

DDI 2014

5th International Workshop on Regulatory Requirements and Current Scientific Aspects on the Preclinical and Clinical Investigation of Drug-Drug Interactions



May 25th to 27th, 2014
Marbach Castle, Germany



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 and increasing polypharmacotherapy”.

BACKGROUND, SCOPE AND AIM

In 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. The workshop was based on an initiative of experts in the field from academia and industry, intrigued by the notion that the field of drug-drug interactions (DDIs) is getting increasingly important and complex in view of continuously emerging new therapies, new drug combinations, 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 of clinically significant DDIs. Therefore, the meticulous investigation, informative labelling, 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 (i.e. understanding) and proper clinical 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 as well as an economic burden on healthcare systems, 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. Apart from metabolism based DDIs, transporter based DDIs, DDIs involving therapeutic proteins, tools extrapolating in vitro results to predict clinical outcomes in vivo (IVIVE) as well as information technology guiding the detection and management of DDIs have gained more importance over recent years. Furthermore, pharmacodynamic DDIs have gained increasing interest given the steady increase in drug combinations in clinical development.

Since its inception in 2010, the International Marbach Castle DDI Workshop has been designed to comprise all of the elements above, to foster a holistic view on

the complex field of drug-drug interactions. In order to facilitate an intense exchange on the topic and networking across company and organizational borders, the Workshop is an exclusive event and is limited to only 70 participants from pharmaceutical industry, contract research organizations and drug regulatory agencies, thus providing a unique opportunity to learn and discuss about the current state-of-the-art in the investigation of DDIs.

The 5th Anniversary Workshop

In its fifth year, the Workshop will, as in previous years, cover a regulatory topic in depth. After the EMA and FDA have updated the DDI guidelines in recent years, the 2014 regulatory session will focus on the changes to regulatory review and drug development induced by the new guidances, introduce the PMDA's draft DDI guideline and cover the submission of PBPK data in support of regulatory decision making, a novel element with rising importance in regulatory submissions. Given the rapid growth of new information on drug transporters and the amount of open questions to be solved, after 2010 and 2012, we will again present a session dealing with transporter mediated drug-drug interactions. A session on herb and food-drug interactions will cover this topic of rising importance given the widespread and increasing use of herbal drugs. Apart from the lectures, a poster session as well as short oral presentations of selected posters will provide you with an opportunity to get feedback on your work and address your current needs related to DDI issues.

As in the previous years, the topics of the 5th International DDI Workshop will be covered by 16 distinguished international scientists and experts from academia, pharmaceutical companies, contract research organizations, consultancies as well as government and regulatory agencies.

We are hoping to welcome you at Marbach Castle in May 2014.

The Workshop Organizers:

Hartmut Derendorf, PhD, FCP

Robert Hermann, MD, FCP

Amin Rostami-Hodjegan, PhD, FCP

Oliver von Richter, PhD, FCP

WHY YOU SHOULD ATTEND

- **Get informed** about the “New Japanese (PMDA) DDI guideline”
- **Focus** on the latest developments related to transporter-drug interactions (tDDIs)
- **Learn more** about employing mass balance trials to determine elimination routes for drugs
- **Gain** insights into herb-drug interactions
- **Display and discuss** your recent work on DDIs during the poster session
- **Realize** important aspects of tDDIs involving endogenous compounds
- **Get introduced** into best practices of PBPK modelling for regulatory submissions
- **Update yourself** on tDDIs involving hepatic uptake transporters
- **Enhance** your knowledge about the regulatory (FDA/EMA/PMDA) guidelines
- **Get to know** implications of the recently introduced changes to EMA and FDA DDI guidelines to drug development programs in a large pharmaceutical company
- **Inform** yourself about the challenges in the assessment of herb-drug interactions
- **Discover** the important differences between metabolism and transporter mediated DDIs
- **And most importantly Meet, Discuss and Network** with scientific and regulatory experts from pharmaceutical- and contract research-industries, international regulatory bodies (ANSM, CBG-MEB, EMA, MHRA, MPA and FDA), and academia.



WORKSHOP PROGRAMME

May 25th, 2014

Sunday	Afternoon	Individual Arrival & Check-in at Marbach Castle
	03:00 p.m.	Registration & Coffee
	04:00 p.m.	Come Together Activities
	06:00 p.m.	Opening of the Poster Exhibition
	08:00 p.m.	Come Together Dinner

May 26th, 2014

Monday	08:00 – 09:00 a.m.	Registration & Coffee
	09:00 – 09:15 a.m.	Welcome Address and Introduction into the Workshop <i>Hartmut Derendorf, PhD, FCP; University of Gainesville, US</i> <i>Robert Hermann, MD, FCP; cr.appliance, Germany</i> <i>Amin Rostami-Hodjegan, PhD, FCP; University of Manchester, UK</i> <i>Oliver von Richter, PhD, FCP; MerckSerono, Germany</i>
	09:15 – 10:00 a.m.	Key Note Lecture I „Fractions and Routes“ – Innovations and Best Practice in Human Mass Balance and Metabolite-Identification Studies <i>Llyod Stevens, PhD; Quotient Clinical, Nottingham, UK</i>
	10:00 – 10:15 a.m.	Discussion
	10:15 – 10:45 a.m.	Coffee Break
		Session I: Regulatory Aspects of Drug-Drug Interactions Chair: Hartmut Derendorf
	10:45 – 11:15 a.m.	The New FDA Guideline – What are the Changes to the Review Process/Labeling? A Regulatory Viewpoint <i>Lawrence Lesko, PhD; University of Gainesville FL, US</i>
	11:15 – 11:25 a.m.	Discussion
	11:25 – 11:55 a.m.	Integration of Guidelines and Science to Assess Drug-Drug Interactions - Are We There Yet? A Viewpoint from Pharmaceutical Industry <i>Richard Peck MD and Dietmar Schwab PhD; Hoffmann La Roche Pharmaceuticals, St. Albans, UK and Basel, Switzerland</i>
	11:55 – 12:05 p.m.	Discussion

12:05 – 12:35 p.m.	Recent Trends and Future Directions in Use of PBPK in Regulatory Submissions - An Outsider View! <i>Amin Rostami-Hodjegan, PhD, FCP; University of Manchester, UK</i>
12:35 – 12:45 p.m.	Discussion
12:45 – 02:00 p.m.	Lunch
02:00 – 02:45 p.m.	Key Note Lecture II The New PMDA Draft DDI Guideline <i>Akihiro Hisaka, PhD and Kazuya Maeda PhD; The University of Tokyo Hospital and University of Tokyo, Japan</i>
02:45 – 03:00 p.m.	Discussion
Poster Session	
03:00 – 04:00 p.m.	Short Presentation of Selected Posters I <i>Moderators: Hartmut Derendorf PhD, FCP; Amin Rostami-Hodjegan, PhD, FCP</i>
04:00 – 04:20 p.m.	Coffee Break
04:20 – 05:20 p.m.	Short Presentation of Selected Posters II <i>Moderators: Hartmut Derendorf PhD, FCP; Amin Rostami-Hodjegan, PhD, FCP</i>
07:30 p.m.	Dinner
09:30 p.m.	2INJOY in Concert <i>Florezelle Amend (voice), Michael Diehl (guitar) present Soul, Pop and Jazz in a new sound.</i>

May 27th, 2014

Tuesday

07:00 – 08:30 a.m.	Breakfast
08:30 – 09:15 a.m.	Key Note Lecture III Drug Metabolism versus Drug Transport: Out of the Frying Pan, into the Fire. A Structure-Based Process for Deciding whether to Conduct <i>in vitro</i> Metabolism or Transport Studies First <i>Andrew Parkinson, PhD; XPD Consulting, Shawnee, US</i>
09:15 – 09:30 a.m.	Discussion
Session II: Drug-Drug Interactions Involving Drug Transporters (tDDI) Chair: Amin Rostami-Hodjegan	
09:30 – 10:00 a.m.	tDDIs Involving Hepatic Drug Transporters <i>Henriette Meyer zu Schwabedissen; University of Basel, Switzerland</i>
10:00 – 10:15 a.m.	Discussion
10:15 – 10:45 a.m.	Coffee Break
10:45 – 11:15 a.m.	Renal Transporter-Mediated Drug-Drug Interactions: <i>in vitro</i> Models and Clinical Importance <i>Martin Fromm MD; University of Erlangen-Nürnberg, Germany</i>
11:15 – 11:30 a.m.	Discussion
11:30 – 12:00 a.m.	tDDIs Involving Endogenous Compounds <i>Robert Hermann MD, FCP; cr-appliance, Gelnhausen, Germany</i>
12:00 – 12:15 p.m.	Discussion
12:15 – 01:30 p.m.	Lunch



01:30 – 02:15 p.m.	Key Note Lecture IV Food-Drug Interactions – Going Back to Square One <i>Werner Weitschies, PhD; University of Greifswald, Germany</i>
02:15 – 02:30 p.m.	Discussion
<p>Session III: Herb-Drug Interactions Chair: Robert Hermann</p>	
02:30 – 03:15 p.m.	Key Note Lecture V – Herb-Drug Interactions <i>Veronika Butterweck PhD; Graduate School for Life Sciences / Institute for Pharmaceutical Technology, Muttenz / Basel, Switzerland</i>
03:15 – 03:25 p.m.	Discussion
03:25 – 05:55 p.m.	A Critical Perspective on Non-Clinical and Clinical Testing of Herb-Drug Interactions <i>Oliver von Richter, PhD, FCP; MerckSerono, Global Clinical Pharmacology, Darmstadt, Germany</i>
03:55 – 04:05 p.m.	Discussion
04:05 – 04:20 p.m.	Coffee Break
<p>Q & A Session</p>	
04:20 – 04:45 p.m.	Q & A Session Involving all Workshop Topics <i>Moderators: Robert Hermann, MD, FCP; Oliver von Richter, PhD, FCP</i>
04:45 – 05:00 p.m.	Concluding Remarks <i>Robert Hermann, MD, FCP; cr.appliance, Germany</i>
05:00 p.m.	End of Meeting & 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, regulatory affairs, pharmacokinetics, clinical pharmacology, exploratory/translational medicine, clinical development, drug safety, biostatistics, business development, medical communications and so forth should attend. All delegates are invited to contribute actively to the poster session and 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. Airport taxi shuttles for Workshop attendees will be organised on Sunday May 25th and Tuesday 27th. Taxi from and to the Airport is approx. 110 Euros. Please find detailed itinerary descriptions posted under the Contact/Travelling menu of the Marbach Castle website, if you arrange the travel yourself.

POSTER EXHIBITION

The Workshop will comprise a poster session for topics related to all aspect of non-clinical and clinical DDI investigations including IVIVE or other pharmacometrics approaches, regulatory, pharmaco-epidemiological as well as labelling aspects of DDIs. Poster presenters need to submit an abstract (limited to 250 words) to karen.grave-hermann@cr-appliance.de. The deadline for abstract submission is on May 3rd 2014.

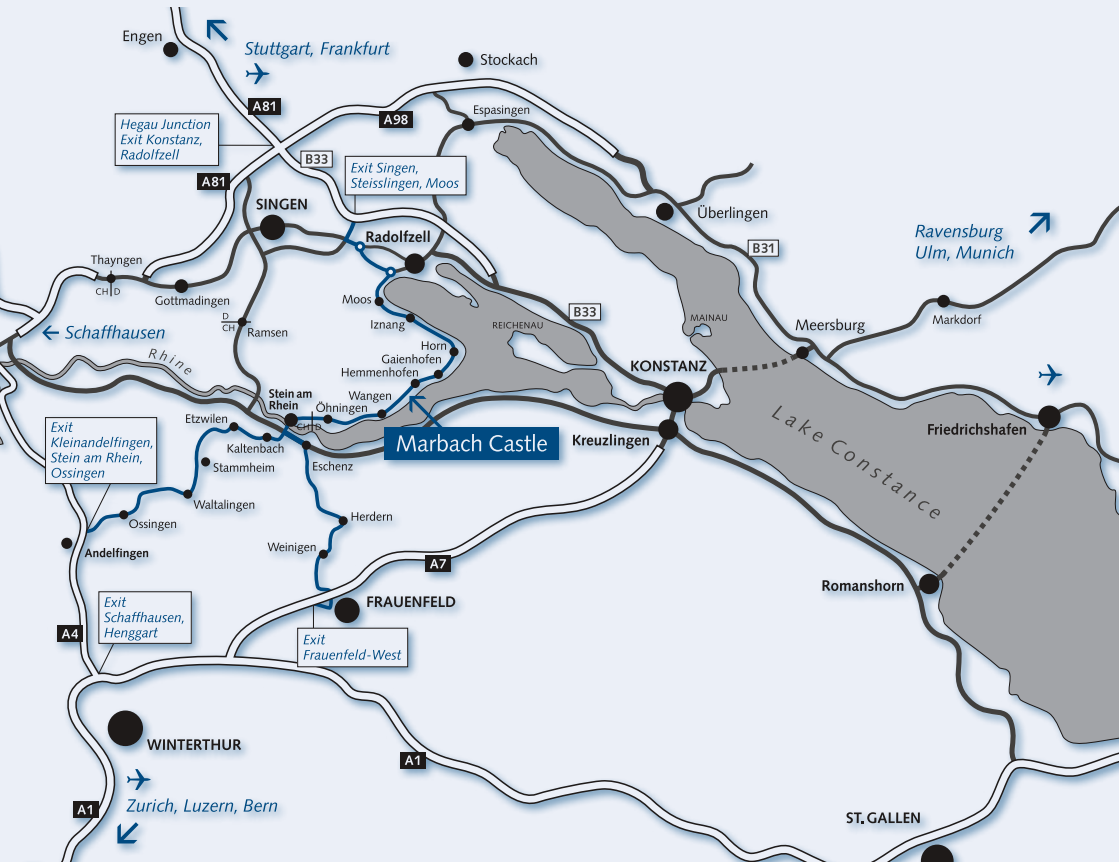
The posters will be displayed on Sunday May 25th from 06:00 p.m. – 08:00 p.m., Monday May 26th from 08:00 a.m. – 05:00 p.m. and on Tuesday May 27th from 08:00 a.m. – 01:30 p.m. The poster format and size must meet the following: portrait format; 140 x 120 cm (55,12 x 47,24 inch).

REGISTRATION INFORMATION

Date, Time and Venue

Date	Workshop May, 25 th to 27 th , 2014	
Venue	Marbach Castle	+49 (0)7735 – 8130 D-78337 Öhningen info@schlossmarbach.de
Times	May 25 th 2014 Afternoon: individual arrival, come together, come together activity, come together dinner	
	May 26 th 2014 Start 09:00 a.m. – End 06:00 p.m.	
	May 27 th 2014 Start 08:30 a.m. – End 05:00 p.m.	
Registration & Coffee	May 25 th 2014	03:00 p.m.
	May 26 th 2014	08:00 a.m.

MAP



Registration Form

Please print your details

Title	First name

Family name	

Position	

Department	

Company	

Address	

City	Post Code

Country	

Tel No.	Fax No.

E-mail	

Date	Signature

You may register by:

Mail: cr.appliance
Heinrich-Vingerhut-Weg 3,
D-63571 Gelnhausen

Fax: +49(0)6051-97 166 93

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For further information please contact Karen Grave-Hermann

Phone: +49(0)6051-97 166 91

Cancellation Policy

- More than 30 days prior to the Seminar: Cancellation fee of 200,00 €.
- 14–29 days prior to the Seminar: 50 % of the fee.
- Less 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.

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

Please tick

Participation from May 25 th to 27 th , 2014	1.830,00 €	<input type="checkbox"/>
Participation from May 25 th to 27 th , 2014, early bird fee, (i.e. registration and payment of workshop fee by end of February 2014 or members of ACCP, DMDG or BioLago)	1.730,00 €	<input type="checkbox"/>
Participation on May 26 th and 27 th , 2014 only	1.730,00 €	<input type="checkbox"/>
Participation on May 26 th and 27 th , 2014 only, in combination with early bird fee or members of ACCP, DMDG or BioLago (conditions see above)	1.630,00 €	<input type="checkbox"/>

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 (175,00 € per night)	<input type="checkbox"/>	<input type="checkbox"/> (= 350 €)
double room (250,00 € per night)	<input type="checkbox"/>	<input type="checkbox"/> (= 500 €)
Category B: single room (127,00 € per night)	<input type="checkbox"/>	<input type="checkbox"/> (= 254 €)
double room (202,00 € per night)	<input type="checkbox"/>	<input type="checkbox"/> (= 404 €)
No hotel accommodation required:		<input type="checkbox"/>

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 be triggered by receipt of the Workshop fees.

Discounted Rates

An “early bird” discount of 100 € will be granted for all binding bookings with actual payment of the workshop fee by end of February 2014. 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.