





11<sup>th</sup> International Workshop on Regulatory Requirements and Current Scientific Aspects of the Preclinical and Clinical Investigation of Drug-Drug Interactions







#### Why You Should Attend



- Get familiarized with the final 2020 FDA Guidance Documents on Drug Interactions (i.e. in vitro and clinical studies).
- Learn how to assign proportional importance to SLC transporters and their contribution the overall clearance and associated DDI
- Find your way out of common mistakes associated with metabolic reaction phenotyping
- Get informed of latest technologies on characterising metabolic activity of given individuals using 'Liquid Biopsy'
- Revisit the interactions between herbal products with prescribed medications
- Build anticipation (or dismissal) of herb-medicine interactions based on in vitro data

- Understand the FDA expectations regarding assessment of food-drug interactions
- Evaluate potentials of modelling and simulation to predict the food-drug interactions and required data for such activities
- Know your gut! (using proteomics to measure the levels of relevant proteins in the wall)
- See how DDI can work for you! (synergies with examples on oncology)
- Go beyond kinetics and review pharmacodynamic interactions
- Hear about DDI in neonates and how they are addressed in the clinic in the absence of prior information from dedicated clinical studies

- Delve into DDI assessment using real-world data in special populations and patients who may have different susceptibility than healthy volunteers
- Become familiar with regulatory perspectives on DDI in paediatric populations and legislation for them
- ... and most importantly meet, discuss and network with a unique selection of scientific and regulatory experts from pharmaceuticaland contract research-industries, international regulatory bodies, non-government organizations and academia.



#### **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 drugdrug 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 poly-pharmacotherapy in particular in ageing and multimorbid populations.

#### Background, Scope and Aim

In June 2010, the International Workshop on Regulatory Reguirements 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 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. More details on the Workshop history have been published recently:

Derendorf H, von Richter O, Hermann R, Rostami-Hodjegan A. Drug-Drug Interactions: Progress Over the Past Decade and Looking Ahead to the Future. Clin Pharmacol Ther. 2019; 105:1289-1291.

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 discussions and exchanges of views for providing a holistic perspective on the complex field of drug-drug interactions.

Robert Hermann MD, FCP Amin Rostami-Hodjegan, PhD, FCP Ping Zhao, PhD



#### The 11<sup>th</sup> Workshop

After the Covid-19 caused cancellation of our DDI Workshop 2020, and the unexpected passing of our long-standing Faculty colleague, friend, and co-founder of the Marbach DDI Workshop series Professor Hartmut Derendorf in November 2020, the Faculty has mutually agreed and decided to carry on with the Workshop series and to run the 2021 DDI Workshop in any case!

The 2021 Marbach DDI meeting is planned to become a special tribute in memoriam of Hartmut and celebrating his life and legacy. To keep Hartmut's memory alive in the Marbach community in the long-run, the Faculty has mutually agreed on the inception of a

# Hartmut Derendorf Young Scientists Award

From 2021 onwards, the Faculty will identify and nominate each year 3 suitably qualified candidates. Upon the agreement of the nominees to participate in the final awardee selection procedure, this will be accomplished by a blinded poll of all speakers and registered workshop attendees using an electronic form at the Marbach DDI Website in advance of the meeting. The elected awardee will then be entitled to present the "Hartmut Derendorf Young Scientists Award Lecture", and will receive a certificate and a trophy along with a certain financial support for his/her scientific work. For financial support of the annual Award, donations will be accepted. Details on how this can be done will be provided by the Workshop Secretary upon request.



## New Marbach DDI Faculty Member

The Marbach DDI Faculty is proud and happy to report that with Dr. Ping Zhao (Bill and Melinda Gates Foundation, Seattle, USA) an outstandingly worthy representative could be allured to join the Faculty as successor of Hartmut Derendorf with immediate effect.

Dr. Zhao is known as an excellent scientist of highest reputation with international recognition in the fields of regulatory science, model-informed drug development and evaluation of drug-drug interactions.

Dr. Zhao has been a contributor to the Marbach events several times and he is familiar with the set up and exclusive nature of this gathering.

We are confident that Dr. Zhao will substantially contribute further under his new role to the maintenance of the high scientific and regulatory standards of our Workshop series and expansion of its global reach.

Many of you may know him! Please join us in welcoming Ping on board!









#### The Workshop Programme 2021

In brief, the Workshop will open with a new feature, a keynote lecture on the philosophy of drug interactions.

This will be followed by a session about food-drug interactions, starting with an overview on the current knowledge of the gut wall proteomics and its relevance to drug absorption and interactions. The following presentation will address the question whether or not formulationdependent food-drug interactions can be predicted. Implications to drug development strategies will be debated. The third talk in this session will familiarize the audience with the IQ Working Group considerations on food-drug interactions, including some food effect case studies. The final presentation in this session details the highlights of the new FDA Guidance on the assessment of food-drug interactions.

As requested by many participants and on the Workshop agenda for years, we will feature a session on pharmacodynamic (PD) drug interactions, with an overview of common PD interactions of clinical importance, and one talk revisiting beneficial and safety-relevant PD interactions in oncology.

The last session of Day 1 will be dedicated to the presentation and discussion of the final 2020 FDA Guidance Documents on Drug Interactions (i.e. in vitro and clinical studies).

Day 2 of the workshop will kick off by a translational DMPK session focusing on in-vitro aspects of DDI studies with an introduction in the liquid biopsy methodology, and its potential role for the characterization of individual hepatic drug elimination capacity. Thereafter, do's and don'ts in metabolic reaction phenotyping, and recent developments in SLC-transporter phenotyping as a new means to quantify the contribution of transporters to the hepatic uptake clearance of drugs will be presented.

For the first time, the workshop will include a new session on evaluating drug interactions in pediatric

populations with clinical as well as regulatory implications.

Finally, the Workshop will conclude with a session on DDIs between herbal drug products and prescription drugs, which will be opened by a presentation of a meta-analysis and novel insights in this topic. A second talk in this session will review 2 decades of clinically relevant DDIs with St. John's Wort, and finally translational approaches to untangle herbdrug interactions will be presented.

All sessions will provide ample opportunity for attendees to ask questions and provide comments.

The topics of the 11th 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 including non-clinical information (especially from in vitro studies), clinical information, as well as in silico simulations (e.g., using PBPK models that integrate non-clinical and clinical knowledge).

We are hoping to welcome you in the newly renovated facilities at Marbach in May of 2021!

The Workshop Organizers



Robert Hermann, MD, FCP



Amin Rostami-Hodjegan, PhD, FCP



Ping Zhao, PhD



# Workshop Programme



Sunday, May 30 <sup>th</sup> , 2021			
Afternoon	Individual Arrival & Check-in at Marbach Castle		
03:00 p.m.	Registration & Coffee		
04:00 p.m.	Come Together Activities		
07:30 p.m.	Come Together Dinner		
09:00 p.m.	Live Music – TBD		

Monday, May	<sup>7</sup> 31 <sup>st</sup> , 2021
08:00 – 08:30 a.m.	Registration & Coffee
08:30 – 08:50 a.m.	Welcome Address and Introduction into the Workshop Amin Rostami
08:50 – 09:25 a.m.	Keynote Lecture – The Philosophy of Drug Interactions Philip D. Hansten, PharmD, Professor Emeritus, University of Washington, USA
09:25 – 09:35 a.m.	Discussion
Session I	Food-Drug Interactions & Beyond Chair: Amin Rostami
09:35 – 10:00 a.m.	Gut Feeling – Proteomics of Gut Wall and Relevance to Drug Absorption and Interactions Stefan Oswald, PhD, University of Greifswald, Germany
10:00 – 10:10 a.m.	Discussion
10:10 – 10:35 a.m.	Can we Predict Formulation-Dependent Food-Drug Interactions? Rodrigo Cristofoletti, PhD, Assistant Professor at the Center of Pharmacometrics & Systems Pharmacology, University of Florida, Gainesville, USA
10:35 – 10:45 a.m.	Discussion
10:45 – 11:10 a.m.	Coffee Break
11:10 – 11:35 a.m.	Food-Drug Interactions – Considerations from the IQ Working Group and Food Effect Case Studies Tycho Heimbach, PhD, Biopharmaceutics, Sterile & Specialty Products Group, Pharmaceutical Sciences, Merck & Co., Inc., Rahway, New Jersey, USA
11:35 – 11:45 a.m.	Discussion
11:45 – 12:05 p.m.	Regulatory Science on Assessing Food Drug Interaction – Highlights from New FDA Guidance Rajanikanth Madabushi, PhD, Office of Clinical Pharmacology, Center for Drug Evaluation and Research, FDA, Silver Spring, MD, USA
12:05 – 12:15 p.m.	Discussion
12:15 – 01:45 p.m.	Lunch

# Workshop Programme



Monday, May 31 <sup>st</sup> , 2021				
Session II	Pharmacodynamic Interactions Chair: Robert Hermann			
01:45 – 02:10 p.m.	Common Pharmacodynamic Interactions of Clinical Importance David Juurlink; MD, PhD, FRCPC, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada			
02:10 – 02:20 p.m.	Discussion			
02:20 – 02:45 p.m.	Revisiting Pharmacodynamic Interactions: Benefits and Watch-outs in Oncology Jin Yan Jin, PhD, Genentech, San Francisco, California, USA			
02:45 – 02:55 p.m.	Discussion			
02:55 – 03:20 p.m.	Coffee Break			
Session III	The Final FDA Guidance Documents on Drug Interactions Chair: Amin Rostami			
03:20 – 03:45 p.m.	Introductory Lecture: What did the FDA Change when it Finalized its In Vitro Drug Interaction Guidance in January, 2020?  Andrew Parkinson, PhD, XPD Consulting, Shawnee KS, USA			
03:45 – 03:55 p.m.	Q & A Session with all Regulatory Attendees			
03:55 – 04:20 p.m.	Introductory Lecture: The Final FDA Guidance on Clinical Drug Interaction Studies – Cytochrome P450 Enzyme- and Transporter- Mediated Drug Interactions. Robert Hermann, MD, Clinical Research Appliance, Gelnhausen, Germany			
04:20 – 04:40 p.m.	Q & A Session with all Regulatory Attendees			
07:00 p.m.	Dinner			

Tuesday, J	lune 1 <sup>st</sup> , 2021

Session IV	Translational DMPK Session Chair: Amin Rostami
08:50 – 09:00 a.m.	Reflections on Day 1 and Opening Remarks Day 2
09:00 – 09:25 a.m.	Liquid Biopsy, its Applications, Limitations, and Potential Role for Characterising Individual Hepatic Drug Elimination Capacity Brahim Achour, PhD, University of Manchester, UK. Appointed Assistant Professor at the Faculty of the College of Pharmacy, University of Rhode Island (URI) (from September 2021)
09:25 – 09:35 a.m.	Discussion
09:35 – 10:00 a.m.	Metabolic Reaction Phenotyping: Do's and Don'ts, and the Oscar Nomination Process (is Metabolism the Best Actor or the Best Supporting Actor?)  Andrew Parkinson, PhD, XPD Consulting, Shawnee KS, USA
10:00 – 10:10 a.m.	Discussion

# Workshop Programme



Tuesday, Jun	<b>e 1<sup>st</sup>, 2021</b> (continued)
10:10 – 10:35 a.m.	"SLC-Phenotyping": Quantifying Contribution of Transporters to the Hepatic Uptake Clearance of Drugs Manthena V Varma, PhD, Pfizer, Groton, CT, USA
10:35 – 10:45 a.m.	Discussion
10:45 – 11:10 a.m.	Coffee Break
Session V	Pediatric DDIs Chair: Ping Zhao
11:10 – 11:35 a.m.	Are Neonates and Young Infants Protected against DDIs Despite their Exposure to a Multitude of Medicines?  Johannes N. van den Anker, MD, PhD, Children's National Hospital, University Children's Hospital Basel, University of Basel, Switzerland
11:35 – 11:45 a.m.	Discussion
11:45 – 12:10 a.m.	Application of Pharmacometric Approaches and Real-World Data to Characterize Drug-Drug Interactions in Infants and Children Daniel Gonzalez, PharmD, PhD, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
12:10 – 12:20 p.m.	Discussion
12:20 – 01:45 p.m.	Lunch
Session VI	Herb-Drug DDIs Chair: Ping Zhao
01:45 – 02:10 p.m.	Herbal Drug-Drug Interactions. A Meta-Analysis and Novel Insights Ingolf Cascorbi, MD, PhD, University of Kiel, Germany
02:10 – 02:20 p.m.	Discussion
02:20 – 02:55 p.m.	Looking Back 2 Decades: Revisiting Clinically Relevant Drug Interactions with St. John's Wort Veronika Butterweck, PhD, Max Zeller und Söhne, Romanshorn, Switzerland
02:55 – 03:05 p.m.	Discussion
03:05 – 03:30 p.m.	Translational Approaches to Untangle Herb-Drug Interactions Mary Paine, RPh, PhD, Washington State University, Spokane, Washington, USA
03:30 – 03:40 p.m.	Discussion
03:40 – 04:05 p.m.	Coffee Break
Session VII	Q & A Session Day 2 Chair: Ping Zhao & Amin Rostami
04:05 – 04:25 p.m.	Q & A Session Involving Sessions IV – VI
04:25 – 04:30 p.m.	Concluding Remarks 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, 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 30<sup>th</sup> and Tuesday June 1<sup>st</sup>. Taxi from and to the Airport is approx. 120 €.

Alternatively, the train form 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

Because of the "hybrid" format of the 2021 Workshop, this year no poster presentation will take place.



#### **Registration Information**



Date, Time and Venue					
Date	Workshop May, 30 <sup>th</sup> to June 1 <sup>st</sup> , 2021				
Venue	Marbach Castle, D-78337 Öhningen +49 (0)7735 – 8130, info@schlossmarbach.de				
Times	May 30 <sup>th</sup> 2021 Afternoon Individual arrival, come together, come together activity, come together dinner, live music (to be defined)  Scientific Programme May 30 <sup>th</sup> 2021 Start 08.30 a.m. – Finish 04.40 p.m.				
	May 31st 2021 Start 08.00 a.m. – Finish 04.30 p.m.				
Registration & Coffee	May 30 <sup>th</sup> 2021 03.00 p.m. May 31 <sup>st</sup> 2021 08.00 a.m.				

Register Online for Workshop and News Feed www.ddi-workshop-marbach.org

#### Registration

Considering the current uncertainties around the course of the Covid-19 pandemic, including the spread of more infectious virus mutations on the one hand, and the progress of the vaccination programs across the world on the other hand, we are currently planning for a "hybrid" meeting this year. This means that speakers and attendees will have the opportunity to opt by certain date (see below) between attendance in person at Marbach Castle or for a virtual attendance via video conference (Zooms).

There are several factors which are beyond our control. These include rules and requirements of local authorities on size of the gatherings for meetings, as well as international and company guidelines governing travel. In case that any of such restrictions will still be in place by end of May, thereby precluding a gathering of a meaningful number of attendees at Marbach Castle, the entire Workshop will be held as a virtual meeting.

#### Registration for Physical Attendance at Marbach Castle

Keeping with the tradition of the Marbach event in the past, to maintain the tradition of Marbach DDI Workshop that assures optimal scientific exchange and interaction at personal level, we limit the number of participants to about 70. Therefore, early registration is recommended, to assure your place at the Workshop. In case the meeting is fully booked, a "standby" registration option will be considered which may come into effect in case of cancellations.

## Registration for Virtual Conference Attendance

Because of the ongoing Covid-19 pandemic, registration for a webbased virtual conference attendance on May 31<sup>st</sup> and June 1<sup>st</sup>, is possible for the Workshop 2021. Only 2-day registrations for the entire event will be accepted. The fees for the virtual conference attendance will

be 50% of the fees applicable for the physical 2-day attendance at Marbach Castle. The number of virtual conference attendees is limited to 50.

### Registration Formalities and Procedures

Workshop participation will be assigned in the sequence of receipt of registration applications. Full confirmation of registration, however, will only be granted upon complete receipt of the Workshop fees, which become payable within 3 weeks after submission of the registration application.

## You may register via the Workshop Secretary by:

- E-Mail: secretary@ddi-workshopmarbach.org
- Fax: +49(0)6051-97 166 93

or by using the registration form below.

# **Registration Form**

Signature



Workshop Fe	e (incl. Lunch, Dinner & Coffee Breaks, incl	. 19 % VAT)		You may register by
3-Day Particip	1.960,00€		Internet	
3-Day Particip (for members	1.860,00 €		www.ddi-workshop-marbach.org <b>E-mail</b>	
2-Day Particip	pation on May 31 <sup>th</sup> and June 1 <sup>st</sup> , 2021 only	1.860,00€		secretary@ddi-workshop- marbach.org
2-Day Participation on May 31 <sup>st</sup> and June 1 <sup>st</sup> , 2021 only, (in combination with discounted rate for members of ACCP, DMDG or BioLago )		1.760,00 €		Fax +49(0)6051-97 166 93
	pation Virtual Conference and June 1st, 2021	930,00€		For further information please contact Karen Grave-Hermann.
Accommodation A limited num			E-mail: secretary@ddi-workshop-marbach.org	
	astle (further Hotel capacities in y available upon request):	1 night 2 ni	ghts	Phone: +49(0)6051-97 166 91  Cancellation Policy
Category A:	single room (198,00 € per night)			More than 30 days prior to the Workshop: Cancellation fee of
	double room (278,00€ per night)			200,00 €.
Category B:	single room (134,00 € per night)			Within 14 – 29 days prior to the Workshop: 50 % of the fee.
	double room (214,00 € per night)			Less than 14 days or if no noti-
No hotel accor	mmodation required:			fication received: Registrant liable to pay FULL
Please print y Salutation (Mr/Ms)	our details			
Title				
First name				
Family name				
Position				
Department				
Company				
Address				
City				
Postal Code				
Country				
Phone				
Fax				
E-Mail				
Date				

#### **Registration Information**



#### **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)
  - 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.

#### **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 rates on the Workshop fee of 100 € will be granted will be granted for members of ACCP, DMDG or BioLago. In addition, a limited number of participants may receive discounted fees based on individual applications of students, personnel from non-profit organizations and registered charities.

#### Cancellation

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

In the event circumstances beyond control, the Workshop Organizers reserve the right to alter the programme, the speakers the date or the venue.



### Marbach Map



