DDI 2016
Marbach DDI Workshop

7th International Workshop on Regulatory Requirements and Current Scientific Aspects on the Preclinical and Clinical Investigation of Drug-Drug Interactions

May 29th to 31st, 2016
Marbach Castle, Germany

MISSION STATEMENT

The DDI workshop series is a non-profit programme to exchange research-based knowledge on drug-drug interactions (DDIs) among all interested stakeholders from pharmaceutical industry, regulatory authorities, academic and health care delivery backgrounds and perspectives.

The overall objective of the International Marbach Castle DDI Workshop series is to disseminate the scientific knowledge about DDIs (incl. food-drug and herb-drug interactions), and to foster communication for efficient preclinical and clinical investigation of DDIs.

The goal is continuous improvement of the safe use of drugs in the light of increasing poly-pharmacotherapy in particular in ageing and multimorbid populations.

BACKGROUND, SCOPE AND AIM

In June 2010, the International Workshop on Regulatory Requirements and Current Scientific Aspects on the Preclinical and Clinical Investigation of Drug-Drug Interactions was held for the first time. The workshop was based on an initiative of experts in the field from academia, consultancy, software and pharmaceutical industry, intrigued by the notion that the field of DDIs is getting increasingly important and complex in view of continuously emerging new therapies, new drug combinations and complex treatment algorithms for many widespread diseases and ageing populations. These factors converge into poly-pharmacotherapy with an increasing risk of clinically significant DDIs. Therefore, the early recognition, meticulous clinical investigation, and informative labelling 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 associated 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 DDIs. In order to facilitate an intense exchange on the topic and networking across company and organisational borders, the Workshop is an exclusive event which it is about 70 participants from academia, pharmaceutical industry, contract research organisations and drug regulatory agencies, thus providing an unique environment to learn and discuss about the current state-of-the-art in the investigation of DDIs.

The 7th Workshop

In it's seventh year, the Workshop will cover three regulatory topics in depth. After the FDA has updated its DDI guideline in 2012, a new food-drug interaction guideline is currently in preparation. A presentation providing an industry perspective on the topic will highlight the expected regulatory changes. Based on the update of the EMA, FDA and PMDA DDI guidelines providing explicit guidance on how to support DDI investigations by PBPK modelling, the number of submissions including PBPK modelling information to these agencies is steadily rising. Therefore, the regulatory session will comprise two presentations from the perspectives of a regulatory agency and from pharmaceutical industry with regard to the use of PBPK for predicting DDIs and food-drug interactions. In November 2015, the FDA held a public meeting on DDIs with hormonal contraceptives (HC) to seek input from experts on the public health concerns associated with use of HCs and interacting drugs that might affect efficacy and safety, pharmacokinetic (PK)/ pharmacodynamic (PD) considerations in designing drug interaction studies, and approaches to translating the results of DDI information into informative labelling and communication. The regulatory session will contain two presentations providing an overview of the topic.

Introduced last year, the Tutorials were well received and will be carried on in 2016 with two presentations focusing on critical input data for PBPK modelling, including the fraction metabolized (f_m) and the fraction unbound (f_u). As in previous years, 4 posters will be selected for oral presentation, allowing participants to presenting their work.

Clinical DDI studies usually study the effect of drug A ("the perpetrator") on drug B ("the victim"). Real life is more complex, though. A session on complex DDIs will therefore present the challenges that arise from complex DDIs in the hospital setting as well as PBPK approaches aiming to tackle those issues.

The clinical session will comprise two presentations on DDIs at the level of renal excretion of drugs (passive as well as active). Given the knowledge accumulated on drug transporters in recent years, this topic has gained increased interest. The two presentations will focus on insights on the clinical relevance of renal DDIs and their underlying mechanisms.

As in the previous years, the topics of the 7th International DDI Workshop will be covered by distinguished international scientists and experts from academia, pharmaceutical companies, contract research organisations, consultancies as well as government and regulatory agencies.

We are hoping to welcome you in Marbach in May of 2016.

The Workshop Organisers:

Hartmut Derendorf, PhD, FCP
Robert Hermann, MD, FCP
Amin Rostami-Hodjegan, PhD, FCP
Oliver von Richter, PhD, FCP

WHY YOU SHOULD ATTEND

- **See** how mechanistic models can help in the evaluation of complex DDIs.
- **Get informed** about drug development and public health implications of DDIs with hormonal contraceptives.
- **Learn** about the current state and future developments of DDI management systems.
- **Update yourself** on the mechanism and clinical impact of DDIs affecting renal elimination of drugs.
- **Get introduced** into the changes of the FDA guidance on the study of food-drug interactions.
- **Discover** how the Bill & Melinda Gates foundation is engaged in research and mitigation of DDIs.
- **Realize** the importance of a correct assessment of the fraction metabolized (f_m).
- **Inform** yourself about variability of fraction unbound of drugs (f_u) and its integration into PBPK models.
- **Gain** insights into regulatory view of predictive performance of PBPK for DDI assessment.
- **Get to know** DDI management systems in the hospital setting.
- **Expand** your knowledge on how to avoid pitfalls when conducting *in vitro* / PBPK DDI studies.
- **Enhance** your knowledge about complex DDIs.
- **Display and discuss** your recent work on DDIs during the poster session.

… **and most importantly meet, discuss and network** with scientific and regulatory experts from pharmaceutical- and contract research-industries, international regulatory bodies, non-government organisations, and academia.

WORKSHOP PROGRAMME

May 29th, 2016

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
07:30 p.m.	Come Together Dinner
09:00 p.m.	Concert: Simon Wahl & Timo Brauwers (Acoustic Guitar Duo)

May 30th, 2016

Monday

08:00 – 09:00 a.m.	Registration & Coffee
09:00 – 09:10 a.m.	Welcome Address and Introduction into the Workshop *Robert Hermann, MD, FCP*
09:10 – 09:55 a.m.	Key Note Lecture I Approaching DDI Challenges in Global Health *Steven E. Kern, PhD; Bill and Melinda Gates Foundation, Seattle WA, USA*
09:55 – 10:05 a.m.	Discussion
10:05 – 10:45 a.m.	Coffee Break / Poster Viewing
	Session I: **Changes in the US Regulatory Landscape** Chair: Hartmut Derendorf
10:45 – 11:15 a.m.	Using PBPK to assess DDI Risk: a Checklist of Predictive Performance *Ping Zhao, PhD; Bethesda MD, USA*
11:15 – 11:30 a.m.	Discussion
11:30 – 12:00 a.m.	Food Effect Assessments in Drug Development – Latest Tools and Guidances *Tycho Heimbach, PhD; Novartis Pharma, East Hanover NJ, USA*
12:00 – 12:15 p.m.	Discussion
12:15 – 01:40 p.m.	Lunch

Session II:
DDIs Affecting Renal Elimination of Drugs

Chair: Amin Rostami-Hodjegan

01:40 – 02:10 p.m.	Renal DDIs: Mechanisms Blocking the Way Out *Maciej Zamek-Gliszczynski, PhD, Glaxo Smith Kline, King of Prussia, PA, USA*
02:10 – 02:20 p.m.	Discussion
02:20 – 02:50 p.m.	Renal DDIs: Focus on Clinical Relevance *Martin Fromm, MD; University of Erlangen-Nürnberg, Erlangen, Germany*
02:50 – 03:00 p.m.	Discussion

Session III:
Revisiting Some Key Principles

Chair: Hartmut Derendorf

03:00 – 03:30 p.m.	f_m is too Important to get it Wrong *Amin Rostami-Hodjegan, PhD, FCP; University of Manchester, Manchester, UK*
03:30 – 03:45 p.m.	Discussion
03:45 – 04:15 p.m.	Coffee Break / Poster viewing
04:15 – 04:45 p.m.	f_u is too Important to be treated as Static *Oliver von Richter, PhD, FCP; Sandoz Biopharmaceuticals, Holzkirchen, Germany*
04:45 – 05:00 p.m.	Discussion

Presentation of Selected Posters

Chairs: Oliver von Richter

05:00 – 06:00 p.m.	Short Presentation of Selected Posters *Presentation of 4 selected posters with 10 minutes presentation and 5 minutes discussion*
07:30 p.m.	Dinner

May 31st, 2016

Tuesday

	Session IV: **DDIs with Hormonal Contraceptives** Chair: Robert Hermann
08:30 – 09:00 a.m.	DDIs with Hormonal Contraceptives: Public Health and Drug Development Implications *Lawrence Lesko, PhD, FCP; University of Florida, Orlando FL, USA*
09:00 – 09:30 a.m.	DDIs with Hormonal Contraceptives: An Industry Perspective on Their Assessment During Drug Development *Joachim Höchel, DVM, PhD; Bayer Pharma AG, Berlin, Germany*
09:30 – 09:45 p.m.	Discussion
	Session V: **Clinical DDI Management** Chair: Robert Hermann
09:45 – 10:15 a.m.	DDI Management Systems in the Hospital Setting – Lost in Information *Walter E. Haefeli, MD; Heidelberg University Hospital, Heidelberg, Germany*
10:15 – 10:30 a.m.	Discussion
10:30 – 11:00 a.m.	Coffee Break
11:00 – 11:30 a.m.	Individualising Management of DDIs *Helen Humphries, PhD; Certara, Sheffield, UK*
11:30 – 11:45 a.m.	Discussion
11:45 – 01:00 p.m.	Lunch

Session VI:
Complex DDIs

Chair: Oliver von Richter

01:00 – 01:30 p.m.	Evaluation of Incidence and Relevance of Complex DDIs in the Clinical Setting *Youssef Daali, PhD; Geneva University Hospital, Geneva, Switzerland*
01:30 – 02:00 p.m.	Complex DDIs: What to do When the Clinical DDI Data does not Agree with the *in vitro* Findings and Predictions *Nina Isoherranen, PhD; University of Washington, Seattle WA, USA*
02:00 – 02:15 p.m.	Discussion
02:15 – 02:45 p.m.	Coffee Break
02:45 – 03:15 p.m.	How to Avoid Common Pitfalls when Conducting PBPK DDI Studies – Wrong Assumptions in = Wrong Results out *Mohamad Shebley, PhD; Abbvie, Chicago IL, USA*
03:15 – 03:45 p.m.	How to Avoid Common Pitfalls when Conducting *in vitro* DDI Studies: It's not all About Metabolism *Brian Houston, BSc, PhD and DSc, Centre for Applied Pharmacokinetic Research, Manchester Pharmacy School, University of Manchester, UK*
03:45 – 04:00 p.m.	Discussion

Q & A Session

Chair: Amin Rostami-Hodjegan

04:00 – 05:00 p.m.	Q & A Session Involving all Workshop Topics
05:00 p.m.	Concluding Remarks End of Meeting & Departure

www.ddi-workshop-marbach.org



WHO SHOULD ATTEND?

This international Workshop on DDIs 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, drug safety, 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: http://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 (ZRH) is about 60 kilometres. Airport taxi shuttles for Workshop attendees will be organised on Sunday May 29th and Tuesday 31st. Taxi from and to the Airport is approx. 110 – 120 €. Please find detailed itinerary descriptions posted under the Contact/Travelling item of the Marbach Castle web site, if you arrange the travel yourself.

POSTER PRESENTATIONS

Poster presentations on topics related to all aspect of non-clinical and clinical DDI investigations including pharmacometrics with emphasis on PBPK, regulatory sciences, pharmaco-epidemiological, pharmacovigilance, management of as well as labelling aspects of DDIs are encouraged. Please submit your poster abstract for approval by the Faculty by April 29th 2016 to: karen.grave-hermann@cr-appliance.com.

ABSTRACT

The abstract must be structured, including the following sections: Aim(s), Methods, Results (some numerical data, including confidence intervals on differences, when appropriate, must be included), and Conclusions. The abstract should not exceed a maximum of 250 words. In addition, authors should provide a written statement on:

What is already known about this subject

This statement should contain a summary of the state of scientific knowledge on this subject before you did your study along with a justification why this study was needed to be done in up to three short bullet points (not more than 50 words in total).

What this study adds

This section should provide a simple answer to the questions "What do we now know as a result of this study that we did not know before?" and "What take-home-message do you want to impart to the readers?" in up to three short bullet point sentences (not more than 50 words in total).

Abstracts of posters will be included in the conference materials and will be made available on the Marbach DDI – Workshop website.

POSTERS

Poster must have **portrait format** and size should be no larger than 120 x 140 cm (47.24 x 55.12 inch). The posters will be displayed on Sunday May 29th from 06:00 p.m. – 08:00 p.m., Monday May 30th from 08:00 a.m. – 05:00 p.m., and on Tuesday May 31st from 08:00 a.m. – 01:30 p.m. Please be prepared to mount your poster during registration on Sunday, May 29th or latest on Monday, May 30th, before the first session begins.

There is no formal poster presentation scheduled. All posters will remain displayed throughout the conference. Poster presenters will therefore have ample time for discussion with attendees during breaks and panel discussions.

A total of 4 Posters will be selected by the Faculty for oral presentation during the Monday afternoon session (10-minute presentations with 5 minutes of discussion). Approved poster applicants are responsible for completing a workshop attendance registration form and payment of fee by April 30th, 2016, and for the shipping of the poster itself.

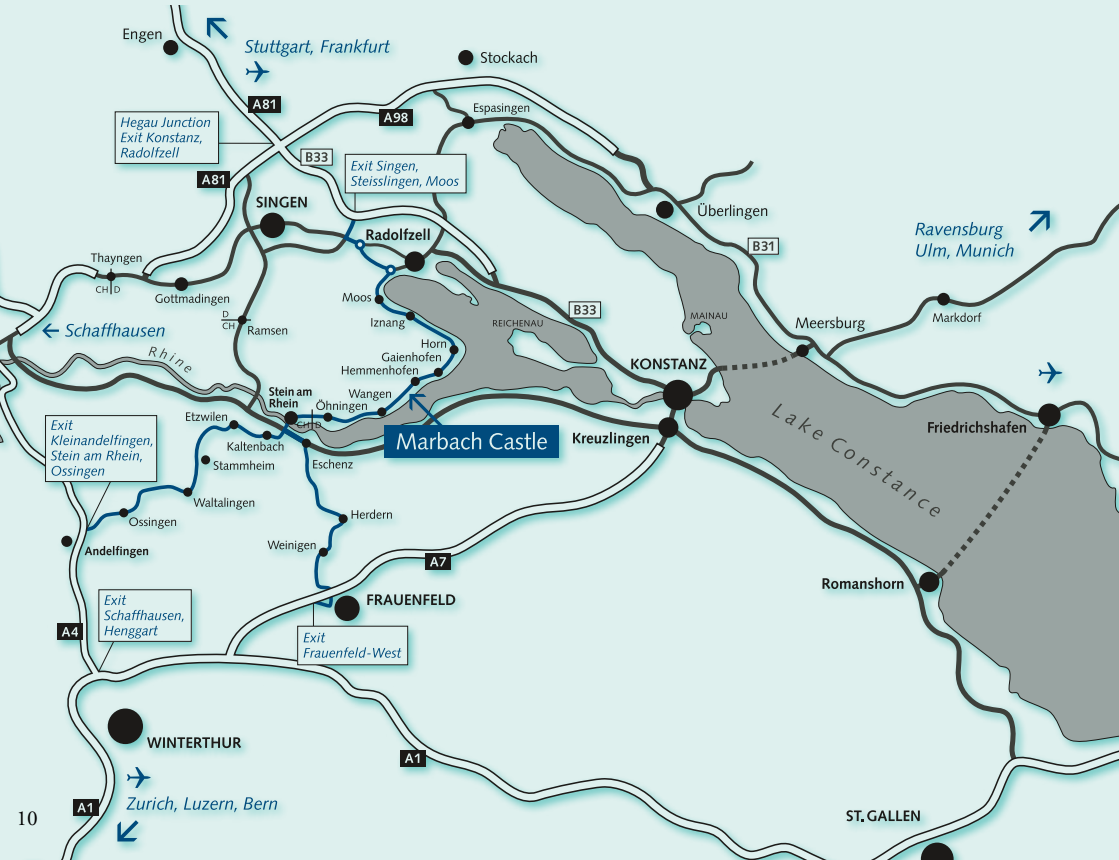
Please contact Karen Grave-Hermann for any questions or comments.

REGISTRATION INFORMATION

Date, Time and Venue

Date	Workshop May, 29th to 31st, 2016
Venue	Marbach Castle +49 (0)7735 – 8130 D-78337 Öhningen info@schlossmarbach.de
Times	May 29th 2016 Afternoon: individual arrival, come together, come together activity, come together dinner, acoustic guitar concert Scientific Programme: May 30th 2016 Start 09.00 a.m. – Finish 06.00 p.m. May 31st 2016 Start 08.30 a.m. – Finish 05.00 p.m.
Registration & Coffee	May 29th 2016 03:00 p.m. May 30th 2016 08:00 a.m.

MAP



Registration Form

Please print your details

Title First name

Family name

Position

Department

Company

Address

City Postal Code

Country

Phone Fax

E-mail

Date Signature

You may register by:

Mail: Karen Grave-Hermann
cr.appliance
Heinrich-Vingerhut-Weg 3,
D-63571 Gelnhausen
Fax: +49(0)6051-97 166 93
Internet: www.ddi-workshop-marbach.org

For further information please contact Karen Grave-Hermann

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

Cancellation Policy

- More than 30 days prior to the Workshop: Cancellation fee of 200,00 €.
- Within 14 – 29 days prior to the Workshop: 50 % of the fee.
- Less than 14 days or if no notification received:
  Registrant liable to pay FULL Workshop fee.

NB: Cancellation must be addressed in writing to (e-mail sufficient) to the Workshop Secretary:
karen.grave-hermann@cr-appliance.com

In the event of circumstances beyond control, the Workshop Organisers reserve 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

3-Day Participation from May 29th to 31st, 2016	1.830,00 €	☐
3-Day Participation from May 29th to 31st, 2016, (Discounted rate for: Early bird registrations or Members of ACCP, DMDG, ISoP or BioLago)	1.730,00 €	☐
2-Day Participation on May 30th and 31st, 2016 only	1.730,00 €	☐
2-Day Participation on May 30th and 31st, 2016 only, in combination with discounted rate (conditions see above)	1.630,00 €	☐

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 (180,00 € per night)	☐	☐
	double room (260,00 € per night)	☐	☐
Category B:	single room (134,00 € per night)	☐	☐
	double room (214,00 € per night)	☐	☐
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

An "early bird" discount on the Workshop fee of 100 € will be granted for all binding bookings with actual payment of the Workshop fee by end of February 2016. Further discounted rates may be granted for a limited number of participants on individual application for students, personnel from non-profit organisations and registered charities.