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Concepts & Solutions in Drug Development

DDI 2012

3rd International Workshop on Regulatory Requirements and Current Scientific Aspects on the Preclinical and Clinical Investigation of Drug-Drug Interactions

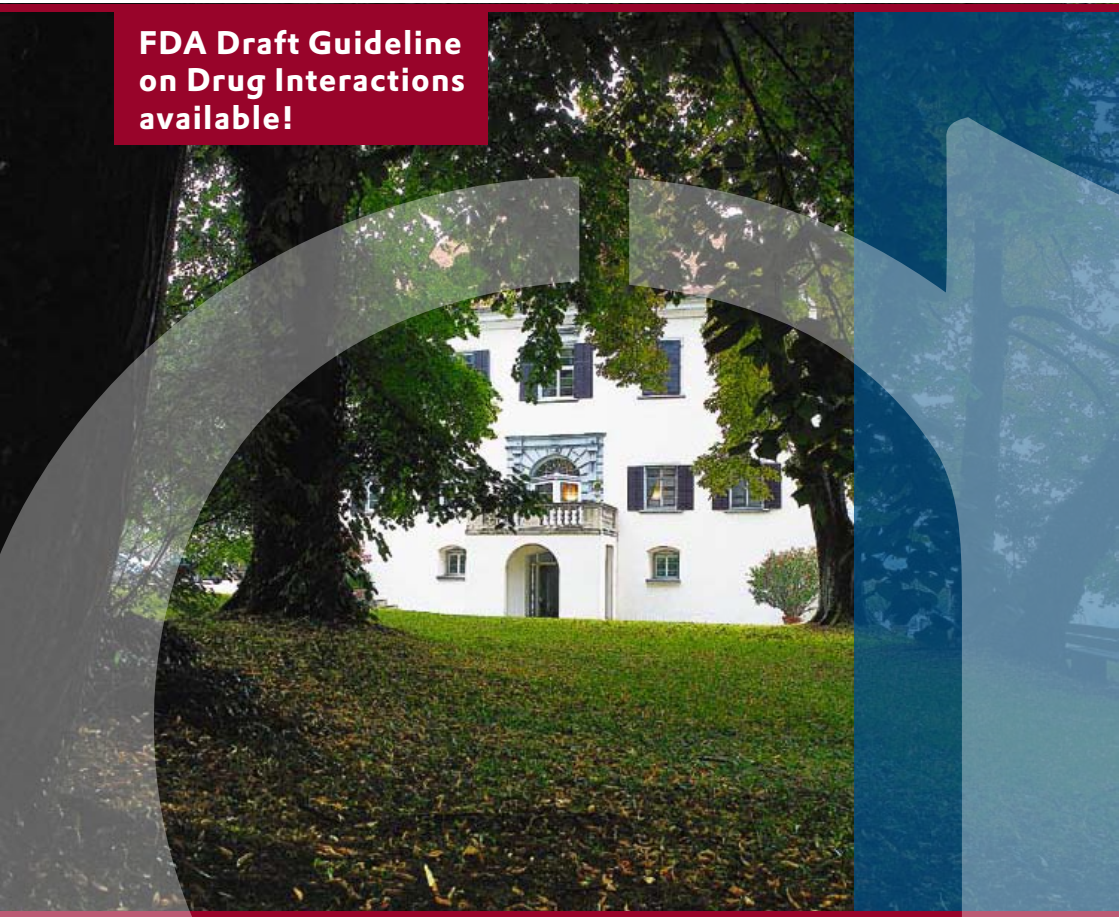
ACCP
American College of Clinical Pharmacology
Advancing Clinical Care through Pharmacology

member of BioLAGO life science network

DM d9 DRUG METABOLISM discussion group

May 06th to 08th, 2012
Marbach Castle, Germany

FDA Draft Guideline on Drug Interactions available!



Final Announcement

MISSION STATEMENT

The overall objective of the International Marbach Castle DDI Workshop series is to improve and disseminate the scientific knowledge about drug-drug interactions (incl. food-drug and herb-drug interactions), to foster their proper preclinical and clinical investigation and communication, thereby improving the safe use of drugs in the light of ageing populations, complex patients with various co-morbidities and increasing poly-pharmacotherapy.

BACKGROUND, SCOPE AND AIM

In May/June 2010 the 1st International Workshop on Regulatory Requirements and Current Scientific Aspects on the Preclinical and Clinical Investigation of Drug-Drug Interactions was held based on the initiative of a group of international scientists and experts in the field from academia and industry. The event was triggered by the notion that the area of drug-drug interactions (DDIs) is getting increasingly important and complex in view of continuously emerging new therapies, complex treatment algorithms for many widespread disease states and ageing populations in the industrialized countries. These factors converge into a frequently employed poly-pharmacotherapy with increasing risk for growing incidences of clinically significant DDIs. Therefore, the meticulous investigation, informative labeling, and early recognition of DDIs represent substantial challenges for the pharmaceutical industry and regulatory bodies in the development, approval and post-marketing surveillance of new medicines. Failures in the early recognition, mechanistic elucidation (understanding) and proper management of DDIs, in turn, have resulted in numerous drug withdrawals from the market in the past and continue to result in a significant health burden to patients, rendering many DDIs serious public safety concerns.

Today, DDIs can be addressed in a more targeted and evidence-based fashion, because considerable progress has been made in the understanding of the underlying mechanisms of DDIs and the subsequent development of methodologies for the investigation of DDI susceptibility, and the extrapolation of outcomes of particular DDIs to other drug combinations. However, apart from metabolism based DDI, transporter based DDIs as well as tools extrapolating *in vitro* results to predict clinical outcomes *in vivo* (IVIVE) have gained more importance over the recent years. Furthermore, pharmacodynamic DDIs have gained increasing interest given the steady increase in drug combination in clinical development.

The 2010 Workshop combined a regulatory update on the investigation of DDIs from the European Rapporteur perspective (MPA, Sweden) along with a scientific update focusing on the investigation of metabolism- and transporter-based DDIs. The 2011 workshop focused on large molecule DDIs, non-metabolic DDIs affecting drug absorption as well as complex DDIs in selected therapeutic areas such as oncology, cardiovascular disorders, as well as immunosuppressant and anti-infective therapies. Around 70 experts (maximum capacity of the venue) from pharmaceutical industry, contract research organizations and drug regulatory agencies from more than 10 European countries and the United States participated in each of the two events. Based on the detailed feedback received from the expert audience on additional areas of interest requiring future consideration, the structure and content of this Workshop were designed. The topics of the 3rd International DDI Workshop meeting will be covered by distinguished international scientists and experts from academia, pharmaceutical companies, contract research organizations, consultancies and regulators. The program will provide a unique opportunity for scientific exchange and networking across company and organizational boarders, and to learning about the current state-of-the-art in the investigation of DDIs.

The organisers:
Hartmut Derendorf PhD, FCP
Robert Hermann MD, FCP
Amin Rostami-Hodjegan PharmD PhD, FCP
Oliver von Richter PhD, FCP

BENEFITS IN ATTENDING

- **Focus** on the latest regulatory aspects and scientific challenges of DDIs related to metabolism and transporter mediated disposition
- **Update yourself** about the current European- and US-perspectives on the regulatory requirements in the *in vitro* and *in vivo* investigation of DDIs
- **Discover** the commonalities and differences between regulatory US- and EU-requirements
- **Inform** yourself about designs, outcomes and implications of the latest DDI trials
- **Enhance** your knowledge about *in vitro* approaches in the assessment of transporter related DDIs by receiving the latest update from PhRMA
- **Realize** important aspects linked to transporter-related DDIs of hepatic uptake and elimination
- **Take time** to reflect about the *in vitro* challenges as well as clinical and strategic impact of drug-drug interactions mediated by UDP-glucuronosyltransferases (UGTs)
- **Learn more** about complex DDIs involving the combined interplay of drug metabolism and transport processes
- **Understand** how mechanistic PBPK modeling can aid in the investigation of transporter mediated DDIs
- **Gain** insights into labeling and post-marketing communications of DDIs
- **Learn about** DDIs based on changes in plasma protein binding and how these are assessed
- **Get informed** on the role of pharmacodynamic DDIs, how they are clinically studied and which modeling & simulation approaches are required to analyze them
- **Find out** how ABCB1 (P-gp) mediated DDIs affecting drug absorption are comprehensively characterized in modern drug development
- **Meet, discuss and network** with scientific and regulatory experts from Pharma and CROs, international regulatory bodies, the International Transporter Consortium and academia

WORKSHOP PROGRAMME

May 6th, 2012

Sunday

Afternoon	Individual Arrival & Check-in at Marbach Castle
03:00 p.m.	Registration & Coffee
04:00 p.m.	Come Together Activities
08:00 p.m.	Come Together Dinner

May 7th, 2012

Monday

08:00 – 09:00 a.m.	Registration & Coffee
09:00 – 09:10 a.m.	Workshop Introduction and Update on Emerging Clinical DDIs 2011/2012 *Robert Hermann, MD, FCP; cr.appliance, Germany*
	Session I (Chair: Hartmut Derendorf): Regulatory Session
09:10 – 09:55 a.m.	The European Guideline on the Investigation of Drug Interactions *Eva Gil Berglund, PhD; Medical Product Agency (MPA), Sweden*
09:55 – 10:10 a.m.	Discussion
10:10 – 10:40 a.m.	Coffee Break
10:40 – 11:25 a.m.	Recent Changes in the FDA's View on the Investigation of Drug Interactions *Larry Lesko, PhD, FCP; University of Florida College of Pharmacy at Lake Nona (Orlando), USA*
11:25 – 11:40 a.m.	Discussion
11:40 a.m. – 12:05 p.m.	Predicting Drug Interaction Potential by Physiologically-Based Pharmacokinetic Models *Manuela Vieira, College of Pharmacy, University of Florida, USA*
12:05 – 12:15 p.m.	Discussion
12:15 – 01:45 p.m.	Lunch

Session I:
Regulatory Session (ctd.)

01:45 – 02:15 p.m.	Getting It Right: Communicating DDI Information in Product Labeling *Helen Winter, PhD, School of Pharmacy, University of Otago, New Zealand*
02:15 – 02:25 a.m.	Discussion
02:25 – 03:30 p.m.	Q & A Session and Plenary Discussion of all Regulatory Talks *Eva Gil Berglund, PhD; Medical Product Agency (MPA), Sweden; Larry Lesko, PhD, FCP; University of Florida College of Pharmacy at Lake Nona (Orlando), USA; Manuela Vieira, College of Pharmacy, University of Florida, USA; Helen Winter, PhD, School of Pharmacy, University of Otago, New Zealand*

Session II (Chair: Amin Rostami-Hodjegan):
UGT-Based DDIs

03:30 – 04:15 p.m.	*In vitro* Assessment of DDIs Mediated by UDP-Glucuronosyltransferases (UGTs): Many Differences to Cytochrome P450s *Andrew Parkinson, PhD; University of Kansas Medical Center, Kansas, USA*
04:15 – 04:25 p.m.	Discussion
04:25 – 04:50 p.m.	Coffee Break
04:50 – 05:30 p.m.	Clinical DDIs Involving UGT-Mediated Metabolism and Disposition of Formed Glucuronides *Robert Hermann, MD, FCP; cr.appliance, Germany*
05:30 – 05:40 p.m.	Discussion

Session III (Chair: Amin Rostami-Hodjegan):
Non-Metabolic / Non-Transport DDIs

05:40 – 06:20 p.m.	Changes in Plasma Protein Binding: A Neglected Mechanism Causing Clinically Relevant DDIs? *Oliver von Richter, PhD, FCP, MerckSerono, Germany*
06:20 – 06:30 p.m.	Discussion
07:30 p.m.	Dinner
08:45 p.m.	Acoustic Guitar Concert – Simon Wahl (fingerstyle guitar)

May 8th, 2012

Tuesday

07:00 – 08:30 a.m.	Breakfast
	Session IV (Chair: Oliver von Richter): Transporter-Based DDIs
08:30 – 09:15 a.m.	The Role of Hepatocellular Efflux Pumps for Drug Interactions. *Dietrich Keppler, MD, German Cancer Research Center (DKFZ), Heidelberg, Germany*
09:15 – 09:25 a.m.	Discussion
09:25 – 10:10 a.m.	The Role of Hepatic Uptake Transporters for DDIs: Linking Hepatic Uptake with Hepatic Metabolism *Mikko Niemi, MD, University of Helsinki, Finland*
10:10 – 10:20 a.m.	Discussion
10:20 – 10:50 a.m.	Coffee Break
10:50 – 11:20 a.m.	Theory and Practice of Determining DDI Potential at Transporter Level *Caroline Lee, PhD on behalf of the PhRMA ABCB1 IC50 consortium, USA*
11:20 – 11:30 a.m.	Discussion
11:30 a.m. – 01:00 p.m.	Lunch

Session IV (Chair: Oliver von Richter): Transporter-Based DDIs (ctd.)

01:00 – 01:40 p.m.	IVIVE of Transporter Related DDIs: A Problem-Based Stepwise Guide *Amin Rostami-Hodjegan, PharmD, PhD, FCP; Faculty of Medical and Human Sciences University of Manchester, UK*
01:40 – 01:50 p.m.	Discussion
01:50 – 02:20 p.m.	Characterisation of P-gp (ABCB1)-Based Absorption Interactions of Dabigatran Etexilate: Clinical Trial Design and Labeling Considerations *Sebastian Härtter, PhD Boehringer Ingelheim Pharma GmbH, Germany*
02:20 – 02:30 p.m.	Discussion
02:30 – 03:00 p.m.	Coffee Break

Session V (Chair: Robert Hermann): Pharmacodynamic DDIs

03:00 – 03:45 p.m.	Evaluation of Pharmacodynamic Drug Interactions. *Hartmut Derendorf, PhD, FCP; College of Pharmacy, University of Florida, USA*
03:45 – 03:55 p.m.	Discussion
03:55 – 04:50 p.m.	Ask the Expert Forum Discussion *Final Q&A Session: Ample Opportunity for Workshop Participants to Address Questions to the Speakers of the Meeting.*
04:50 – 05:00 p.m.	Concluding Remarks *Robert Hermann, MD, FCP; cr.appliance, Germany*
05:00 p.m.	End of Meeting & Individual Departure

WHO SHOULD ATTEND?

This international Workshop on drug-drug interactions is designed to meet the requirements and expectations of professionals from the pharmaceutical industry, contract research organisations, regulatory agencies and academia.

Department heads, project managers, scientists and consultants in R&D, in regulatory affairs, pharmacokinetics, clinical pharmacology, exploratory / translational medicine, clinical development, biostatistics, business development, medical communications and so forth should attend. All delegates are invited to contribute actively to the scientific discussions.

LANGUAGE

English will be the language of the Workshop. No simultaneous translation will be provided.

VENUE & LOCATION

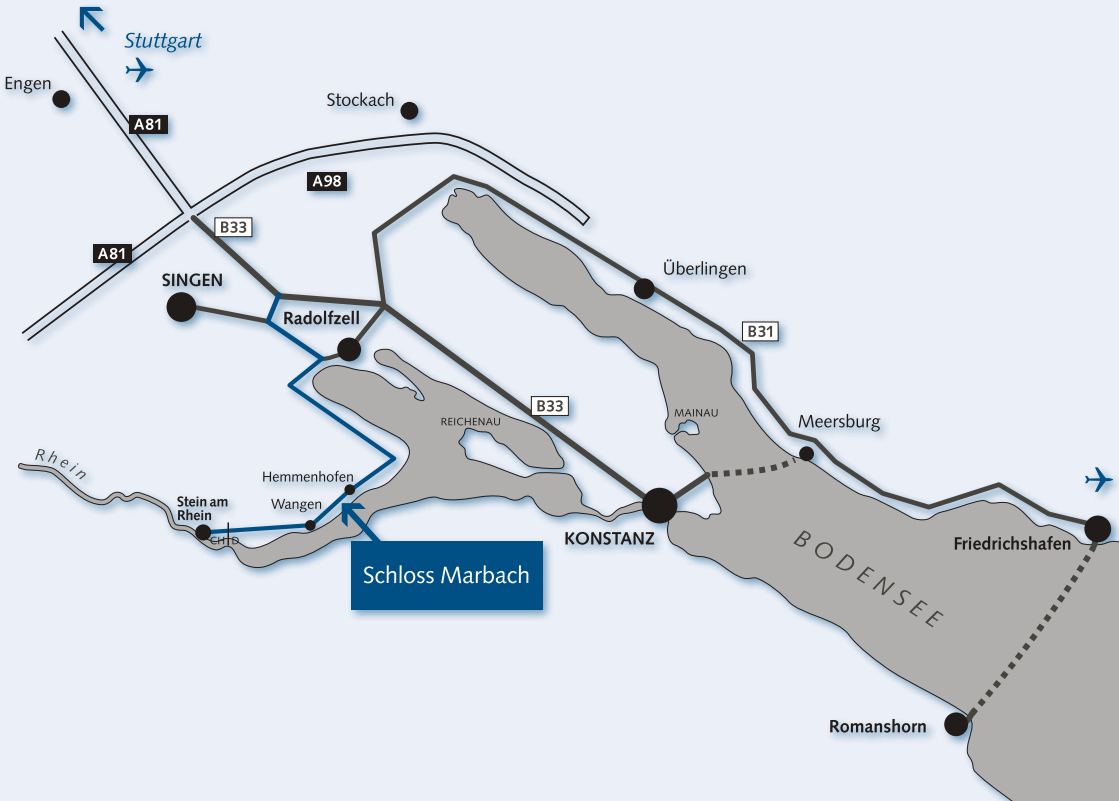
The Workshop will take place at the Marbach Castle Conference Centre (see the following web site: www.schlossmarbach.de), located close to the Swiss border amidst the beautiful surrounding of the Western shore of Lake Constance in close proximity to the historic town of Stein am Rhein. The old town centre of Stein am Rhein is characterised by striking medieval buildings such as the City Church, the former Monastery of St. Georgen, burghers' houses, gates and towers, as well as buildings dating from the early modern age, including the Town Hall and the Arsenal.

Marbach Castle is within easy reach of the major cities in the area (Zurich, Basel, Stuttgart). The distance to Zurich International Airport is about 60 kilometres. Taxi from and to the Airport is approx. 90 Euros. Airport taxi shuttles for Workshop attendees can be organised upon request. If driving, please find detailed itinerary descriptions posted under the Contact / Travelling item of the Marbach Castle web site.

REGISTRATION INFORMATION

Date	Workshop May, 6th to 8th, 2012	
Venue	Marbach Castle D-78337 Öhningen	+49 (0)7735 – 8130 info@schlossmarbach.de
Times	May 6th 2012 Afternoon: individual arrival, come together activities, come together dinner May 7th 2012 Start 09:00 a.m. – Finish 06:30 p.m. May 8th 2012 Start 08:30 a.m. – Finish 05:00 p.m.	
Registration & Coffee	May 6th 2012 – 03:00 p.m. May 7th 2012 08:00 a.m.	

MAP



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Registration Form

Please print your details

Title _____ First name _____

Family name _____

Position _____

Department _____

Company _____

Address _____

City _____ Post Code _____

Country _____

Phone _____ Fax _____

E-mail _____

Date _____ Signature _____

You may register by:

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For further information please contact Karen Grave-Hermann
Phone: +49 (0)7732-820 951

Cancellation Policy

- Over 30 days prior to the Seminar: Cancellation fee of 150,00 €.
- 14 – 29 days prior to the Seminar: 50 % of the fee.
- Fewer than 14 days or if no notification received: Registrant liable to pay FULL seminar fee.

NB: Cancellation must be addressed in writing to karen.grave-hermann@cr-appliance.com

In the event circumstances beyond control, cr.appliance reserves the right to alter the programme, the speakers, the date or the venue.

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Workshop Fee (incl. Lunch, Dinner & Coffee Breaks, incl. 19 % VAT)

Please tick

Participation from May 6th to 8th, 2012	1.790,00 €	☐
Participation from May 6th to 8th, 2012 members of ACCP, DMDG, or BioLago	1.690,00 €	☐
Participation on May 7th and 8th, 2012 only	1.690,00 €	☐
Participation on May 7th and 8th, 2012 only, in combination with membership of ACCP, DMDG, or BioLago	1.590,00 €	☐

Accommodation (incl. Breakfast and 19 % VAT)

A limited number of bedrooms are available at Marbach Castle (further Hotel capacities in close proximity available upon request):		1 night	2 nights
Category A:	single room (170,00 € per night)	☐	☐ (= 340 €)
	double room (210,00 € per night)	☐	☐ (= 420 €)
Category B:	single room (117,00 € per night)	☐	☐ (= 234 €)
	double room (157,00 € per night)	☐	☐ (= 314 €)
No Hotel accommodation required:			☐

Application to Register

To ensure the personal workshop character of the event and to provide maximum knowledge transfer benefits for the attendees, the overall number of participants is limited. Workshop participation will be assigned in the sequence of receipt of registration applications. Full confirmation of registration will occur by receipt of the Workshop fees.

Discounted Rates

Discounted rates may be granted for a limited number of participants on individual application for students, personnel from non-profit organizations and registered charities.