, UK*

Case Study: Application of Dissolution Testing in Industrial Drug Product Development

- Special dosage forms
- Fixe dose combinations
- Extended release formulations
- Coprecipitate formulations
- Influence of stability testing on dissolution

DR KERSTIN PAULI, *Bayer HealthCare Pharmaceuticals*

Country-specific Dissolution Requirements and Challenges: Japan, Korea, Taiwan, etc.

DR THOMAS FÜRST, *Boehringer Ingelheim, Germany*

Expectations of an FDA Reviewer with regard to the Submission of Dissolution Data

BARBARA M. DAVIT, *Division of Bioequivalence, Office of Generic Drugs, CDER, FDA, USA (invited)*

Conference Exhibition

Leading suppliers of Dissolution apparatus and Dissolution systems are invited to exhibit their products. Please contact Ms Susanne Ludwig for further information on the opportunity to exhibit at the conference: Phone ++49-(0)62 21-84 44 44, Fax ++49-(0)62 21-84 44 34, e-mail: ludwig@concept-heidelberg.de

Already registered Exhibitors

ERWEKA GmbH, Heusenstamm, Germany

SOTAX AG, Allschwil, Switzerland

Visit of the Dissolution Laboratories at Bayer HealthCare Pharmaceuticals, Berlin

In the afternoon of the second course day all participants and speakers are invited to a guided tour to the new dissolution laboratory at Bayer HealthCare Pharmaceuticals in Berlin. The dissolution lab is equipped with various automated dissolution systems applicable to cover multiple aspects occurring during research and development:

- The new RoboDis: several fully automated robotic system (equipped with HPLC-, UV/VIS- and fibre optics technology) developed in cooperation with ERWEKA
- Several semi-automated UV/VIS systems
- Semi-automated "Paddle-over disk" dissolution system

- Fully automated Sotax AT 70 smart dissolution systems

- Various semi-automated HPLC systems

There will be a bus transfer to the laboratory and back to the hotel.
The number of participants for the lab visit is limited.

Speakers

DR CHRISTOPHER BURGESS, *Burgess Analytical Consultancy Limited, UK*
Dr Burgess is a Chartered Chemist and has more than 38 years experience in the pharmaceutical industry primarily with Glaxo in Quality Assurance and Analytical R&D. He is a "Qualified Person" and a member of the European QP Association advisory board. He has been appointed to the United States Pharmacopoeia's Council of Experts 2010 to 2015 and is a visiting professor of the University of Strathclyde's School of Pharmacy and Biomedical Sciences (SIPBS).

DR THOMAS FÜRST, *Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany*
Dr Fürst is Senior Principal Scientist at the Development Unit of Boehringer Ingelheim. He is responsible for the scientific quality of submissions and the QOS. Before joining Boehringer Ingelheim, Dr Fürst was with Schering AG, Berlin, where he worked in a production facility for oral dosage forms and the analytical development department before heading the Pharmaceutical Development Services group of Schering AG, Berlin.

DR KERSTIN PAULI, *Bayer HealthCare Pharmaceuticals, Berlin, Germany*
Kerstin Pauli studied Food Chemistry and Pharmacy at the University of Bonn and received her PhD in Pharmaceutical Analytics. In her position as head of a group of project laboratories in Global Drug Development within Bayer HealthCare Pharmaceuticals she is responsible for all aspects regarding the analytical part of product development. In her first position she was specialised in the area of dissolution testing (including development and validation of dissolution methods, submission of development projects and handling of post approval changes, life cycle management and patent protection of market products) and also for automation in dissolution testing (Robot Technology).

DR JOCHEN SCHER, *Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany*
Dr Scher studied pharmacy and conducted his PhD at the University of Saarland at the Institute of Pharmacognosy and Analytical Phytochemistry and at the University of Otago in Dunedin. He is a specialised pharmacist for pharmaceutical analytics and for seven years he is working at Boehringer Ingelheim Pharma GmbH & Co. KG in Biberach (Germany). He is principal scientist in the Analytical Development.

Social Event

We are looking forward to welcome all participants and speakers to a nice evening in a relaxed atmosphere after the first course day.

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
Wednesday, 17 October 2012, 9.00 h – 18.00 h
(Registration and coffee 8.30 – 9.00 h)
Thursday, 18 October 2012, 8.30 h – 18.30 h
Friday, 19 October 2012, 08.30 – 15.30 h

Venue
Steigenberger Hotel Berlin
Los-Angeles-Platz 1
10789 Berlin
Germany
Phone + 49 / (0) 30 / 2127 - 0
Fax + 49 / (0) 30 / 2127 - 799

Fees
ECA Members € 1,790.- per delegate plus VAT
APIC Members € 1,890.- per delegate plus VAT
(does not include ECA Membership)
Non-ECA Members € 1,990.- per delegate plus VAT
EU GMP Inspectorates € 995.- 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 three 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 event. Please use this form for your room reservation to receive the specially negotiated rate for the duration of your stay (single room € 125,- per night, incl. breakfast). Reservation should be made directly with the hotel not later than 16 September 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
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
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www.concept-heidelberg.de

For questions regarding content:
Dr Günter Brendelberger (Operations Director) at +49-62 21 / 84 44 39, or per e-mail at brendelberger@concept-heidelberg.de.
For questions regarding reservation, hotel, organisation etc.:
Susanne Ludwig (Organisation Manager) at +49-62 21 / 84 44 44, or per e-mail at ludwig@concept-heidelberg.de.

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Reservation Form (Please complete in full)

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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 %
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