DDI 2018
Marbach DDI Workshop

ACCP
American College of Clinical Pharmacology

DMdg

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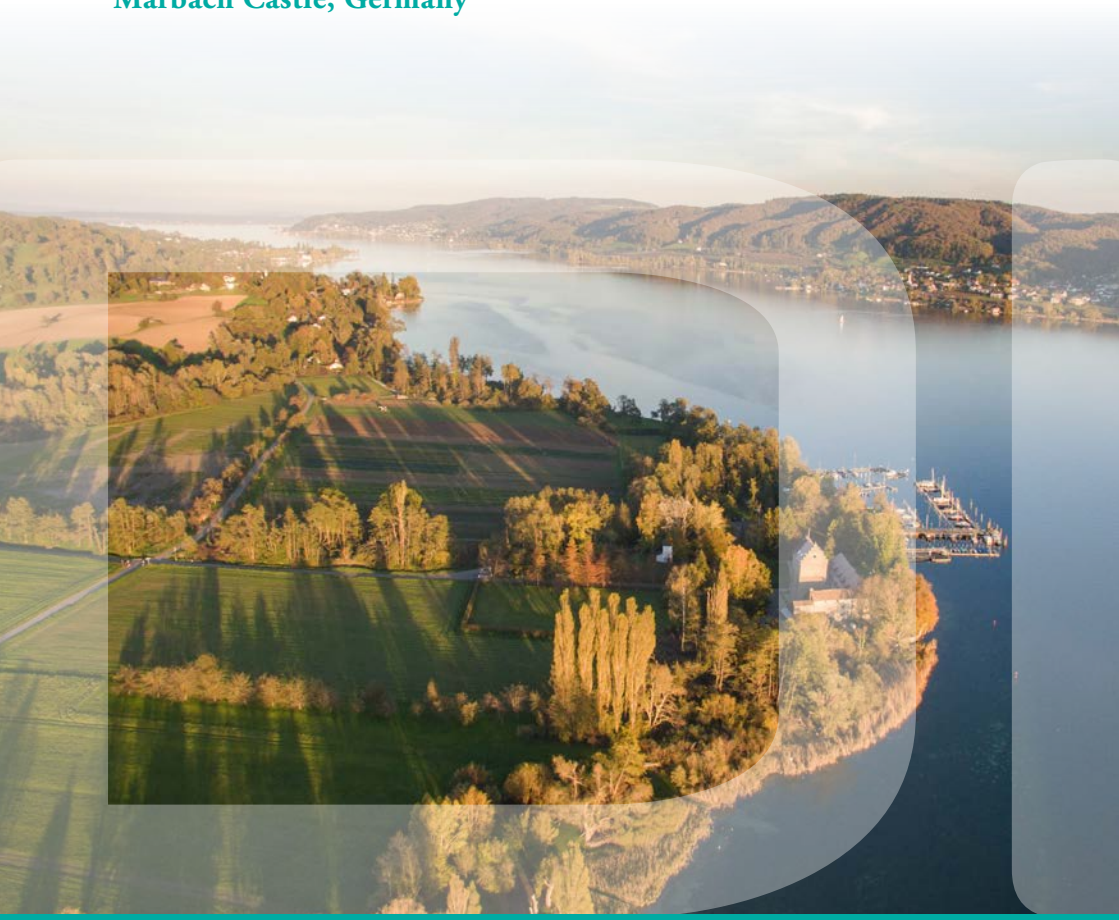
life science network

9th International Workshop on Regulatory Requirements and Current Scientific Aspects on the Preclinical and Clinical Investigation of Drug-Drug Interactions

May 27th to 29th, 2018
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 & 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 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 9th Workshop

In its 9th year, the Workshop will cover a number of highly important regulatory topics in depth. The entire first day of the meeting will be dedicated to current regulatory issues.

The US FDA released two new drug-drug interaction (DDI) Guidance documents in October 2017 to replace the 2012 draft DDI Guidance. The two documents are entitled "Guidance on Clinical Drug Interaction Studies – Study Design, Data Analysis, and Clinical Implications" and "Guidance on In Vitro Metabolism- and Transporter-Mediated Drug-Drug Interaction Studies". Both provide pharmaceutical companies comprehensive guidance on how to evaluate investigational drugs for potential clinical DDIs and drug labeling.

In the "Clinical Drug Interaction Studies Guidance", the timing of clinical DDI trials, the design and conduct of the DDI studies, the reporting and interpreting of such study results and labeling recommendations are provided.

In turn, the "In Vitro Metabolism- and Transporter-mediated DDI Studies Guidance" provides recommendations on the in vitro approaches to the evaluation of potential DDIs that involved metabolizing enzymes and/or transporters, and how in vitro outcomes can inform clinical DDI studies. The presentation of both Gui dance documents will examine and discuss the changes of the new guidances and their impact on in vitro and clinical study requirements. A second presentation on the In Vitro Metabolism- and Transporter-Mediated Guidance will provide an expert perspective on practical implications.

A second part of the regulatory session will comprise a Consortium perspective on the important issue of PBPK model qualification and reporting procedures for regulatory submissions, and a presentation on dynamic drug labels for optimal management of DDIs in patient care. Finally, a representative of the French Agency ANSM will share concepts of the regulatory assessment of two DDIs involving the activation of prodrugs by a distinct enzyme and their consequences.

Two regulatory panel discussions will provide ample opportunity for a lively discussion of the audience with the presenters.

The second meeting day will start with a session on mechanistic models and PBPK sensitivity assessment. In the latter, sensitivity analyses towards model credibility, uncertainty, verification and validation will be presented, while the talk on mechanistic models will address the search of sensitive endogenous markers for transporter DDIs, with coproporphyrin I as examples for renal and hepatic uptake-transporter DDI markers.

Furthermore, the 2018 workshop programme comprises two sessions dealing with the mechanistic assessment of pharmacokinetic DDIs (Session "Phenotyping Revisited") including presentation of a microdosing cocktail approach for direct acting oral anticoagulants (DOACs), and a session on non-CYP related metabolic DDIs with a particular emphasis on UDP-glucuronyltransferase (UGT)-based DDIs.

The topics of the 9th 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 2018!

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 new FDA DDI Guidance on Clinical Drug Interaction Studies – Study Design, Data Analysis, and Clinical Implications.
- **Get informed** about the new FDA Guidance on In Vitro Metabolism- and Transporter-Mediated Drug-Drug Interaction Studies.
- **Learn** about a practice perspective on the new FDA Guidance on In Vitro Metabolism- and Transporter-Mediated Drug-Drug Interaction Studies.
- **Inform yourself** about a Consortium perspective on PBPK model qualification and reporting procedures for regulatory submissions.
- **Enhance your knowledge** about dynamic drug labels for optimal management of DDIs in patient care.
- **Gain insights** into the regulatory assessment of DDIs involving a distinct enzyme and their consequences on morbidity and mortality.
- **Expand your knowledge** on global sensitivity analyses in PBPK – model credibility, uncertainty, verification and validation.
- **Get introduced** into the search of sensitive endogenous markers for transporter DDIs.
- **Update yourself** on the mechanistic assessment of pharmacokinetic DDIs – phenotyping revisited.
- **Discover** the usefulness a micro-dosed cocktail approach of direct-acting oral anticoagulants (DOACs) in the prediction of DOAC-mediated DDIs.
- **Enjoy an update** on non-CYP related metabolic DDIs with particular emphasis on UGT-based 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.

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

WORKSHOP PROGRAMME

May 27th, 2018

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: Eckhard Freund & Özkan Yalkinoglu Guitar Duo – Inspiring & Meditative Guitar Music

May 28th, 2018

Monday

08:00 – 08:30 a.m.	Registration & Coffee
08:30 – 08:40 a.m.	Welcome Address and Introduction into the Workshop *Hartmut Derendorf, PhD, FCP*
	Session I: **Changes in the US/EU Regulatory Landscapes Part I** Chair: Hartmut Derendorf
08:40 – 09:20 a.m.	Keynote Lecture Drug Interactions From Lab to Labeling – A Regulatory Perspective *Joseph A. Grillo, PharmD, Associate Director for Labeling and Health Communication, FDA/CDER/OTS/Office of Clinical Pharmacology, Washington D.C., USA*
09:20 – 09:30 a.m.	Discussion
09:30 – 10:10 a.m.	Keynote Lecture The new FDA Guidance on *In Vitro* Metabolism- and Transporter-Mediated Drug-Drug Interaction Studies *Aleksandra Galetin, PhD, Centre for Applied Pharmacokinetic Research, The University of Manchester, Manchester, UK*
10:10 – 10:20 a.m.	Discussion
10:20 – 10:50 a.m.	Coffee Break & Visit of the Poster Exhibition
10:50 – 11:30 a.m.	Keynote Lecture The new FDA *In Vitro* Metabolism- and Transporter-Mediated Drug-Drug Interaction Guidance – A Perspective from Practice *Andrew Parkinson, PhD, XPD Consulting, Shawnee KS, USA*

11:30 – 11.40 a.m.	Discussion
11:40 – 12:10 a.m.	Q & A of the Regulatory Session Panel Discussion *Joseph Grillo, PharmD, FDA, USA; Aleksandra Galetin, PhD, University of Manchester, UK; Andrew Parkinson, PhD, XPD Consulting, USA*
12:10 – 01:40 p.m.	Lunch
	Session I : **Changes in the US/EU Regulatory Landscapes Part II** Chair: Amin Rostami-Hodjegan
01:40 – 02:20 p.m.	Keynote Lecture PBPK Model Qualification and Reporting Procedures for Regulatory Submissions: A Consortium Perspective *Edgar L. Schuck, PhD, Modeling and Simulation, Clinical Pharmacology Sciences, MDC, Eisai, USA*
02:20 – 02:30 p.m.	Discussion
02:30 – 03:10 p.m.	Dynamic Drug Labels for Optimal Management of DDIs in Patient Care *David Burger, PharmD, Radboud University Medical Center, Nijmegen, The Netherlands*
03:10 – 03:20 p.m.	Discussion
03:20 – 03:50 p.m.	Assessment of Two DDIs Involving a Distinct Enzyme and Their Consequences on Morbi-Mortality *Béatrice Saint-Salvi, PhD, DDI Unit, ANSM, France*
03:50 – 04:00 p.m.	Discussion
04:00 – 04:30 p.m.	Coffee Break & Visit of the Poster Exhibition
	Session II **Phenotyping Revisited Part I** Chair: Robert Hermann
04:30 – 05:00 p.m.	Can DDIs of Direct-Acting Oral Anticoagulants (DOACs) be Predicted by Using a Micro-Dosed DOAC Cocktail Approach? *Gerd Mikus, MD, Heidelberg University Hospital, Heidelberg, Germany*
05:00 – 05:10 p.m.	Discussion
07:30 p.m.	Dinner

May 29th, 2018

Tuesday

Session III:
Sensitivity Assessment in PBPK: Foe or Friend
Chair: Amin Rostami-Hodjegan

08:30 – 09:05 a.m.	Deciphering Sensitivity Analysis in PBPK: Model Credibility, Uncertainty, Verification and Validation *George D. Loizou, PhD, Head of Computational Toxicology Team, Health Risks, HSL: HSE's Health & Safety Laboratory, Buxton, Derbyshire, UK*
09:05 – 09:15 a.m.	Discussion
09:15 – 09:50 a.m.	In Search of Sensitive Endogenous Markers for Transporter DDIs – Mechanistic Models for Creatinine and Coproporphyrin I *Aleksandra Galetin, PhD, Centre for Applied Pharmacokinetic Research, The University of Manchester, Manchester, UK*
09:50 – 10:00 a.m.	Discussion
10:00 – 10:30 a.m.	Coffee Break & Visit of the Poster Exhibition

Session II:
Phenotyping Revisited Part II
Chair: Robert Hermann

10:30 – 11:10 a.m.	Keynote Lecture Mechanistic Assessment of Pharmacokinetic DDIs – Phenotyping Revisited *Uwe Fuhr, MD, University of Cologne, Cologne, Germany*
11:10 – 11:20 a.m.	Discussion

Session I (Continued): Changes in the US/EU Regulatory Landscapes Part II

Chair: Amin Rostami-Hodjegan

11:20 – 11:50 a.m.	Q & A of the Regulatory Session Panel Discussion *Edgar L. Schuck, PhD, Eisai, USA; David Burger, PharmD, Radboud University Medical Center, The Netherlands; Béatrice Saint-Salvi, PhD, DDI Unit, ANSM, France*
11:50 – 01:30 p.m.	Lunch

Session IV: Non-CYP Related Metabolic DDIs

Chair: Robert Hermann

01:30 – 02:15 p.m.	Non-CYP Related Metabolic DDIs with Particular Emphasis on UGT-based DDIs *Janne T. Backman, MD, Department of Clinical Pharmacology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland*
02:15 – 02:25 p.m.	Discussion
02:25 – 03:00 p.m.	Coffee Break & Visit of the Poster Exhibition

Poster Session: Presentation of Selected Posters

Chair: Oliver von Richter

03:00 – 04:00 p.m.	Short Presentation of Selected Posters *Presentation of 4 selected posters with 10 minutes presentation and 5 minutes discussion*

Q & A Session

Chair: Hartmut Derendorf & Oliver von Richter

04:00 – 04:30 p.m.	Q & A Session Involving Sessions II – IV
04:30 p.m.	Concluding Remarks End of Meeting & Departure

For more information please also visit:
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 request for Sunday, May 27th and Tuesday May, 29th. Taxi from and to the Airport is approx. 100 Euros. 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 2018 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 27th from 06:00 p.m. – 08:00 p.m., Monday May 28th from 08:00 a.m. – 05:00 p.m., and on Tuesday May 29th from 08:00 a.m. – 01:30 p.m. Please be prepared to mount your poster during registration on Sunday, May 27th or latest on Monday, May 28th, 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, 2018, 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, 27th to 29th, 2018
Venue	Marbach Castle +49 (0)7735 – 8130 D-78337 Öhningen info@schlossmarbach.de
Times	May 27th 2018 Afternoon: individual arrival, come together, come together activity, come together dinner, acoustic guitar concert Scientific Programme: May 28th 2018 Start 08:30 a.m. – Finish 05:00 p.m. May 29st 2018 Start 08.30 a.m. – Finish 04:30 p.m.
Registration & Coffee	May 27th 2018 03:00 p.m. May 28th 2018 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

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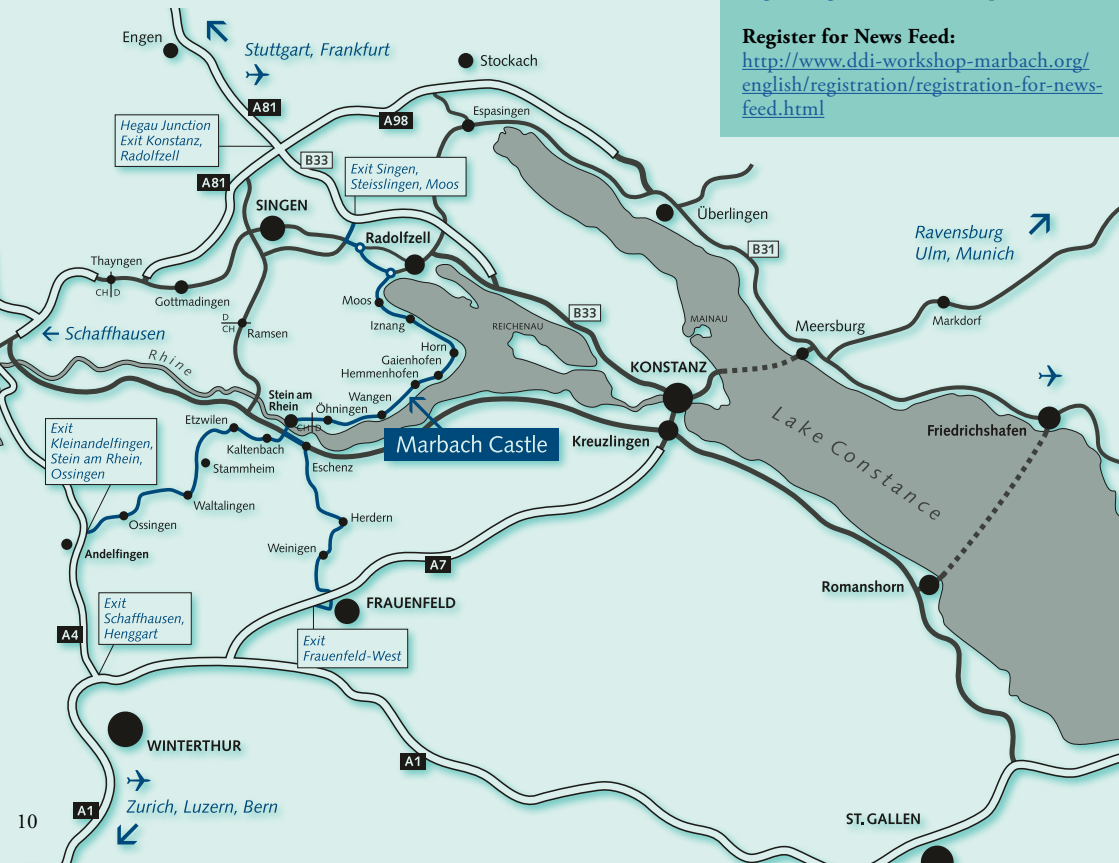

Registration Form

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 27th to 29th, 2018	1.960,00 €	☐
3-Day Participation from May 27th to 29th, 2018, early bird fee, (i.e. registration and payment of workshop fee until end of February 2018 or members of ACCP, DMDG or BioLago)	1.860,00 €	☐
2-Day Participation on May 28th and 29th, 2018 only	1.860,00 €	☐
2-Day Participation on May 28th and 29th, 2018 only, in combination with early bird fee (conditions see above)	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 2018. 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.