DDI 2017
Marbach DDI Workshop

ACCP
American College of Clinical Pharmacology

DM dg DRUG METABOLISM discussion group

BioLAGO
life science network

8th International Workshop on Regulatory Requirements and Current Scientific Aspects on the Preclinical and Clinical Investigation of Drug-Drug Interactions

May 28th to 30th, 2017
Marbach Castle, Germany

Second Announcement

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 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 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 vivo* 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 organisational borders, the Workshop is an exclusive event which it is limited to 70 participants from academia, pharmaceutical industry, contract research organisations and drug regulatory agencies, thus providing a unique environment to learn and discuss about the current state-of-the-art in the investigation of DDIs.

The 8th Workshop

In it's eighth year, the Workshop will cover a number of regulatory topics in depth. After the FDA has updated its DDI guideline in 2012, the final guideline is about to be released in 2017. The final guideline will be presented by an FDA speaker as well as by a representative of a drug company providing insights into changes to the drug development process resulting from the final DDI guidance. As second regulatory highlight, the new EMA Draft Guideline on the qualification and reporting of physiologically based pharmacokinetic (PBPK) modelling and simulation will be introduced by the Rapporteur involved in generating the Guideline. In addition, the current regulatory experience of EMA on DDI submissions involving PBPK modelling will be presented. Following last year's presentation on the regulatory standards for PBPK submission by an FDA representative, the regulatory session is flanked by a presentation on the successful use of PBPK supporting DDI investigations for a development program in oncology, laying out the hurdles but also the gains as well as the implications for labelling.

Following the update of the food-drug interaction guideline by the FDA last year, the 8th workshop will cover an important aspect of food-drug interactions, i.e. formulation dependent interactions as well as interactions with alcohol.

Introduced in 2015, Tutorials were well received and will be carried on in 2017 rebranded as "Concepts revisited". The session will comprise a presentation on sample size consideration for DDI studies, a topic that is often neglected given the important information, which are drawn from DDI studies and presented in drug labels. The second topic in this session is dealing with drug interactions related to changes in intracellular drug partitioning, i.e. lysosomal trapping.

Furthermore, the 2017 workshop program comprises two sessions dealing with drug-interactions based on drug transporters as well as an important physiological barrier, i.e. the blood brain-barrier. Presentations will comprise a review of blood-brain-barrier physiology as well as tools on how to study those interactions *in vivo*. A keynote lecture will deal with the latest *in vitro* tools to study DDI rounded up by a presentation on the initial validation of the initial clinical evaluation of a transporter probe-drug cocktail.

As in the previous years, the topics of the 8th 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. All topics will be presented from different angles by presenting non-clinical information from *in vitro* studies, clinical studies as well as PBPK simulations linking non-clinical and clinical data.

We are hoping to welcome you in Marbach in May of 2017!

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

- **Get introduced** into the final FDA DDI Guideline
- **Update yourself** on the new EMA Draft Guidance for conducting PBPK modelling
- **Get informed** about practical challenges in implementing and conducting M&S for DDI in lieu of clinical studies
- **Learn** about formulation-dependent DDI and formulation dependent interactions with alcohol
- **Enhance** your knowledge on the interplay of formulations and gut-wall metabolism and its implications for formulation-dependent DDI
- **Inform** yourself about the role of transporters in the blood-brain-barrier and applications of CNS imaging for the examination of DDI
- **Gain** insights into the uptake and efflux transporters expressed in the microvascular endothelial cells of the blood-brain-barrier, and the Choroid Plexus, the anatomical correlate of the blood-cerebrospinal fluid-barrier (BCSFB)
- **Expand** your knowledge on drug transporters and transporter-based DDI beyond ITC and DDI Guideline transporter panels
- **Get introduced** into the first clinical evaluation of a transporter probe-drug cocktail
- **Recapitulate and expand your knowledge** on sample-size considerations in planning *in vivo* DDI studies
- **Enjoy an update** on the mechanisms and pharmacokinetic & toxicological consequences of ion partitioning of drugs into lysosomes
- **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.

For more information please also visit:
www.ddi-workshop-marbach.org

WORKSHOP PROGRAMME

May 28th, 2017

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: Live Concert – 2Injoy (Soul, Pop & Jazz) & Michael Diehl (Fingerstyle Guitar) *www.2injoy.de & www.michaeldiehl-fingerstyle.de*

May 29th, 2017

Monday

08:00 – 09:00 a.m.	Registration & Coffee
09:00 – 09:10 a.m.	Welcome Address and Introduction into the Workshop *Oliver von Richter, PhD, FCP*
	Session I: **Changes in the US/EU Regulatory Landscapes** Chair: Amin Rostami-Hodjegan & Hartmut Derendorf
09:10 – 09:55 a.m.	Key Note Lecture Philosophy and Specific Recommendations for Preclinical and Clinical DDI Studies *Shiew-Mei Huang, PhD; FDA, Silver Spring, MD, USA*
09:55 – 10:15 a.m.	Discussion
10:15 – 10:45 a.m.	Coffee Break / Poster Viewing
10:45 – 11:15 a.m.	How should Pharmaceutical Industry Interpret and Comply with the New FDA DDI Guidance? *Vikram Sinha, PhD; MSD, North Wales, PA, USA*
11:15 – 11:25 a.m.	Discussion
11:25 – 11:55 a.m.	The Current Experience of EMA on DDI Submissions Involving PBPK Modelling *Susan Cole; MHRA, London, UK*
11:55 – 12:05 p.m.	Discussion
12:05 – 01:30 p.m.	Lunch

Session I (ctd.):
Changes in the US/EU Regulatory Landscapes
Chair: Amin Rostami-Hodjegan & Hartmut Derendorf

01:30 – 02:00 p.m.	The New Draft EMA Guidance on PBPK Submissions and Feedback from Public Consultation *Anna Nordmark, PhD; Medical Products Agency, Uppsala, Sweden*
02:00 – 02:15 p.m.	Discussion
02:15 – 02:45 p.m.	Practical Challenges in Implementing and Conducting M&S for DDI in Lieu of Clinical Studies: Convincing Various Players and the Anticipated Rewards *Venkatesh Pilla Reddy, PhD, AstraZeneca, Cambridge, UK*
02:45 – 03:00 p.m.	Discussion
03:00 – 03:30 p.m.	Coffee Break / Poster Viewing
03:30 – 04:00 p.m.	Q &A of the Regulatory Session Panel Discussion *Shiew-Mei Huang PHD, FDA, USA; Susan Cole, MHRA, UK; Anna Nordmark PHD, MPA, Sweden; Vikram Sinha PHD, MSD, USA; Venkatesh Pilla Reddy PHD, AstraZeneca, UK*

Session II:
Formulation Dependent DDI
Chair: Robert Hermann

04:00 – 04:45 p.m.	Keynote Lecture Formulation Dependent DDI and Formulation Dependent Interactions with Alcohol *Henning Blume, PhD; SocraTec R&D, GmbH, Bad Homburg, Germany*
04:45 – 05:00 p.m.	Discussion
05:00 – 05:30 p.m.	Interplay of Formulation and Gut Wall Metabolism and its Implications for Formulation Dependent DDI *Andrés Olivares-Morales, Pharm D, PhD; F. Hoffmann-La Roche, Basel, Switzerland*
05:30 – 05:45 p.m.	Discussion
07:00 p.m.	Dinner

May 30th, 2017

Tuesday

	Session III: **The Role of Transporters at the Blood-Brain-Barrier (BBB) and Applications of Imaging DDI at the BBB** Chair: Hartmut Derendorf
08:15 – 09:00 a.m.	The Uptake and Efflux Transporters Expressed in the Microvascular Endothelial Cells of the Blood-Brain Barrier and in other Brain Barriers *Jean Michel Scherrmann, PhD; Inserm, UMR-S Université Paris Descartes, Paris, France*
09:00 – 09:15 a.m.	Discussion
09:15 – 10:00 a.m.	Keynote Lecture The Role of Transporters in the Blood-Brain-Barrier (BBB) and Applications of Imaging DDI at the BBB *Jashvant Unadkat, PhD; University of Washington, Seattle, WA, USA*
10:00 – 10:15 a.m.	Discussion
10:15 – 10:45 a.m.	Coffee Break / Poster Viewing
	Poster Session: **Presentation of Selected Posters** Chair: Amin Rostami-Hodjegan
10:45 – 11:45 a.m.	Presentation of Selected Posters *Presentation of 4 selected posters with 10 minutes presentation and 5 minutes discussion*
11:45 – 01:00 p.m.	Lunch

For more information please also visit:
www.ddi-workshop-marbach.org

Session IV:
tDDI
Chair: Robert Hermann

01:00 – 01:45 p.m.	Keynote Lecture Nucleoside Transporters – A Family of Transporters with Emerging Importance *Peter Krajcsi, PhD; Solvo Biotechnology, Budaörs, Hungary*
01:45 – 02:00 p.m.	Discussion
02:00 – 02:30 p.m.	Clinical Evaluation of the First Established Transporter Probe-Drug Cocktail *Peter Stopfer, PhD; Boehringer Ingelheim, Biberach, Germany*
02:30 – 02:45 p.m.	Discussion
02:45 – 03:15 p.m.	Coffee Break / Poster Viewing

Session V:
Concepts Revisited
Chair: Oliver von Richter

03:15 – 03:45 p.m.	Sample Size Assessment in DDI studies – Food for Thoughts *Sibylle Neuhoff, PhD; Certara, Sheffield, UK*
03:45 – 04:00 p.m.	Discussion
04:00 – 04:30 p.m.	The Mechanism and Pharmacokinetic & Toxicological Consequences of Ion Partitioning of Drugs into Lysosomes *Andrew Parkinson, PhD, XPD Consulting, Shawnee KS, USA*
04:30 – 04:45 p.m.	Discussion

Q & A Session
Chair: Amin Rostami-Hodjegan & Oliver von Richter

04:45 – 05:00 p.m.	Q & A Session Involving Sessions II – V
05:00 p.m.	Concluding Remarks End of Meeting & Departure

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 request for Sunday, May 28th and Tuesday May, 30th. German taxi fare from and to the airport is approx 120 €, while Swiss airport taxi fares are substantially higher. 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 28th 2017 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 28th from 06:00 p.m. – 08:00 p.m., Monday May 29th from 08:00 a.m. – 05:00 p.m., and on Tuesday May 30th from 08:00 a.m. – 01:30 p.m. Please be prepared to mount your poster during registration on Sunday, May 28th or latest on Monday, May 29th, 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 AND WORKSHOP INFORMATION

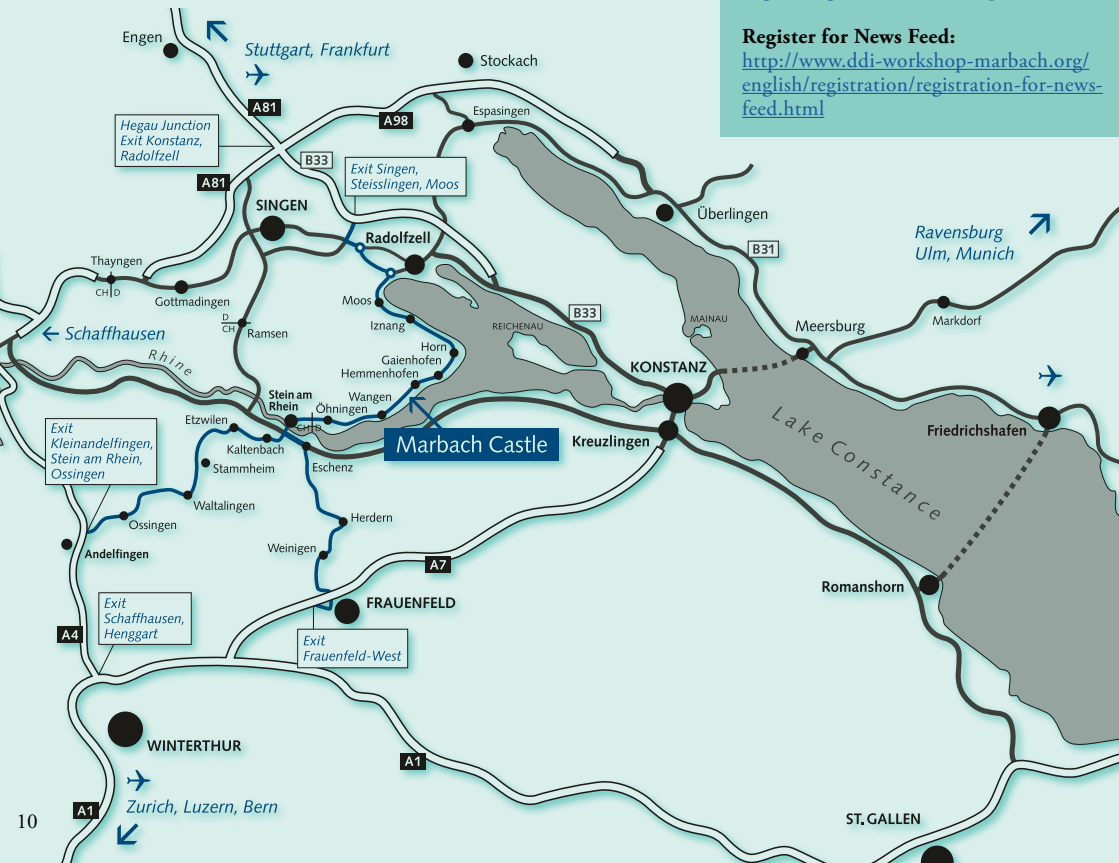
Date, Time and Venue

Date	Workshop May, 28th to 30th, 2017
Venue	Marbach Castle +49 (0)7735 – 8130 D-78337 Öhningen info@schlossmarbach.de
Times	May 28th 2017 Afternoon: individual arrival, come together, come together activity, come together dinner, concert Scientific Programme: May 29th 2017 Start 09:00 a.m. – Finish 05:45 p.m. May 30st 2017 Start 08.15 a.m. – Finish 05:05 p.m.
Registration & Coffee	May 28th 2017 03:00 p.m. May 29th 2017 08:00 a.m.

Register Online
http://www.ddi-workshop-marbach.org/english/registration/workshop.html

Register for News Feed:
http://www.ddi-workshop-marbach.org/english/registration/registration-for-news-feed.html

MAP



Registration Form

Please print your details

Salutation (Mr/Ms) 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

E-mail: karen.grave-hermann@cr-appliance.com

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 28th to 30th, 2017	1.960,00 €	☐
3-Day Participation from May 28th to 30th, 2017, early bird fee, (i.e. registration and payment of workshop fee until end of February 2017 or members of ACCP, DMDG or BioLago)	1.860,00 €	☐
2-Day Participation on May 29th and 30th, 2017 only	1.860,00 €	☐
2-Day Participation on May 29th and 30th, 2017 only, in combination with early bird fee (conditions see above) or members of ACCP, DMDG or BioLago)	1.760,00 €	☐

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 2017. 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.