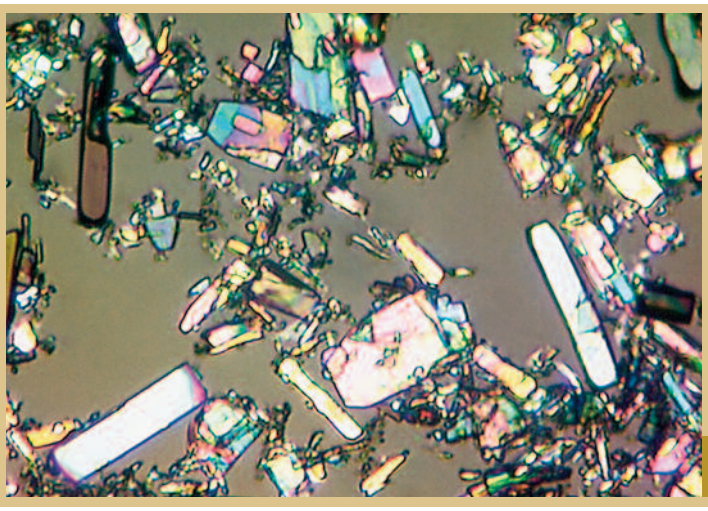
Science based design of formulations and manufacturing processes for oral solid dosage forms – from preformulation to capable commercial processes

APV Expert Workshop: The Preformulation Tool Box: The Key to Enter Successful Drug Development



23 to 24 October 2018
Frankfurt, Germany

Course No. 6740

Hot Topics

Target audience

This seminar is aimed at all pharma professionals engaged in the development and evaluation of drug formulations, in particular in early development phase. The seminar will cover all aspects of this topic starting from the solid state characteristics of drug substances of significance, the basics for the different formulation principles, guidance as to which principle to choose for which type of API, and recent development in the testing and evaluation of formulations with respect to bioavailability. Relevant case studies presented by experts in the field will open up the discussion of connected issues in groups. These group discussions may suggest alternative approaches or strategies and add to the profit for each seminar participant. There is also room to discuss further cases coming from the audience.

APV
MAKING SCIENCE WORK

Hot Topics

A seminar organised by the APV focus group

Objectives

Preformulation is the key to successful drug development.

In the preformulation phase, the physicochemical properties of APIs are characterized, potential liabilities are identified, and step by step various formulation approaches are screened and compared in order to turn Active Pharmaceutical Ingredients (APIs) into drugs which progress into (pre-)clinical programs. This requires a critical set of compound sparing assays that gain information about solid state properties (e.g. crystallinity, melting point, hygroscopicity, polymorphism), solubility (thermodynamic and respectively kinetic), dissolution (intrinsic dissolution and from powder), permeability, and stability (chemical, physical). This sound data package is the basis for the rational choice of formulation principles and for (preclinical) formulation development that takes bioavailability, manufacturability, and potential development risks into account. Formulations considered during the course range from conventional to enabling formulations such as solubility- (e.g. cosolvents, cyclodextrins, lipids)), dissolution- (e.g. salts, amorphous solid dispersions), permeability-enhancing (e.g. Pg-p inhibitors) formulations or formulations stabilizing supersaturated states.

This course covers the "whys" and "hows" of preformulation work and provides guidance for efficient preclinical formulation development.

Organisers

Prof. Dr. Annette Bauer-Brandl, University of Southern Denmark, Odense M
Dr. Christoph Saal, Merck KGaA

Presenters/Contributors

Dr. Jochem Alsenz, Hoffmann-La Roche
Prof. Dr. Martin Brandl, University of Southern Denmark
Prof. Dr. Jennifer Dressman, Universität Frankfurt
Dr. Kerstin Julia Schäfer, Boehringer Ingelheim
Dr. Réne Holm, Janssen R&D
Dr. Jörg Rosenberg, AbbVie

Program

Tuesday, 23 October 2018 10:00 to 18:00

Welcome and organization
Introduction of participants and alignment of expectations
Annette Bauer-Brandl, University of Southern Denmark, Odense M, Denmark
Christoph Saal, Merck KGaA, Darmstadt, Germany

Part 1: Introduction and Overview
Christoph Saal, Merck KGaA, Darmstadt, Germany

Physicochemical Background
- Solubilities of recently approved APIs
- Reasons for poor solubility
- Targets, indications and technologies

Solid State
- Salts, polymorphs, co-crystals
- Solvates and Hydrates
- Solubility improvement: expected extent
- Properties of significance for production and handling

Examples and discussions in groups

Part 2: Improving Solubility
Christoph Saal, Merck KGaA, Darmstadt, Germany

Solubility as the main parameter of evaluation/ optimization
- Definition of kinetic and thermodynamic solubility
- Methods to measure kinetic and thermodynamic solubility
- Connection between solid state and thermodynamic solubility measurement
- Optimization of the solid substance with respect to solubility

Supersaturation – how to reach, how to keep
- Definition of supersaturation
- How can supersaturation be achieved?
- Thermodynamic and kinetic reasoning
- Choice of solid state form and formulation
- Induction of re-crystallization in supersaturated systems
- Crystallization inhibition

Case study and group work
Christoph Saal, Merck KGaA, Darmstadt, Germany

The Preformulation Tool Box: The Key to Enter Successful Drug Development

Part 3: Which formulation for which API?

Formulation principles for poorly soluble drugs
- The main types of enabling formulations
- General rules for choosing enabling formulations

Jochem Alsenz, F. Hoffmann-La Roche Ltd, Basel, Switzerland

Formulations in early development phases
- Formulations for formulation screening
- Preparation of preclinical samples

Jochem Alsenz, F. Hoffmann-La Roche Ltd, Basel, Switzerland

Formulating oral solutions with cyclodextrins
- Types of cyclodextrins and variations of importance
- Physical chemical principles of cyclodextrin work
- How to optimize a cyclodextrin formulation
- Biopharmaceutical consideration using cyclodextrins
- Short overview of the toxicological status of the various types of cyclodextrins

René Holm, The Janssen Pharmaceutical Companies of Johnson & Johnson, Beerse, Belgium

Amorphous solid dispersions (ASD)
- Types
- Screening methods in preformulation settíngs
- Preparation and Characterization
- Limitations / Challenges

Jörg Rosenberg, Abbvie Deutschland GmbH & Co. KG, Ludwigshafen, Germany

Nano-Crystals
- Nanocrystals: why and when?
- Preparation and characterization
- Limitations / Challenges
- Examples
- Biopharmaceutical considerations

Jörg Rosenberg, Abbvie Deutschland GmbH & Co. KG, Ludwigshafen, Germany

Lipid based formulations for oral applications
- Formulation classifications
- Solubility screening and general characterizations
- Formulation design, inducing supersaturation
- Predictive tools (biorelevant media) for selecting the best formulation before clinical studies, in vitro and in vivo

René Holm, The Janssen Pharmaceutical Companies of Johnson & Johnson, Beerse, Belgium

Networking Dinner

We are delighted to invite you to join us for dinner. Come and meet colleagues and specialists in your field from around the world in an enjoyable and relaxed atmosphere.

Wednesday, 24 October 2018 09:00 to 16:30

Silica-based carriers
- Types of Silica carriers
- Examples for manufacturing and characterization
- Use of precipitation inhibitors
- in vivo performance – examples
- Loading capacity as a critical parameter

Christoph Saal, Merck KGaA, Darmstadt, Germany

Preclinical formulation screening in animals
- Species challenges
- Dosing volume and route of administration
- Formulations and excipient effects on drug disposition
- Formulations for parenteral use

Jochem Alsenz, F. Hoffmann-La Roche Ltd, Basel, Switzerland

Specific examples of substances: Which enabling formulation to choose?

Group work and discussion of possible approaches and strategies in groups
Discussion of the cases in plenum
Jochem Alsenz, F. Hoffmann-La Roche Ltd, Basel, Switzerland

Part 4: Testing, evaluation and ranking

Bioavailability of enabling formulations
- A retrospective overview and summary
- Comparison of in vivo performance of oral enabling formulations
- Comparison of bioavailability enhancement and predictability thereof

Annette Bauer-Brandl, University of Southern Denmark, Odense, Denmark

Dissolution
- Biorelevant media – the Levels pyramid
- Validation of Biorelevant testing – ring studies
- The OrBiTo Decision Tree for selecting the right test
- Case example – weak bases

Jennifer Dressman, Johann Wolfgang Goethe-Universität, Frankfurt, Germany

The Preformulation Tool Box: The Key to Enter Successful Drug Development

In vitro permeation / absorption: the basics
- Basic principles of permeation and absorption
- Approaches in drug discovery and drug development
- Permeability screening

Martin Brandl, University of Southern Denmark, Odense, Denmark

Case studies and group work:
Comparison of in vitro characteristics to in vivo performance (conventional tools)
Martin Brandl, University of Southern Denmark, Odense, Denmark

Discussion in plenum

Prediction of bioavailability
- Permeation of the API from formulations
- The role of colloidal states for permeation
- Effect of biomimetic media
- Dissolution / permeation interplay

Martin Brandl, University of Southern Denmark, Odense, Denmark

Innovative Experimental Approaches for Prediction & Ranking

Dissolution models with a sink
- Biphasic dissolution for biopharmaceutical analysis in early formulation development
- Model overview
- When are biphasic dissolution models useful?
- Analysis of output parameters

Kerstin Schäfer, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany

Dissolution / permeation between compartments separated by artificial barriers
- Functional properties of the optimum barrier
- Diffusion vs. permeation
- The role of sampling on output parameters
- Experimental approaches; minitiaturized models

Annette Bauer-Brandl, University of Southern Denmark, Odense, Denmark

Tools and Ranking
- Prediction and predictability of formulation performance using miniaturized models: current developments and outlook

Martin Brandl, University of Southern Denmark, Odense, Denmark

Case studies and group work:
Comparison of in vitro characteristics to in vivo performance
(similar cases – novel tools)

Discussion and wrap-up

Program is subject to change

Registration by fax +49 6131 9769-69

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Location

Best Western Premier IB Hotel
Friedberger Warte
Homburger Landstraße 4
60389 Frankfur am Main
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Fax: +49 69 76 80 64 555
email:
info@ibhotel-frankfurt.bestwestern.de

I herewith repealable authorise APV to use my E-mail address to send me APV relevant material including current program information. My acceptance can be cancelled at any time in writing.

Date

Preformulation Toolbox
Course no. 6740
from 23 October 2018 10:00
to 24 October 2018 16:30

Registration fee

Course no. 6740

Industry	1490 EUR
Authorities/Academia	745 EUR
Students*	178 EUR

(free of VAT according to § 4,22 UStG)
Coffee breaks, lunches, dinner and electronic proceedings included.

*Limited places for full time students available; written evidence must be submitted.

Registration

APV-Geschäftsstelle
Kurfürstenstraße 59
55118 Mainz/Germany
Phone: +49 6131 9769-0
Fax: +49 6131 9769-69
e-mail: apv@apv-mainz.de

You will receive a confirmation of your registration with the invoice.

Hotel reservation

Best Western Premier IB Hotel
Friedberger Warte
Homburger Landstraße 4
60389 Frankfur am Main
Phone: +49 69 76 80 64 0
Fax: +49 69 76 80 64 555
email:
info@ibhotel-frankfurt.bestwestern.de

Participants should make their own hotel reservation referring to the APV seminar.

Deadline for special conference rate: 21 September 2018.

Special rate:
Single room incl. breakfast buffet from 129 EUR per night.

Mainz, May 2018

APV Expert Workshop: The Preformulation Toolbox, 23 to 24 October 2018, Frankfurt/Main, Course no. 6740

Registration
As soon as you have found a seminar of your interest, it is very easy to register for it via fax, e-mail or online. We will process your registration promptly and certainly are available for any questions that may arise.

Registration confirmation
After your registration was successfully processed, you will receive a confirmation.

Before the event
A few days before the event starts, you will receive important information about the seminar, such as time, date, addresses etc.

After the event
You will receive a certificate confirming your participation. Furthermore, we would like to ask you to fill-in our evaluation sheet to make sure we get better every time.

Follow-up
After the event, we are open to receive any suggestions and critique that might arise during the seminar and will certainly help you with further questions you may have.

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