DIE AKADEMIE FRESENIUS

Where Experts Meet!

International Akademie Fresenius Conference

Regulatory Toxicology of Active Substances in Plant Protection Products

2 and 3 December 2019 in Mainz/Germany

Highlights

In vitro comparative metabolism studies

- Report from the EFSA Workshop: Data requirement, human relevance of animal data

EFSA future developments

- Development of adverse outcome pathways (AOP)
- In vitro screening battery

Cumulative assessment and combined exposure

- Cumulative assessment groups and tools used to draft scientific reports
- Dietary and non-dietary combined risk assessment

QSAR and read-across

- Assessment of genotoxicity and general toxicity of metabolites in residues
- Use of in silico tools

Genotoxicity of active substances

- Hurdles and challenges
- In vivo comet assay

Impurities

- Impurity profiles of active substances

Evaluation of public literature

- Relevance and reliability
- SciRAP tool

Benchmark dose modelling

- Current state of the approach
- Regulatory use

The Experts

Anna Beronius Karolinska Institute | **Bas Bokkers** Dutch National Institute for Public Health and the Environment (RIVM) | **Damian Bowen** ERM – Environmental Resources Management | **Susy Brescia** British Health and Safety Executive, Chemicals Regulation Division (HSE CRD) | **Agathi Charistou** Benaki Phytopathological Institute | **Tamara Coja** Austrian Agency for Health and Food Safety (AGES) | **Mark Cronin** Liverpool John Moores University | **Markus Frericks** BASF | **Ellen Fritsche** IUF – Leibniz Research Institute for Environmental Medicine | **Susanne Hougaard Bennekou** Danish Technical University (DTU) | **Johann Kaltenhäuser** German Federal Institute for Risk Assessment (BfR) | **Carsten Kneuer** German Federal Institute for Risk Assessment (BfR) | **Alfonso Lostia** European Food Safety Authority (EFSA) | **Bette Meek** University of Ottawa | **Susanne Rudzok** German Federal Institute for Risk Assessment (BfR) | **Rositsa Serafimova** European Food Safety Authority (EFSA) | **Emanuela Testai** Italian National Institute of Health (ISS) | **Manuela Tiramani** European Food Safety Authority (EFSA)

INSTITUT FRESENIUS

SGS

The Programme

Get-Together on Sunday, 1 December 2019

Will you arrive on Sunday? Come to the hotel bar at 8 p.m. and meet other participants and experts in a relaxed atmosphere.

Monday, 2 December 2019

9.00 Registration and coffee and tea

9.30 Welcome address by Akademie Fresenius and the Chair

Tamara Coja, Austrian Agency for Health and Food Safety (AGES), Austria

Metabolism studies

9.40 Report from the 2018 EFSA Workshop „In vitro comparative metabolism studies in regulatory pesticide risk assessment": Data requirement in vitro comparative metabolism study

- Minimum amount of information to be included in the study protocols and provided
- Key elements to be considered for the interpretation of the study's outcome

Emanuela Testai, Italian National Institute of Health (ISS), Italy

10.05 In vitro comparative metabolism studies in regulatory pesticide risk assessment: Human relevance of animal data

- Assessment of the potential for thyroid disruption for human health and investigation whether liver enzyme induction is responsible for thyroid disruption
- Key elements to be measured to evaluate the liver enzyme induction-mediated thyroid disruption

Alfonso Lostia, European Food Safety Authority (EFSA), Italy

10.30 Panel discussion
10.50 Coffee and tea break

Cumulative assessment

11.20 Cumulative assessment groups from a toxicological point of view – example: "Establishment of cumulative assessment groups of pesticides for their effects on the nervous system/thyroid" – tools used to draft scientific reports, e.g. basic principles of

- Scientific Opinion on the guidance on the use of the weight of evidence (WoE) approach in scientific assessments
- Guidance on expert knowledge elicitation in food and feed safety risk assessment

Susanne Hougaard Bennekou, Danish Technical University (DTU), Denmark

11.45 What can we take from cumulative assessment groups (CAG) for dietary and non-dietary combined risk assessment?

- Basis of CAGs and their validity
- Application to dietary and non-dietary combined risk assessment

Susy Brescia, Health and Safety Executive, Chemicals Regulation Division (HSE CRD), UK

12.10 Panel discussion
12.30 Lunch

Evaluation of public literature

13.30 Assessment of public literature – how to appropriately decide upon relevance and reliability?

Johanna Kaltenhäuser, German Federal Institute for Risk Assessment (BfR), Germany

13.55 Systematic evaluation of in vitro and in vivo data for health risk assessment of chemicals – the SciRAP tool

- Evaluation of data for health risk assessment and movement towards systematic review methodology in health risk assessment – advantages and challenges
- The SciRAP initiative and tool

Anna Beronius, Karolinska Institute, Sweden

14.20 Panel discussion
14.40 Coffee and tea break

Benchmark dose modelling

15.10 The benchmark dose (BMD) approach: Basic principles and recent developments

- Deriving a point of departure for risk assessment
- Incorporating all model results by model averaging

Bas Bokkers, National Institute for Public Health and the Environment (RIVM), The Netherlands

15.35 Overcoming hurdles in regulatory use of the BMD concept

Susanne Rudzok, German Federal Institute for Risk Assessment (BfR), Germany

16.00 Panel discussion
16.20 Short break

Substance evaluation

16.35 Genotoxicity and active substance evaluation: Hurdles and challenges, some examples and obstacles

- Member State perspective

Carsten Kneuer, German Federal Institute for Risk Assessment (BfR), Germany

17.00 Genotoxicity and active substance evaluation: Applicability of follow-up in vivo tests, especially in vivo comet assay

- Overview of positive in vitro data
- Appropriate in vivo follow up

Damian Bowen, ERM – Environmental Resources Management, UK

17.25 Panel discussion
17.45 End of the first conference day

18.30 Departure time for the evening event

After the first conference day Akademie Fresenius would like to invite you to a leisurely evening at the vineyard of Joachim Flick in the wine-growing region Rheingau. You have the opportunity of better getting to know other participants you met during the day over a relaxed wine tasting and meal. Don't miss out on this opportunity!

Tuesday, 3 December 2019

8.30 Welcoming speech by the Chair

Susanne Hougaard Bennekou, Danish Technical University (DTU), Denmark

QSAR and read-across

8.40 In silico prediction of the toxicity and genotoxicity of metabolites in residues

- Application of QSAR to predict the toxicity of metabolites and read-across of data from the parent substance to the metabolite
- Methods to assess uncertainties in predictions of toxicity

Mark Cronin, Liverpool John Moores University, UK

9.05 Use of QSAR and read-across for assessment of genotoxicity and general toxicity of metabolites in residues of plant and animal origin – how far we are and how certain do we want to be? Industry perspective

- Chemical descriptors, applicability domain, chemical similarity, data quality and ownership
- Training of QSAR models, read-across and weight of evidence for higher tier evaluation

Markus Frericks, BASF, Germany

9.30 Read-across and metabolites: A few thoughts from a regulator and an example

- When does a "grouping concept" make sense and when it does not?
- Difficulties in identification of a "lead molecule" for potential toxicity testing

Tamara Coja, Austrian Agency for Health and Food Safety (AGES), Austria

9.55 Panel discussion
10.25 Coffee and tea break

10.55 Use of in silico tools for prediction of genotoxicity of pesticides and their metabolites – results from a recent EFSA project related to use of in silico methods for prediction of genotoxicity of pesticides and their metabolites

- Main findings, main conclusions and recommendations

Rositsa Serafimova, European Food Safety Authority (EFSA), Italy

11.25 Questions & answers

Impurities

11.35 The impurity profile of an active substance – assessment of the toxicological relevance of the impurities: Hurdles and challenges – Member State perspective

- Assessment of the reference source specifications during the renewal of active substance approval
- Toxicological relevant impurities

Agathi Charistou, Benaki Phytopathological Institute, Greece

12.00 Panel discussion
12.15 Lunch

EFSA future developments

13.45 Current developments on EFSA level: Projects, ongoing activities, outputs

Manuela Tiramani, European Food Safety Authority (EFSA), Italy

14.15 Questions & answers

14.25 Application of AOPs to address biological plausibility of associations observed in epidemiological studies for pesticides

- Assessing mechanistic knowledge to support regulatory application in adverse outcome pathway (AOP) descriptions
- Systematic consideration of the extent of supporting mechanistic data for regulatory application

Bette Meek, University of Ottawa, Canada

14.50 An in vitro screening battery for developmental neurotoxicity evaluation: Past and current scientific and regulatory activities

Ellen Fritsche, IUF – Leibniz Research Institute for Environmental Medicine, Germany

15.15 Panel discussion
15.40 End of the conference

Information available online at:
www.akademie-fresenius.com/2730

The Experts

Anna Beronius is an Assistant Professor and a Lecturer at the Institute of Environmental Medicine, Karolinska Institute, Stockholm. Her research focuses on structured methods for evidence evaluation and integration in health risk assessment of chemicals. She is one of the initiators and developers of the SciRAP web-based platform.

Bas Bokkers is a Modeller and Toxicologist and has been working at the Dutch National Institute for Public Health and the Environment (RIVM) since 2017, currently at the RIVM Centre for Safety of Substances and Products. His work primarily concerns benchmark dose (BMD) modelling, kinetic modelling of chemicals and probabilistic risk assessment.

Damian Bowen is a Mammalian Toxicologist working for ERM for over 9 years within the regulatory services group. He has spent time within the contract research organisation arena working as a Genetic Toxicology Study Director.

Susy Brescia works as a Regulatory Toxicologist at the UK HSE CRD and has many years of experience in the risk assessment of pesticides, biocides and industrial chemicals.

Agathi Charistou is a Regulatory Toxicologist in the Laboratory of Toxicological Control of Pesticides at the Benaki Phytopathological Institute in Greece with long experience in the evaluation of mammalian toxicology studies and non-dietary exposure assessment to both plant protection products and biocides.

Tamara Coja is a Biologist and has been working as a Regulatory Toxicologist and Senior Expert at the Austrian Agency for Health and Food Safety in Vienna, Division for Plant Protection Products, Department of Toxicology since 2007. Her special regulatory interest is in toxicity of metabolites in residues of plant and animal origin and in groundwater.

Mark Cronin is a Professor of Predictive Toxicology at Liverpool John Moores University, England. He has been working in the area of computational toxicology for over 30 years to predict both the human health and environmental effects of chemicals.

Markus Frericks is a Biologist and Toxicologist and works as a Regulatory Toxicologist at BASF in Mannheim. He is the Vice Chair of the Working Group on Computational Toxicology from the German Society of Toxicology and the Chair of the ECPA Working Group on Genotoxicity-QSAR.

Ellen Fritsche is appointed as a full Professor by the Heinrich-Heine-University in Dusseldorf. She holds a Group Leader position at the IUF - Leibniz Research Institute for Environmental Medicine.

Susanne Hougaard Bennekou joined the Division of Risk Assessment and Nutrition at the National Food Institute of the Technical University of Denmark as a Senior Advisor in toxicology in January. She has previously worked as a Senior Advisor in the Pesticide Division of the Danish EPA. She was the Vice-Chair of the EFSA PPR panel and since last year she has been a Vice-Chair of the EFSA Scientific Committee.

Johanna Kaltenhäuser has been working in the Unit "Steering and Overall Assessment" in the Pesticides Safety Department of the German Federal Institute for Risk Assessment.

Carsten Kneuer is a Toxicologist and the Head of the Unit "Toxicology of Active Substances and their Metabolites" in the Pesticides Safety Department of the German Federal Institute for Risk Assessment.

Alfonso Lostia is a Biochemist and joined EFSA in 2018 where he works in the Pesticide Unit on the pesticide risk assessment. Before joining EFSA, he has worked at the Joint Research Centre in the Unit of Chemical Safety in the area of predictive toxicology.

Bette Meek is the Associate Director of Chemical Risk Assessment at the McLaughlin Centre for Risk Science, Faculty of Medicine, University of Ottawa. She has managed chemical risk assessment programmes within Health Canada and contributed to or led initiatives in developing methodology in chemical risk assessment.

Susanne Rudzok is a Biochemist and a Toxicologist and has been working as a Scientific Officer in the Unit "Toxicology of Active Substances and their Metabolites" in the Pesticides Safety Department of the German Federal Institute for Risk Assessment.

Rositsa Serafimova has been working as a Scientific Officer in EFSA since 2012, first in the Food Ingredients and Packaging Unit and currently in the Pesticides Peer Review Unit. Before joining EFSA she worked at the European Commission Joint Research Centre and at the Laboratory of Mathematical Chemistry, Burgas University.

Emanuela Testai is a Toxicologist in the Environment and Health Department at the ISS, the Italian National Institute of Health. Her expertise is focused on mammalian toxicology, alternative methods, toxicokinetics and risk assessment, dealing with research and regulatory activities as well.

Manuela Tiramani has been working as the Head of the Pesticide Peer Review Unit in the Department of Scientific Evaluation of Regulated Products at EFSA since this year. She joined EFSA in 2005 as a Scientific Officer in the Pesticide Unit and became Head of the FEED Unit in 2015.

About

Who do you meet?

Groups that should take part:
Managing directors, boards of directors, managers, consultants and scientists in the fields of:

- Toxicology
- Registration
- Marketing & distribution
- Human exposure & risk assessment
- Research & development
- Product stewardship & responsible care
- Human/Consumer safety – crop protection

Sectors that should take part:

- Agrochemical industry
- Research institutes
- Authorities (agricultural inspection offices, registration and control authorities)
- Professional associations
- Contract laboratories

Trade Exhibition

Our conference provides you with the opportunity of presenting your company in a trade display. Present your products and services and reach out to your specific target groups. We would be happy to provide you with information on all the various options available – from displaying product information to an exhibition stand – with no further obligation on your part.

Use the attached fax reply sheet to request our information material. Or simply call us. We would be more than pleased to assist you personally.

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The Organiser

For 25 years, Akademie Fresenius has been your partner for practice-orientated training on all the latest topics surrounding the safety and quality of food, consumer goods and chemical products along the whole production chain. Our portfolio not only includes international conferences but also offers national trade meetings, intensive practical seminars and training in small work groups.

Our events are designed to promote an active exchange amongst our participants and offer the perfect platform for bringing the industry, the scientific sector, the authorities and the consulting field together. Excellent service, all-inclusive. Our wide-ranging advanced training opportunities contribute to giving our customers the competitive edge in all quality assurance, risk assessment, legal, production and technical questions.

Akademie Fresenius is a joint venture between Cognos, one of the largest private and independent education groups in Germany, and SGS Institut Fresenius, one of the leading German providers of chemical laboratory analysis.

You can find details on upcoming and new events at

www.akademie-fresenius.com

29 to 30 October 2019 in Cologne/Germany

3rd International Akademie Fresenius MIXTOX Conference "Toxicity of Chemical Mixtures: Risk, Hazard and Exposure Assessment"

Please request more information now!
www.akademie-fresenius.com/2717

Do you have any questions?

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Registration

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DIE AKADEMIE FRESENIUS

Participation

- ◯ I would like to take part in the International Akademie Fresenius Conference **„Regulatory Toxicology of Active Substances in Plant Protection Products", 2 and 3 December 2019 in Mainz/Germany.** Fee: € 1,895.00 plus VAT.
- ◯ I am a **representative of an authority or a public university** and therefore eligible for a reduced fee of € 795.00 plus VAT (please provide evidence). The reduced fee cannot be combined with other rebates.
- ◯ I would like to take part in the **evening event on 2 December 2019** (included in the above price).

Event Documentation

- ◯ Unfortunately, I am unable to attend. Please send me the complete documentation for € 295.00 plus VAT.

Trade Exhibition

- ◯ Please send me information on available options for trade exhibition and presenting product information.

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Terms of Participation and Purchase
The registration fee includes the event participation, event documentation, lunch, coffee breaks, beverages as well as the evening event. You will receive written confirmation of your registration. Upon receiving our invoice, please transfer the amount due without further deductions before the event begins.
The price of the event documentation includes a hard copy of the documentation as well as an access code to the secure Akademie Fresenius download area. Both the documents and the secure access code will be dispatched around two weeks after the event and as soon as advance payment has been received.

Group Reductions
For joint bookings received from one company we grant a 15% discount from the third participant onwards.

Terms of Cancellation
Written cancellations or transfers will be accepted free of charge up to four weeks prior to the start of the event. After this date and up to a week prior to the start of the event we will reimburse 50% of the registration fee. We cannot, unfortunately, provide refunds for later cancellations. Please note that you can name a substitute free of charge at any time.

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By registering, you agree to our General Terms and Conditions as well as to our Privacy Policy. You can find our GTC on the internet (www.akademie-fresenius.com/general-terms) or receive them on request.

Personal Data
The Akademie Fresenius will keep your data for the purpose of organising this event. We will under no circumstances use your data for commercial trade purposes. In signing this form you consent to our occasionally contacting you by mail, email, fax or phone (please strike through if unwanted) in order to provide you with further information from our company. You can, of course, withdraw your consent whenever you wish. Occasionally we go around taking photos and videos at our events. These are then published anonymously on our website. Further information can be found at: www.akademie-fresenius.com/dataprotection.

Picture Credit

Venue

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We have reserved a limited number of rooms for our participants at reduced rates at the hotel. These rooms can be booked up to four weeks prior to the start of the event. Please book early and directly through the hotel quoting "Akademie Fresenius" as reference.