ECA Academy
Your GMP/GDP Information Source

GMP Certification Programme
Certified Quality Control Manager

Speakers

Dr Kerstin Hartisch
Bayer AG

Dr Ragna Hoffmann
Boehringer Ingelheim

Dr Gerd Michael Maier
Boehringer Ingelheim

Dr Alexander Pontius
Bayer AG

Dissolution Testing

Development / Quality Control and *in vivo* Relevance

11/12 February 2020 | Prague, Czech Republic

Image: ERWEKA GmbH, Germany

Highlights

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

Objective

This GMP Education Course on Dissolution Testing aims at providing delegates with a sound understanding of the principles and best practices in dissolution testing.
As Dissolution represents a very interdisciplinary topic, a broad variety of areas within the development and commercial phase will be discussed. You will get to know

- how to characterize formulations
- how to support formulation and process development:
- how to evaluate the impact of formulation and process parameters changes
- how to control the quality (QC tool) of clinical trial supplies and the commercial product
- how to support drug product stability testing
- how to justify formulation/production changes (e.g., according to SUPAC, Biowaivers)
- how to predict in vivo performance

Due to the wide range of applications and the sensitivity of dissolution testing, sound method development and validation is of essential importance. Furthermore also knowledge on dissolution apparatus qualification, dissolution specification setting, dissolution profile comparison and handling of OOS/OOE results will be trained and discussed.

Background

The dissolution test is a key test parameter for assessing the performance of 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 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. A dissolution test should therefore have adequate discriminatory power to detect relevant Drug Product changes.

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 many dissolution 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 GMP Education Course will, therefore, cover the following topics:

- physicochemical and biopharmaceutical foundations
- dissolution method development,
- validation of the dissolution methodology
- approaches for setting specifications
- OOS and OOE 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 course is to cover all aspects of dissolution testing with a focus on practical examples. Workshops are also part of the course in order to encourage the exchange of experience and to allow interactive and in depth discussions of the subject.

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
- Fraction of a dose absorbed classification system
- Hurdles and limitations of dissolution testing

Dissolution Testing throughout the Drug Product Development Lifecycle

- Use of dissolution testing during Drug Product development
- What is Biorelevance? Meaning and Misconceptions
- How to establish a link between dissolution and bioavailability
- The role of IVIVC
- Setting biorelevant dissolution specifications
- BCS based biowaivers
- Waivers based on proportional similarity
- Country specific regulatory differences
- Case studies

Dissolution Testing – Regulatory Guidelines

- Prerequisites of international and mostly harmonized pharmacopeias (USP, EP, Pharm Jap)
- Miniaturization of dissolution tests
- General guidelines for dissolution testing
- Contents and differences in Chinese pharmacopeia

- Validation of dissolution test methods
- Bioequivalence considerations
- Special in vitro bioequivalence applications in Japan
- Waiving dissolution tests by disintegration tests

Development of Dissolution Methods - The balancing Act between Quality Control and Clinically Relevance

- Method development for Immediate Release, Extended Release and Delayed Release Formulations
- Regulatory recommendations
- Dissolution apparatus and medium selection
- Use of surfactants
- Adequate discriminatory capability
- Standard Dissolution Test Conditions
- Evaluation of bio-relevance
- Dissolution methods for developing an IVIVE/C to gain regulatory flexibility
- Case studies

Mechanical Calibration & Performance Verification Test (PVT)

- Regulatory basis
- Fundamentals of instrument qualification
- Qualification and calibration of dissolution apparatuses
- Mechanical calibration
- USP Performance Verification Test (PVT)
- Deviations and OOC

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

WORKSHOP I
How to Set Specifications: Sharing Information of the Learned Theories

- Presentation of Case Studies and discussion of potential results
- Q&A Session

OOS Results in Dissolution Testing

- Regulatory aspects
- Dissolution methods having appropriate discriminatory power
- General OOS procedure for dissolution testing
- Defining and handling of OOS results including CAPA
- OOS evaluation for immediate release products
- OOS evaluation for capsules
- OOS evaluation for modified-release products
- OOT/OOE results: Evaluating stability effects by applying dissolution testing

Automation in Dissolution Testing

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

Analytical Validation of Dissolution Testing Methods

- Pharmacopoeial and Regulatory Recommendations (e.g., ICH Q2 (R1),USP <1092>, RDC No. 166/2017)
- Validation characteristics:
  - Specificity, Linearity, Precision, Accuracy and Robustness
  - Validation of automated procedures
- Some practical recommendations for performing the validation and recommended acceptance criteria
- Dissolution method transfer

WORKSHOP II
Analytical Validation of Dissolution Methods
Putting theory to work (case studies):

- Develop validation protocol for validation of dissolution methods for solid oral dosage forms
- Pitfalls in performing the experiments

Dissolution Profile Comparison; Approaches and Issues

- Importance of dissolution profile comparisons during drug product development and for a commercial product
- Regulatory requirements concerning dissolution profile comparison
- Different approaches to compare dissolution profiles: Model dependent and independent approaches
- Examples

Case Study
Application of Dissolution Testing in Industrial Drug Product Development
Discussion of various case studies occurring during product development

Speakers

Dr Kerstin Hartisch
Bayer AG, Berlin, Germany

Kerstin Hartisch studied Food Chemistry and Pharmacy at the University of Bonn and received her PhD in Pharmaceutical Analytics. In her position as head of Analytical Development within Bayer, Chemical and Pharmaceutical Development she is responsible for all aspects regarding special analytical techniques in product development, i.e. dissolution testing, , particle identification, packaging materials, excipient testing and also sample and data management (LIMS). She is specialised in the area of dissolution testing including all aspects of automation (Robot Technology).

Dr Ragna Hoffmann
Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany

Dr Ragna Hoffmann is a pharmacist by training and received her PhD in pharmaceutical technology from the Eberhard-Karls University of Tuebingen. She joined Boehringer Ingelheim in 2007 and has since worked in different areas of drug product development (preformulation, formulation development, and analytical development). Dr. Hoffmann is currently heading a dissolution lab within the Analytical Development Department at Boehringer Ingelheim in Biberach, Germany.

Dr Gerd Michael Maier
Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany

Dr. Gerd-Michael Maier is a chemist by training and did his PhD graduation in bioinorganic chemistry at the University of Konstanz. He joined Boehringer Ingelheim in 1997 where he started in the Drug Regulatory Affairs department and worked as a regulatory affairs manager. After three years as team leader Regulations & Training in the Quality Systems group Gerd-Michael joined the department of Drug Dicovery Support in research leading a CMC lab for almost 10 years. Since 2014 he holds the position of a dissolution lab head within the Analytical Development Department at Boehringer Ingelheim, Biberach, Germany.

Dr Alexander Pontius
Bayer AG, Leverkusen, Germany

Alexander is a pharmacist by training and did his PhD graduation in biopharmaceutical analytics. He was heading a QC group in the global pharmaceutical development division and was responsible for all aspects of the dissolution methodology. This work covered the development and validation of dissolution methods, bio-pharmaceutical evaluations, dossier submission of innovative drug products, handling of post approval changes as well as support of life cycle management and patent protection of market products. At present, Alexander is working as Quality System Manager within the enterprise-wide Corporate Quality function. He is responsible for the regulation management within the overarching Quality Management System at Bayer.

Date
Tuesday, 11 February 2020, 9.00 h – 18.00 h
(Registration and coffee 8.30 – 9.00 h)
Wednesday, 12 February 2020, 8.30 h – 16.00 h

Venue
Corinthia Hotel Prague
Kongresova 1
14069 Prague 4, Czech Republic
Phone +420 (261) 191 111
Email prague@corinthia.com

Fees (per delegate, plus VAT)
ECA Members € 1,590
APIC Members € 1,690
Non-ECA Members € 1,790
EU GMP Inspectorates € 895
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/ POG when you have registered for the course. Reservation should be made directly with the hotel. 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
ECA has entrusted Concept Heidelberg with the organisation of this event.

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organisation etc. please contact:
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thiel@concept-heidelberg.de.

Social Event
At the end of the first course day 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.

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Reservation Form (Please complete in full)

Dissolution Testing, 11/12 February 2020, Prague, Czech Republic

Title, first name, surname

Department Company

Important: Please indicate your company's VAT ID Number Purchase Order Number, if applicable

City ZIP Code Country

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