

Speakers



Dr Corinna Bode
Bayer



Dr Jan Joseph
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Dr Gerd Michael Maier
Boehringer Ingelheim



Dr Johanna Milsmann
Boehringer Ingelheim

Dissolution Testing

Development/Quality Control and *in vivo* Relevance

26/27 June 2024 | Hamburg, Germany



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 guidance 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

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

Dissolution Testing – Regulatory Requirements (Guidelines, Pharmacopoeias, etc.)

- Prerequisites of international and mostly harmonized pharmacopoeias (USP, EP, Pharm Jap)
- Miniaturization of dissolution tests
- General guidelines for dissolution testing
- Contents and differences in Chinese pharmacopoeia
- Validation of dissolution test methods

- Bioequivalence considerations
- Special in vitro bioequivalence applications in Japan
- Waiving dissolution tests by disintegration tests

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

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



Case Study

Application of Dissolution Testing in Industrial Drug Product Development

Discussion of various case studies occurring during product development

Automation in Dissolution Testing

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

Dissolution Testing throughout the Drug Product Development Lifecycle: In vivo relevance and Bio-waivers

- 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 bio waivers
- Waivers based on proportional similarity
- Country specific regulatory differences
- Case studies

OOS Results in Dissolution Testing (incl. OOE)

- 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

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

Conference Exhibition

Leading suppliers of Dissolution apparatus and Dissolution systems are invited to exhibit their products.

Please contact Mr Niklaus Thiel for further information on the opportunity to exhibit at the conference:

Phone: +49 (0)62 21-84 44 43

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Speakers



Dr Corinna Bode
Bayer AG, Elberfeld, Germany

Dr Corinna Bode is a pharmacist by training and received her PhD in pharmaceutical technology from the Université de Lille, France. Her doctoral thesis focused on biodegradable implants (both pre-formed and in situ-forming) and the underlying mechanisms for drug release and degradation. She joined Bayer in 2020 and is heading a dissolution lab within the Drug Product Development department.



Dr Jan Joseph
Bayer AG, Berlin, Germany

Dr Jan Joseph is a pharmacist by training and obtained his PhD in Pharmaceutical and Medicinal Chemistry from Freie Universität Berlin, where he was heading a unit of the departments core facility for chromatography and mass spectrometry focusing on (bio-)pharmaceutical analyses for three years. In 2020 he joined Bayer's Analytical Development department within Chemical and Pharmaceutical Development and is currently heading a dissolution lab within the Drug Product Development department.



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 Discovery 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 Johanna Milsmann
Boehringer Ingelheim Pharma GmbH & Co.
KG, Biberach, Germany

Dr Johanna Milsmann joined the Analytical Development Department at Boehringer Ingelheim in Biberach, Germany, as a Postdoc in 2018. Currently, she is heading a dissolution laboratory at Boehringer Ingelheim in Biberach, which is responsible for the development and validation of QC dissolution methods. In addition, she is leading all biorelevant dissolution activities as well as oversees all dissolution activities concerning novel formulations such as long acting injectables. Prior joining Boehringer Ingelheim she was a Postdoc at Abbvie in Ludwigshafen, Germany, focusing on discriminative dissolution setups for ASD formulations. Johanna studied Food Science and Technology and received her PhD from the University of Kiel.

Date

Wednesday, 27 June 2024, 9.00 h – 18.00 h
(Registration and coffee 8.30 – 9.00 h)
Thursday, 28 June 2024, 8.30 h – 15.30 h

Venue

Barceló Hotel Hamburg
Ferdinandstrasse 15
20095 Hamburg
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Phone: +49 (0) 40 22 63 62 0
hamburg@barcelo.com

Fees (per delegate, plus VAT)

ECA Members € 1,690
APIC Members € 1,790
Non-ECA Members € 1,890
EU GMP Inspectorates € 945

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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For questions regarding reservation, hotel, organisation etc. please contact:
Mr Niklaus Thiel (Organisation Manager) at
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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.

Your Benefits

Internationally Acknowledged Certificate from ECA Academy



The EU GMP Guide requires:

„... All personnel should be aware of the principles of Good Manufacturing Practice that affect them and receive initial and continuing training,...“
This is why you receive an acknowledged participant certificate, which lists the contents of the seminar in detail and with which you document your training.

This Training Course is recognized for the GMP/GDP Certification Scheme „Certified Quality Control Manager“



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GERMANY

Reservation Form (Please complete in full)

Dissolution Testing | 26/27 June 2024, Hamburg, Germany

Title, first name, surname

Department

Company

Important: Please indicate your company's VAT ID Number

Purchase Order Number, if applicable

City

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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:
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Important: This is a binding registration and above fees are due in case of can-

cellation 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 July 2022).

German law shall apply. Court of jurisdiction is Heidelberg.

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