

**DDI 2019 – 10th International
Workshop on Regulatory Requirements
and Current Scientific Aspects on the
Preclinical and Clinical Investigation of
Drug-Drug Interactions**

May 26th to 28th, 2019
Marbach Castle, Germany



10 years
Marbach DDI Workshop



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 drug-drug interactions (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 polypharmacotherapy 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 DDIs 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 polypharmacotherapy 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 drug-drug interactions.

THE 10TH WORKSHOP

In its 10th anniversary year, the Workshop will cover a number of highly important regulatory topics in depth. The Workshop will open with a historic review of past, present and future of the investigation of DDIs, featuring presentations from an academic and industrial point of view. This will be followed by a session focusing on Metabolism-Based DDIs & Clinical Management of DDIs, reviewing approaches of predicting DDI with integrated model-informed drug development capability as well as the clinical management of DDIs in future. We will also address changes in the regulatory DDI landscape from an European and international point of view. Recent international DDI guidelines on DDIs and PBPK will be presented discussed and implications to drug development strategies will be debated.

On the second day we will be fortunate to have presentations from global leaders in the field of transporter-based DDIs, focusing on uptake transporters in the gut and the utility of endogenous biomarkers in early clinical trials. Also on the menu is an update on an ongoing transporter probe-cocktail study. The last session is dedicated to a special topic of great interest, namely DDIs with hormonal contraceptives. There will be a number of presentations to shed light on this issue from an academic, regulatory and industrial perspective, covering the opportunities for translation from pre-clinical *in vitro* studies.

As always, there will be an opportunity for Workshop participants to submit abstracts for poster presentations throughout the Workshop. The best abstract also will be selected for short oral presentations.

All sessions will provide plenty of opportunity to ask questions and provide comments.

The topics of the 10th International DDI Workshop will be covered by distinguished international scientists and experts from academia, pharmaceutical companies, contract research organizations, 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 2019!

The Workshop Organizers
Hartmut Derendorf, PhD, FCP
Robert Hermann, MD, FCP
Amin Rostami-Hodjegan, PhD, FCP

WHY YOU SHOULD ATTEND

- **Get a comprehensive review** on the historical landscape in investigating DDI
 - **Get informed** about current trends in industry on wider employment of modelling and simulation in general, and specific aspects affecting DDI studies
 - **Update yourself** on EMA Guidances impacting the assessment of DDIs
 - **Learn** about the Japanese (PMDA) DDI guideline and potential future links to PBPK guideline
 - **Expand your knowledge** on regulatory expectations and clinical guidance concerning translation of preclinical information to clinical DDIs affecting hormonal contraceptives
 - **Enjoy an introduction** to what the future DDI decision support tools for clinicians may look like in the era of precision dosing
- ... **and most importantly meet, discuss and network** with a unique selection of scientific and regulatory experts from pharmaceutical- and contract research-industries, international regulatory bodies, non-government organizations, and academia

WORKSHOP PROGRAMME

May 26th, 2019

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, Michael Diehl & 2InJoy – Fingerstyle Guitar and Soul, Pop & Jazz Double Concert: www.simonwahl.com , www.2injoy.de & www.michaeldiehl-fingerstyle.de

May 27th, 2019

Monday

08:00 – 08:30 a.m.	Registration & Coffee
08:30 – 08:40 a.m.	Welcome Address and Introduction into the Workshop <i>Amin Rostami-Hodjegan</i>
	Session I: Past, Present and Future of the Investigation of DDIs Chair: Amin Rostami-Hodjegan
08:40 – 09:20 a.m.	Keynote Lecture An Academic Review on the History & Evolution of DDI Investigations <i>Malcolm Rowland, PhD, DSc; Professor Emeritus, University of Manchester, Manchester, UK</i>
09:20 – 09:30 a.m.	Discussion
09:30 – 10:10 a.m.	Keynote Lecture An industry view on the evolution of modelling and simulation in drug development with emphasis on DDI studies over the past decade <i>Richard Lalonde, PharmD, Adjunct Professor University of Florida and Consultant, Bradenton, Florida, USA</i>
10:10 – 10:20 a.m.	Discussion
10:20 – 10:50 a.m.	Coffee Break & Visit of the Poster Exhibition

Session II: Changes in the International Regulatory DDI Landscapes

Chair: Hartmut Derendorf

10:50 – 11:30 a.m.	Update on EMA Guidances Impacting the Assessment of DDIs <i>Kevin Blake, MD, PhD, European Medicines Agency (EMA), London, UK</i>
11:30 – 11:40 a.m.	Discussion
11:40 – 12:20 p.m.	The Japanese (PMDA) DDI Guideline and application of PBPK modeling in DDI evaluation <i>Kiyomi Ito, PhD, Research Institute of Pharmaceutical Sciences, Musashino University, Tokyo, Japan</i>
12:20 – 12:30 p.m.	Discussion
12:30 – 02:00 p.m.	Lunch

Session III: PBPK Modeling of Metabolism-Based DDIs

Chair: Andrew Parkinson

02:00 – 02:40 p.m.	Predicting DDI with Integrated MiDD Capability <i>Ping Zhao, PhD, Bill and Melinda Gates Foundation, Seattle, Washington, USA</i>
02:40 – 02:50 p.m.	Discussion
02:50 – 03:20 p.m.	Coffee Break & Visit of the Poster Exhibition

Session IV: Clinical Management of DDIs

Chair: Robert Hermann

03:20 – 04:05 p.m.	Getting Over Fatigue of DDI Warnings: What the Future Decision Support Tools Hold for Clinicians in the Era of Precision Dosing <i>Jean-Luc Reny, MD, Geneva University Hospital, Geneva, Switzerland</i>
04:05 – 04:15 p.m.	Discussion
04:15 – 04:35 p.m.	Late Breaking Topic! Ketoconazole and Liver Injury – A Five-Year Update <i>Gerd Mikus, MD, Heidelberg University Hospital, Heidelberg, Germany</i>
04:35 – 04:45 p.m.	Discussion

Q & A Session Day 1

Chair: Andrew Parkinson & Amin Rostami-Hodjegan

04:45 – 05:15 p.m.	Q & A Session Involving Sessions I - III
07:30 p.m.	Dinner

May 28th, 2019

Session V:

Transporter-Based DDIs Revisited

Chair: Hartmut Derendorf

08:30 – 09:10 a.m.	The Role of Intestinal Influx Transporters in Drug-Nutrient, Drug-Excipient and Drug-Drug Interactions <i>Kathleen Giacomini, PhD, Department of Bioengineering and Therapeutic Sciences, Schools of Pharmacy and Medicine, University of California, San Francisco, USA</i>
09:10 – 09:20 a.m.	Discussion
09:20 – 10:00 a.m.	Can Endogenous Biomarkers be Applied in Phase I Clinical Trials to Facilitate Subject Phenotyping and DDI Prediction? <i>Yuichi Sugiyama, PhD; RIKEN Cluster for Science, Technology and Innovation Hub, Japan</i>
10:00 – 10:10 a.m.	Discussion
10:10 – 10:40 a.m.	Coffee Break & Visit of the Poster Exhibition
10:40 – 11:10 a.m.	The Effect of Inhibitors of Drug Transport on a Probe-Drug Cocktail Consisting of Digoxin, Furosemide, Metformin, and Rosuvastatin <i>Peter Stopfer, PhD; Boehringer Ingelheim, Biberach, Germany</i>
11:10 – 11:20 a.m.	Discussion

Session VI:

DDIs with Hormonal Contraceptives Revisited

Chair: Robert Hermann

11:20 – 12:00 a.m.	Regulatory Guidance Versus Clinical Guidance on Drug Interactions of Combined Hormonal Contraceptives <i>Lawrence J. Lesko, PhD, FCP; Professor Emeritus and Founding Director, Center for Pharmacometrics and Systems Pharmacology Department of Pharmaceutics, College of Pharmacy, University of Florida, USA</i>
12:00 – 12:10 p.m.	Discussion
12:10 – 01:40 p.m.	Lunch

Tuesday



Session VI: DDIs with Hormonal Contraceptives Revisited (ctd)

Chair: Robert Hermann

01:40 – 02:10 p.m.	Closing the Knowledge Gap on Potential Differences in the Sensitivity to CYP3A4 Induction between Common Progestins used in Oral Contraceptives Relative to Midazolam <i>Joachim Höchel DVM, PhD & Herbert Wiesinger, PhD; Bayer AG, Berlin, Germany</i>
02:10 – 02:20 p.m.	Discussion
02:20 – 02:50 p.m.	Assessment of Drug Interactions with Oral Contraceptives using PBPK Modelling: A Best Practice Approach Using Case Studies <i>Karen Rowland Yeo, PhD, Vice President PBPK Consultancy Services, Certara, Sheffield UK</i>
02:50 – 03:00 p.m.	Discussion
03:00 – 03:30 p.m.	Coffee Break & Visit of the Poster Exhibition
	Poster Session: Oral Presentation of Selected Posters Chair: Hartmut Derendorf
03:30 – 04:30 p.m.	Short Presentation of Selected Posters <i>Presentation of 4 selected posters with 10 minutes presentation and 5 minutes discussion</i>
	Q & A Session Day 2 Chair: Andrew Parkinson & Amin Rostami-Hodjegan
04:30 – 05:00 p.m.	Q & A Session Involving Sessions IV - VI
05:00 p.m.	Concluding Remarks End of Meeting & Departure

Tuesday

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, 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: 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 26th and Tuesday 28th. Taxi from and to the Airport is approx. 120€. Alternatively, the train from Zurich Airport to Stein am Rhein (train change in Winterthur) can be used (train departs in Zurich every 10 minutes and the connecting train in Winterthur every 40 minutes; average travel time 1.5 hours; 20 to 30€). In case of train travel the Congress Secretary needs to be informed about the travel schedule and arrival time in Stein am Rhein in order to organize a taxi shuttle from Stein am Rhein to Marbach Castle. 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. Further details regarding poster submission can be found on the DDI Website: www.ddi-workshop-marbach.org/english/registration/posters.html

Please submit your poster abstract for approval by the Faculty by April 26th 2019 to:

Professor Hartmut Derendorf: hartmut@cox.net

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 × 140 cm (47.24 × 55.12 inch). The posters will be displayed on Sunday May 26th from 06:00 p.m. – 08:00 p.m., Monday May 27th from 08:00 a.m. – 05:00 p.m., and on Tuesday May 28th from 08:00 a.m. – 01:30 p.m. Please be prepared to mount your poster during registration on Sunday, May 26th or latest on Monday, May 27th, 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 Tuesday 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, 2019, and for the shipping of the poster itself.

Please contact Professor Hartmut Derendorf (hartmut@cox.net) for any questions or comments.

EUROPEAN PROTECTION LAW (EDPL)

By filling out the registration form, the participant gives consent to the DDI Workshop Faculty to process the data provided within the framework of the conference and in compliance with the EDPL Legislation. This includes the following, unless registered participants object:

- All personal details needed for the applicant’s participation at the event - invoicing, participant list, Certificate of Attendance, contact about the registration, specific diet information, etc
- Pictures taken during the conference:
 - Accessible only by participants (PW-protected Website area)
 - Accessible by Website visitors (public Website area)

Data collection and processing: Personal Data and Contact Information will be exclusively used within the framework of registration to the aforementioned event and will not be shared publicly. The collected data is stored on a secured server.

Right of access: applicants have a right to access and ask for changing or deleting their personal data and pictures.

REGISTRATION INFORMATION

Date, Time and Venue

Date Workshop May, 26th to 28th, 2019

Venue Marbach Castle +49 (0)7735 – 8130
D-78337 Öhningen info@schlossmarbach.de

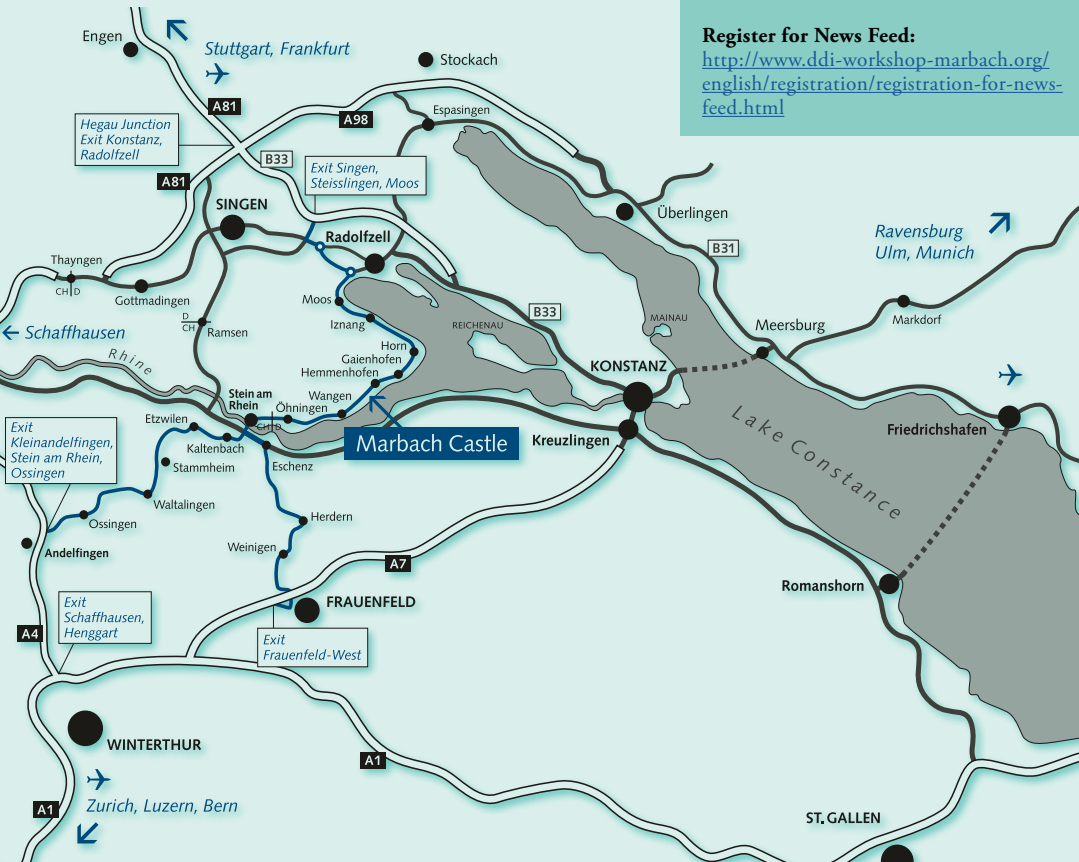
Times May 26th 2019 Afternoon:
Individual arrival, come together, come together activity,
come together dinner, acoustic guitar concert

Scientific Programme:

May 26th 2019 Start 06:00 p.m. – Opening Poster Session
May 27th 2019 Start 08:30 a.m. – Finish 05:15 p.m.
May 28st 2019 Start 08:30 a.m. – Finish 05:00 p.m.

Registration & Coffee May 26th 2019 03:00 p.m.
May 27th 2019 08:00 a.m.

MAP



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>

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

Please tick

3-Day Participation from May 26 th to 28 th , 2019	1.960,00 €	<input type="checkbox"/>
3-Day Participation from May 26 th to 28 th , 2019, early bird fee, (i.e. registration and payment of workshop fee until end of February 2019 or members of ACCP, DMDG or BioLago)	1.860,00 €	<input type="checkbox"/>
2-Day Participation on May 27 th and 28 th , 2019 only	1.860,00 €	<input type="checkbox"/>
2-Day Participation on May 27 th and 28 th , 2019 only, in combination with early bird fee (conditions see above)	1.760,00 €	<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 (198,00 € per night)	<input type="checkbox"/>	<input type="checkbox"/>
	double room (278,00 € per night)	<input type="checkbox"/>	<input type="checkbox"/>
Category B:	single room (134,00 € per night)	<input type="checkbox"/>	<input type="checkbox"/>
	double room (214,00 € per night)	<input type="checkbox"/>	<input type="checkbox"/>
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 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 2019. 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.

Registration Form

Please print your details

Salutation (Mr/Ms)	Title	First name
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Family name		
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Position		
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Department		
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Company		
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Phone	Fax	
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E-mail		
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Date	Signature	
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You may register by:

Mail: 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: secretary@ddi-workshop-marbach.org

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.

**Note: Cancellation must be addressed in writing to (e-mail sufficient) to the Workshop Secretary:
secretary@ddi-workshop-marbach.org**

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