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Concepts & Solutions in Drug Development

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AMERICAN COLLEGE OF CLINICAL PHARMACOLOGY

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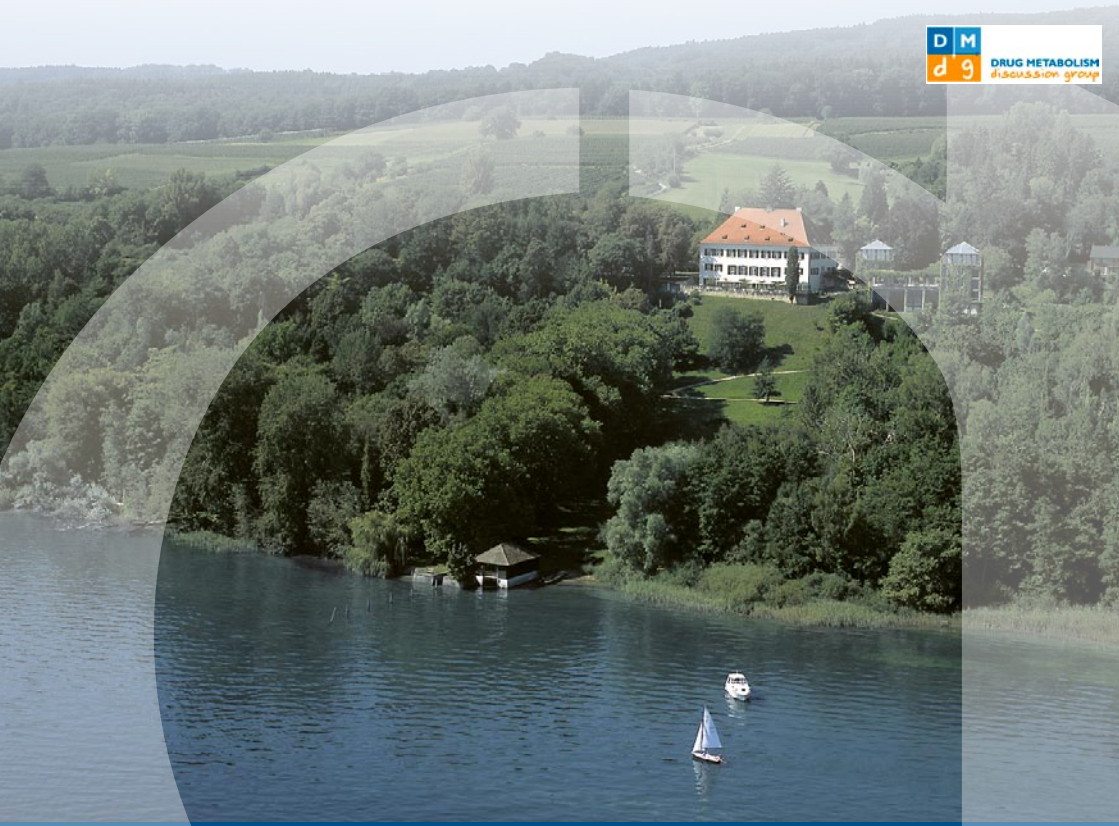
DM d9 DRUG METABOLISM discussion group

New Regulatory Requirements and Current Scientific Aspects on the Preclinical and Clinical Investigation of Drug-Drug Interactions

May 30th to June 01st, 2010
Marbach Castle, Germany



Final Announcement

SCOPE AND AIM

The present **European Note for Guidance on the Investigation of Drug Interactions** (CPMP / EWP / 560 / 95) by the European Agency for the Evaluation of Medicinal Products (EMEA) was issued more than a decade ago in December 1997. Over the last years, however, considerable progress has been gained about underlying mechanisms of drug-drug interactions (DDIs) and the applied methodologies for the investigation of DDI susceptibility, and the extrapolation of outcomes to other drug combinations. To integrate and transfer current scientific evidence into regulatory guidance and drug development practice, the DDI Note for Guidance document has been recently subjected to revision by the European Medicines Agency (EMA) to update several areas. A draft of the revised „Guideline on the Investigation of Drug Interactions" (EMA/CHMP/EWP/125211/2010) has been released on April 22, 2010 for public consultation.

The Workshop event will combine a regulatory update on the investigation of DDIs along with a scientific update on the investigation of DDIs. Four sessions comprising a "regulatory update", "metabolic drug-drug interactions (mDDI)", "non-metabolic DDIs & PGx of DDIs", and "tools in design & evaluation of DDI-trials for better timing of DDI-trials in course of clinical development" will address the latest knowledge and strategies in this key area of drug development. Commonalities and differences between US and EU regulatory requirements in conducting DDI studies will also be addressed.

The topics will be covered by international experts from European regulatory authorities, pharmaceutical companies / consultancies and academia. The program will provide a unique opportunity to learn about the European perspective on the investigation of DDIs and to gain a better understanding on "which studies are needed when?", and "how these should be performed / interpreted?"

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 upcoming 2010 revision of the EMEA Guideline on the investigation of drug interactions
- **Learn and discuss** regulatory requirements for *In Vitro* and *In Vivo* drug-drug interaction (DDI) studies in Europe
- **Hear** the current US-perspective on the investigation of DDIs
- **Discover** the commonalities and differences between regulatory US- and EU-requirements
- **Understand** the usefulness and application of "Cocktail Studies" for the investigation and prediction of *In Vivo* DDI potential
- **Gain** a thorough understanding of type of *In Vitro* data and models which are useful for mechanistic prediction of metabolism-based DDIs
- **Understand** the knowledge base required for designing the most appropriate clinical DDI studies and good decision making
- **Update yourself** the clinical relevance of transporter-based DDIs and the difficulties in predicting these from *In Vitro* data
- **Learn more** about the complexity of DDIs involving plasma protein binding
- **Consider** pharmacogenetic aspects and implications for DDI trial designs
- **Inform** yourself about useful tools in designing and evaluating DDI trials
- **Optimize** the timing of DDI studies to manage risks and resources in development
- **Meet, discuss and network** with scientific and regulatory experts from Pharma- and CRO-industries, international regulatory bodies, and academia

FINAL WORKSHOP PROGRAMME

May 30th, 2010

Sunday

Afternoon	Individual Arrival & Check-in at Marbach Castle
04:00 p.m.	Registration & Coffee
05:00 – 07:30 p.m.	Come Together Lake Constance Boat – Ride
08:00 p.m.	Come Together Dinner

May 31st, 2010

Monday

08:00 – 09:00 a.m.	Registration & Coffee
	Session I: Clinical & Regulatory Update on the Investigation of Drug Interactions
09:00 – 09:10 a.m.	Welcome & Introduction to the Workshop Robert Hermann, MD, FCP; cr.appliance, Germany
09:10 – 09:50 a.m.	The Burden of Drug-Drug Interactions: The Clinical Perspective. *Robert Hermann, MD, FCP; cr.appliance, Germany*
09:50 – 10:30 a.m.	The European Note for Guidance on the Investigation of Drug Interactions: What is New in the 2010 Revision? *Eva Gil Berglund, PhD; Medical Product Agency (MPA), Sweden*
10:30 – 10:45 a.m.	Initial Open forum Discussion on EMEA DDI GL Aspects
10:45 – 11:15 a.m.	Coffee Break & Collection of Written Questions from the Audience
11:15 – 12:00 a.m.	Drug Interaction Issues Addressed in the 2009 EMEA Q&A Document of the EWP-PK Subgroup: Cocktail Studies for Investigating and Predicting *In Vivo* Drug Interaction Potential. *Uwe Fuhr, MD; Clinical Pharmacology, University of Cologne, Germany*
12:00 – 12:30 p.m.	Concluding Open Forum Discussion on EMEA DDI GL Aspects
12:30 – 02:00 p.m.	Lunch

May 31st, 2010

Session II: Clinical & Regulatory Update on the Investigation of Drug Interactions

02:00 – 02:45 p.m.	The US-Perspective on Drug-Drug Interactions: Commonalities and Differences between Regulatory US- and EU- Requirements. *Hartmut Derendorf, PhD, FCP; College of Pharmacy, University of Florida, USA*
02:45 – 03:30 p.m.	Break-out Sessions into Four Groups. Group-Discussions of Most Common Issues in Assessing the Need for DDI-Studies: Design, Timing, Conduct and Evaluation in the Light of Current Guidelines. *Group Moderators: Amin, Hartmut, Oliver, Robert* (Note: Coffee will be available during the break-out sessions. Therefore no extra coffee break scheduled.)
03:30 – 04:10 p.m.	Summary Reports from Each Group. *1 – 2 Rapporteurs from each Group, 10 Minutes per Group*

Session III: Scientific Update on the Investigation of DDIs. Metabolic drug-drug interactions (mDDI)

04:15 – 05:00 p.m.	Metabolism Based DDIs: Requirements for Good Decision Making – *In Vitro* Data and Models. *Amin Rostami-Hodjegan, PharmD, PhD, FCP; Faculty of Medical and Human Sciences, University of Manchester, UK.*
05:00 – 05:15 p.m.	Discussion
05:15 – 06:00 p.m.	Metabolism Based DDIs: Practical *In Vitro – In Vivo* Extrapolation Approaches (IVIVE) – Common Pitfalls and Determinants of Successful Data Integration. *Amin Rostami-Hodjegan, PharmD, PhD, FCP; Faculty of Medical and Human Sciences, University of Manchester, UK.*
06:00 – 06:15 p.m.	Discussion & Conclusion of Meeting Day 1 Scientific Programme
07:00 p.m.	Dinner
08:30 p.m.	Making Blues in Concert *Ignaz Netzer; vocal, guitar, harp and Albert Koch; vocal harp*

Tuesday

June 01st, 2010

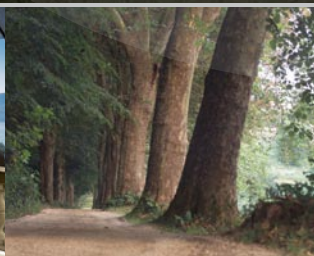
Session III ctd. and Session IV: Scientific Update on the Investigation of DDIs (ctd.). Non-Metabolic Drug-Drug Interactions & PGx of DDIs

07:00 – 08:30 a.m.	Breakfast
08:30 – 09:00 a.m.	System-dependent inhibition – When should CYP inhibition studies be conducted in hepatocytes? *Andrew Parkinson, PhD; CSO XenoTech LLC, Lenaxa, Kansas, USA*
09:00 – 09:45 a.m.	Transporter Based DDIs (trDDI) – Evidence For and Against Clinical Importance of trDDI. *Oliver von Richter, PhD, FCP; Dept. Exploratory Medicine, Merck Serono, Germany*
09:45 – 10:00 a.m.	Discussion
10:00 – 10:30 a.m.	Transporter Based DDIs (trDDI) – Prediction from *In Vitro* Information and Current Regulatory Requirements: Are We There Yet? *Oliver von Richter, PhD, FCP; Dept. Exploratory Medicine, Merck Serono, Germany*
10:30 – 10:40 a.m.	Discussion
10:40 – 11:00 a.m.	Coffee Break
11:00 – 11:45 a.m.	DDIs Involving Plasma Protein Binding: Complexity of Deciphering Multiple Effects. *Hartmut Derendorf, PhD, FCP; College of Pharmacy, University of Florida, USA*
11:45 – 11:55 a.m.	Discussion
11:55 – 12:35 a.m.	Pharmacogenetic Aspects and Inter-Subject Variability of DDIs, and Implications for Designing DDI Trials. *Isabelle Ragueneau-Majlessi, MD; Dept. of Pharmaceutics, University of Washington, USA*
12:35 – 12:45 p.m.	Discussion
12:45 – 02:00 p.m.	Lunch

June 01st, 2010

Session V:
Scientific Update on the Investigation of DDIs (ctd.). Tools in Design & Evaluation of DDI Trials; Timing of Clinical DDI Trials

02:00 – 02:30 p.m.	Useful Tools in Designing and Evaluating DDI Trials: The University of Washington Metabolism & Transport DDI Database (DiDB). *Isabelle Ragueneau-Majlessi, MD; Dept. of Pharmaceutics, University of Washington, USA*
02:30 – 02:40 p.m.	Discussion
02:40 – 03:40 p.m.	Useful Tools in Designing and Evaluating DDI Trials: Automated Prediction of DDIs and Related Inter-Subject Variabilities: Introduction to Simcyp™ Population Based ADME Predictor. *Amin Rostami-Hodjegan, PharmD, PhD, FCP; Faculty of Medical and Human Sciences University of Manchester, UK.*
03:40 – 03:50 p.m.	Discussion
03:50 – 04:15 p.m.	Coffee Break
04:15 – 04:50 p.m.	Implementation of DDI Trials into Clinical Development Programs: Timing of DDI Studies to Manage Risks and Resources, and Optimize Timelines in Development. *Robert Hermann, MD, FCP; cr.appliance, Germany*
04:50 – 05:00 p.m.	Discussion
05:00 – 05:15 p.m.	Concluding Remarks and Wrap-up of the Meeting *Hartmut, Amin, Oliver, Robert*
05:15 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 research based and generic industry, CROs, regulatory agencies and academia.
Department heads, project managers, scientists and consultants in R&D, in regulatory affairs, pharmacokinetics, clinical pharmacology, exploratory 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

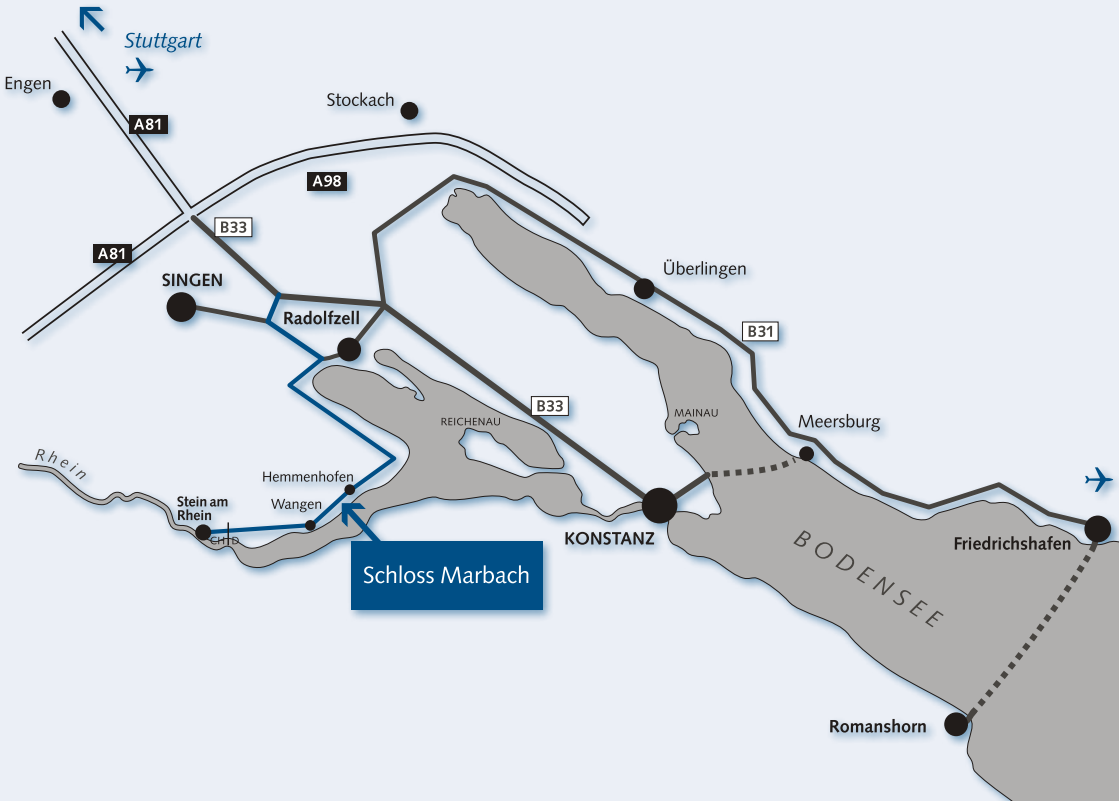
The Workshop will take place at the Marbach Castle Conference Centre (see the following web site: www.schlossmarbach.de), located close to the Swiss border on the beautiful surrounding of the Western shore of Lake Constance in close proximity to the historic town of Stein am Rhein. The old town centre of Stein am Rhein is characterised by striking medival 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, Constance, Freiburg). The distance from the Zurich International Airport Airport is about 60 kilometres. Taxi from and to the Airport is approx. 80 Euros. Airport taxi shuttles for Workshop attendees can be organised upon request. If driving, please find detailed itinerary descriptions posted under the Contact / Travelling menue of the Marbach Castle web site.

REGISTRATION INFORMATION

Date	Workshop May 30th to June 01st, 2010
Venue	Marbach Castle, D-78337 Öhningen Phone +49 (0)7735 – 8130, info@schlossmarbach.de
Times	30 May 2010 Afternoon: Individual arrival, come together, Lake Constance boat-ride, come together dinner 31 May 2010 Start 09.00 a.m. – Finish 07.15 p.m. 01 June 2010 Start 09.00 a.m. – Finish 05.15 p.m.
Registration & Coffee	30 May 2010 – 04.00 p.m. 31 May 2010 – 08.00 a.m.

MAP



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Registration Form

Please print your details

Title First name

Family name

Position

Department

Company

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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
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Cancellation Policy

- Over 30 days prior to the Seminar: Cancellation fee of 75,00 €.
- 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.de

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 30th to June 01st, 2010	1.750,00 €	☐
Members of AGAH, ACCP, DMDG and BioLago (Full participation from May 30th to June 01st, 2010)	1.650,00 €	☐
Participation on May, 31st **and** June 01st, 2010 **only**	1.650,00 €	☐
Member of AGAH, ACCP, DMDG and BioLago (participation on May, 31st **and** June 01st, 2010 **only**)	1.550,00 €	☐

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 (205,00 € per night)	☐	☐ (=410 €)
Category B:	single room (117,00 € per night)	☐	☐ (=234 €)
	double room (152,00 € per night)	☐	☐ (=304 €)
No Hotel accommodation required:			☐

Application to Register

To ensure the personal workshop character of the event and 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 workshop fees for members of ACCP, AGAH, DMDG and BioLago will be granted as indicated in the respective table based on proven evidence of current membership (e.g. membership card).

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