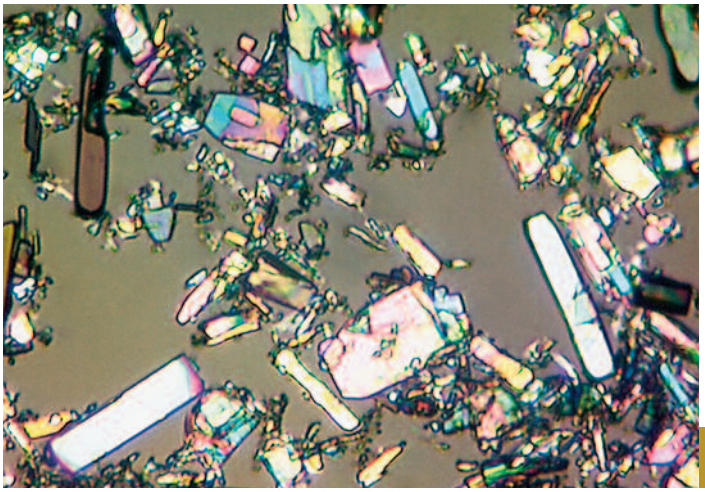
Science based design of formulations and manufacturing processes for oral solid dosage forms – from preformulation to capable commercial processes

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



08 to 09 May 2017
Berlin, Germany

Course No. 6692

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 participant. There is also room to discuss further cases coming from the audience.

APV
MAKING SCIENCE WORK

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 pakkage 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.

Program

Monday, 08 May 2017 10:00 to 19:15

Welcome and organization
Introduction of participants and alignment of expectations
Annette Bauer-Brandl
Department of Physics Chemistry and Pharmacy
University of Southern Denmark, Odense M, Denmark
Christoph Saal
Director Site Operations I Analytics
Merck KGaA, Darmstadt, Germany

Part 1: Introduction and Overview

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

Christoph Saal

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

Christoph Saal

Examples and discussions in group work

Part 2: Improving Solubility

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

Christoph Saal

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

Christoph Saal

Solubilization – the basics
- Biomemetic and biorelevant media
- BCS / DCS scheme
- intrinsic dissolution; intrinsic dissolution rate
- Case study

Christoph Saal

Case study and group work

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
Expert Scientist, Preformulation – Pre-Clinical CMC
F. Hoffmann-La Roche Ltd, Basel, Switzerland

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

Jochem Alsenz

Amorphous solid dispersions
- Types
- Examples for manufacturing
- Characterization
- in vivo performance-examples
- Loading capacity as a critical parameter

Jochem Alsenz

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

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 toxilogical status of the various types of cyclodextrins

Réne Holm
Head and Scientific Director, Liquids & Parenterals
The Janssen Pharmaceutical Companies of Johnson & Johnson, Beerse, Belgium

Amorphous solid dispersions (ASD)
- Types
- Screening methods for ASD
- Manufacturing and characterization of ASD
- Limitations/challenges of ASD

Bernard Van Eerdenbrugh
Novartis Pharma AG, Switzerland

Milling
- Micronization / nanomilling
- Nanomilling: why and when?
- Preparation and characterization of anosuspensions
- Limitations/challenges of nanosuspensions
- Examples
- Biopharmaceutical considerations

Bernhard Van Eerdenbrugh

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

Réne Holm

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

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.

Tuesday, 09 May 2017 08:30 to 16:45

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

Specific examples of substances:
- Which enabling formulation to choose?
- Discussion of possible approaches and strategies in group work
- Discussion of the cases in plenum

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

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

Martin Brandl
Department of Physics Chemistry and Pharmacy
University of Southern Denmark, Odense M, Denmark

Case studies: Comparison of in vitro characteristics to in vivo performance (conventional tools) in group work

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

Conventional dissolution testing
- Capabilities and restrictions

Annette Baur-Brandl

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

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
- Case studies
Kerstin Julia Frank
Boehringer Ingelheim Pharma GmbH & Co. KG,
Biberach/Riss, 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

Tools and Ranking
• Prediction and predictability of formulation performance using miniaturized models
Martin Brandl

Case studies: 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

MAKING SCIENCE WORK

Location

Holiday Inn Berlin City-East
Landsberger Allee 203
13055 Berlin
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Phone: +49 30 97808-0
Fax: +49 30 298988-399
email: info@hibce.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. 6692
from 08 May 2017 10:00
to 09 May 2017 16:45

Registration fee

Course no. 6692
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

Holiday Inn Berlin City-East
Landsberger Allee 203
13055 Berlin
Germany
Phone: +49 30 97808-0
Fax: +49 30 298988-399
email: info@hibce.de

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

Deadline for special conference rate: 27 March 2017.

Special rate:
Single room incl. breakfast buffet from 85 EUR per night.

Mainz, February 2017

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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