Past, Present and Future Challenges in Risk Assessment – Strengthening Consumer Health Protection

Joint International Symposium, November 30th and December 1st, 2017, Berlin

MINISTRY OF FOOD AND DRUG SAFETY
National Institute
of Food and Drug Safety Evaluation

DTU Food
National Food
Institute

anses
French agency for food, environmental and occupational health & safety
Investigate, evaluate, protect

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Past, Present and Future Challenges in Risk Assessment – Strengthening Consumer Health Protection

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1 Greetings from Professor Dr Dr Andreas Hensel and Professor Dr Reiner Wittkowski (BfR)

President and Vice-President of the German Federal Institute for Risk Assessments (BfR), Berlin, Germany

Dear Guests,

Professor Dr Dr Andreas Hensel

we are honoured to welcome you at our Joint International Symposium “Global Past, Present and Future Challenges in Risk Assessment – Strengthening Consumer Health Protection”, which we have organised in cooperation with ANSES, DTU and NIFDS in order to celebrate the BfR’s 15th anniversary.

Over the past 15 years, the German Federal Institute for Risk Assessment (BfR) has been working for consumer health protection in Germany and Europe. We are very delighted to jointly look back on the last one and a half decades of risk assessment. During the next days we will discuss current activities and future challenges in consumer health protection on the national and the international level!

Professor Dr Reiner Wittkowski

Ensuring food safety and consumer protection has always been a complex task.
Yet, in an ever more interconnected world it is becoming an increasingly complex undertaking. The globalisation of food production and trading inevitably entails new challenges for consumer health protection. The safety of food and feed has to be guaranteed along global and intricate supply chains. In Germany and Europe, the supply of and reliance on food from all over the world is steadily growing. Consequently, consumer health protection agencies have to continuously improve and adapt the requirements that have to be met for rigorous scientific assessment as well as the reduction and effective communication of risks.

Global threats require global responses – only together we will be able to tackle the issues the future holds in store. This symposium is an opportunity to bring you together, to form networks and future alliances for international cooperation in the field of risk assessment.

We are very much looking forward to many interesting discussions on ideas and visions that will help us to succeed in our joint quest for common solutions.

Sincerely,

Professor Dr Dr Andreas Hensel

Professor Dr Reiner Wittkowski

2 Greetings from Dr Sunhee Lee (NIFDS)

Director General, National Institute of Food and Drug Safety Evaluation (NIFDS), Republic of Korea

With technological developments, we now lead more comfortable lives, but we also face greater risks for public health and safety. The emerging hazards and insufficient information on safety have, therefore, increased demands on roles of governments. As threats are connected across-borders, global cooperation and response to risks is significant for safety.

Dr Sunhee Lee

The National Institute of Food and Drug Safety Evaluation (NIFDS), an affiliated organisation of the Ministry of Food and Drug Safety (MFDS), is responsible for risk assessment of foods and medicinal products for human use. The NIFDS signed an MoU with the German Federal Institute of Risk Assessment (BfR) in 2010, the first step of cooperation with European countries. Since then the NIFDS and BfR have been working together in various sectors, especially for exchange of technologies and human resources, and organising joint symposiums.

As a close partner, the NIFDS sincerely congratulates the BfR to its 15th anniversary. We believe that over those 15 years, the BfR has become one of the most reliable institutes for accurate risk assessments in the field of public health protection. We are very pleased and grateful to have the opportunity to participate in this symposium in Berlin with many organisations for risk assessment such as the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) and the Danish National Food Institute (DTU Food).

This symposium will be a good chance to discuss the past, present, and future challenges of risk assessment. I am sure that the symposium will provide a good opportunity for all participating institutes to strengthen international collaboration for improving health and safety.

Thank you.

3 Greetings from Dr Roger Genet (ANSES)

Director General of the French Agency for Food, Environmental and Occupational Health & Safety (ANSES), France

The many challenges we all face in food safety can only be met if we work together in a global approach for risk assessment and consumer protection.

Dr Roger Genet

Just like food knows no borders, science also has no borders, which is why cooperation, at European and international level, is so important for the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) in order to ensure the highest level of food safety for our citizens.

It is thus of paramount importance to develop strong European and international scientific collaborations. They may be formalised in agreements such as the tripartite collaboration agreement signed in 2010 between the German Federal Institute for Risk Assessment (BfR), the National Food Institute at the Technical University of Denmark (DTU-Food) and ANSES, and the Memorandum of understanding signed in 2016 between the National Institute of Food and Drug Safety Evaluation (NIFDS) of the Republic of Korea and ANSES. These collaborations favour facilitating greater scientific and technical cooperation, enabling us to develop knowledge and exchange information and thus improve our ability to carry out our respective missions in the areas of food safety and consumer protection.

This joint event illustrates the variety of challenges that we faced in the past, currently face and may face in the future. The co-organisation of this event is a strong message that we would like to give about the importance of cooperating at European and at international level, to tackle the many challenges in risk assessment. Special thanks to the BfR for hosting this event as part of its 15 years anniversary.

4 Greetings from Dr Flemming Bager (DTU)

Head of Division, Division for Risk Assessment and Nutrition, National Food Institute (DTU), Denmark

Dear Guests,

Dr Flemming Bager

we are honored to welcome you at our Joint International Symposium “Global Past, Present and Future Challenges in Risk Assessment – Strengthening Consumer Health Protection”, which we have organised in cooperation with ANSES, DTU and NIFDS in order to celebrate the BfR’s 15th anniversary!

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Ensuring food safety and consumer protection has always been a complex task. Yet, with an ever more interconnected world it is becoming an even more complex undertaking. The increasing globalisation of food production and trading inevitably entails new challenges for consumer health protection. The safety of foods and feeds has to be guaranteed along global and increasingly intricate supply chains. In Germany and Europe, the supply of and reliance on food from all over the world is steadily growing. Consequently, consumer health protection agencies have to continuously improve and adapt the requirements that have to be met for rigorous scientific assessment as well as the reduction and effective communication of risks.

Global threats require global responses – only together will we be able to tackle the issues the future holds in store. We therefore want to use this symposium as an opportunity to bring you together, to form networks and future alliances for international cooperation in the field of risk assessment.

We are very much looking forward to an exciting symposium with many interesting discussions, ideas and visions that help us to succeed in our joint quest for common solutions.

5 Programme

Thursday 30th November 2017

Opening

9:00–9:15 am
Welcome and opening remarks from BfR
Prof. Dr Dr Andreas Hensel, BfR, Germany

9:15–9:25 am
Opening remarks from NIFDS
Dr Sunhee Lee, NIFDS, Republic of Korea

9:25–9:35 am
Opening remarks from ANSES
Dr Roger Genet, ANSES, France

9:35–9:45 am
Opening remarks from DTU
Dr Flemming Bager, DTU, Denmark

Past

Chair: Prof. Dr Dr Andreas Hensel, BfR

9:45–10:30 am
2002 – A new dawn in European food safety
Prof. Dr Tony Hardy, European Food Safety Authority, EFSA

10:30–11:00 am
Microbiological threats: how have Germany and France responded to the crisis with enterohemorrhagic *E. coli* (EHEC) and what about the future?
Dr Elisabeth Hauser, BfR, Germany
Dr Patrick Fach, ANSES, France

11:00–11:30 am
The fascinating world of analytical chemistry – a continuing story of contaminants in food
Prof. Dr Jørn Smedsgaard, DTU, Denmark

11:30 am–1:00 pm
Lunch

Present: Parallel Sessions A–C

Session A: Microbiological safety

Chair: Dr Sara Pires, DTU

1:00–1:30 pm
Antimicrobial resistance I: Situation and strategies in Europe
Dr Sofia Duarte, DTU, Denmark

1:30–2:00 pm
Antimicrobial resistance II: Situation and strategies in the Republic of Korea
Dr Soo Hwan Suh, NIFDS, Republic of Korea

2:00–2:30 pm
Emerging pathogens: foodborne viruses
Prof. Dr Reimar Johne, BfR, Germany

2:30–2:50 pm
Coffee

2:50–3:20 pm
Microbial food safety in the age of whole genome sequencing
Maria Borowiak, BfR, Germany

3:20–3:50 pm
Contribution of whole genome sequencing to source attribution of campylobacteriosis in France
Amandine Thépault, ANSES, France

Session B: Chemical safety

Chair: Dr Meekyung Kim, NIFDS

1:00–1:30 pm
Endocrine disruptors: EU-criteria and guidance document
Dr Vera Ritz,
Dr Philip Marx-Stölting,
BfR, Germany

1:30–2:00 pm
Risk assessment of aflatoxins
Prof. Dr Hyang Sook Chun, NIFDS, Republic of Korea

2:00–2:30 pm
Facing new facts: marine biotoxins as a challenge for seafood safety
Dr Charlotte Grastilleur, ANSES, France

2:30–2:50 pm
Coffee

2:50–3:20 pm
Analytical challenges for nanomaterials in risk assessment
Dr Katrin Löschner, DTU, Denmark

3:20–3:50 pm
Fighting unknown chemicals: analytical strategies for risk prioritisation
Eelco Pieke, DTU, Denmark

Session C: Methodologies and harmonisation

Chair: Prof. Dr Gérard Lasfargues, ANSES

1:00–1:30 pm
Data challenges to improve dietary exposure assessments
Sisse Fagt, DTU, Denmark
Dr Oliver Lindtner, BfR, Germany
Dr Chris Roth, ANSES, France

1:30–2:00 pm
Mixtures prioritisation based on exposure and hazard
Dr Amélie Crépet, ANSES, France

2:00–2:30 pm
Lessons learned from recent food fraud in Korea
Young-Ho Koh, NIFDS, Republic of Korea

2:30–2:50 pm
Coffee

2:50–3:20 pm
How to build a crystal ball – the art of emerging risk identification
Dr Tobin Robinson, European Food Safety Authority, EFSA

3:20–3:50 pm
Risk-benefit assessment of foods
Dr Maarten Nauta, DTU, Denmark

Poster Session

3:50–6:00 pm
Current topics in risk assessment

Friday 1st December 2017

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Chair: Dr Antje Grobe, Dialog Basis

Tools and methods

9:00–9:45 am
Keynote: Using 21st century science to improve risk-related evaluations
Dr Ellen Mantus, National Academy of Sciences, USA

9:45–10:05 am
Introduction of the data management and risk assessment program: its application and expected effects on risk assessment for the future
Dr Myung-Sil Hwang, NIFDS, Republic of Korea

10:05–10:25 am
Risk assessment modelling and knowledge integration platform
Matthias Filter, BfR, Germany

10:25–11:00 am
Coffee

Societal challenges

11:00–11:20 am
Linking risk and sustainability assessment to meet current and future challenges in circular economy, food safety, and consumer protection
Prof. Dr Peter Fantke, DTU Management, Denmark

11:20–11:40 am
Trust in science, interaction with stakeholders and risk communication
Prof. Dr Gérard Lasfargues, ANSES, France

11:40 am–12:00 pm
Globalised markets – local risk assessment?
Prof. Dr Dr Andreas Hensel, BfR, Germany

Poster award

12:00–1:15 pm
Prof. Dr Dr Andreas Hensel, BfR, Germany

Panel discussion

12:15–13:00 pm
Future challenges and solutions in risk assessment
Dr Ellen Mantus, National Academy of Sciences, USA
Dr Meekyung Kim, NIFDS, Republic of Korea
Prof. Dr Peter Fantke, DTU Management, Denmark
Dr Charlotte Grastilleur, ANSES, France
Prof. Dr Dr Andreas Hensel, BfR, Germany

Conclusion and farewell

1:00–1:15 pm
Prof. Dr Dr Andreas Hensel, BfR, Germany

6 Abstracts

6.1 2002: a new dawn in European food safety

Prof. Dr Tony Hardy
European Food Safety Authority, EFSA, Hampshire, UK

Major European food scares in the 1980s and 1990s, principally bovine spongiform encephalopathy (BSE) and dioxin contamination of animal feed, caused widespread of consumer trust in food safety, loss of confidence in food trade and seriously damaged trust in public authorities. This resulted in coordinated action at European and national levels to separate risk assessment from risk management, to separate specialist committees from policy and to increase transparency. In 2002 the EU General Food Law Regulation (Reg EC 178/2002) laid down the principles and requirements of food law and created the independent European Food Safety Authority (EFSA). National legislations established National Food Agencies in Member States.

The last 15 years have seen the strengthening of this new food safety infrastructure accompanied by the further development of scientific methodologies, increased transparency of the risk assessment process, the greater independence of specialist scientific experts drawn primarily from Member States, rigorous evaluation of data and its sources, advances in technology and digital platforms, data sharing and greater collaboration across Europe and beyond, underpinned by internationally funded research. Examples will illustrate some of these changes and consider how food safety has improved. Technology, global data availability and wider sharing will provide both challenges and opportunities for the future.

6.2 Microbiological threats: how have Germany and France responded to the crisis with enterohemorrhagic *E. coli* (EHEC) and what about the future?

Dr Patrick Fach[1], Dr Elisabeth Hauser[2]

[1] French Agency for Food, Environmental and Occupational Health & Safety (ANSES), Maisons-Alfort, France
[2] German Federal Institute for Risk Assessment (BfR), Berlin, Germany

In 2011, a large outbreak of an unusual bacterial strain occurred in Europe. This strain was characterised as a hybrid of an enteroaggregative *Escherichia coli* (EAEC) and a Shiga toxin-producing *E. coli* (STEC) strain of the serotype O104:H4. The National Reference Laboratory for *E. coli* in Germany (BfR) and the genomic 'IdentyPath Platform' of ANSES merged their efforts to face this exceptional *E. coli* outbreak. Based on the work of a PhD student shared by ANSES and the BfR, the two laboratories had published, just before the crisis, a Micro-array for the identification of the most common STEC seropathotypes associated with hemorrhagic colitis and Hemolytic Uremic Syndrome. This Micro-array included in particular genetic markers for detecting *E. coli* O104 and the gene encoding the Shiga toxin 2 (Stx2). The system was rapidly adapted to detect the major genetic markers (stx2, rfb_{O104}, $flic_{H4}$, ter, and aggR) characteristic of the O104:H4 outbreak strain and was made commercially available for rapid screening of food samples and confirmation of pure isolates. The molecular method developed by ANSES and the BfR was rapidly provided to all the EU member states via the European reference laboratory for *E. coli*.

Genotypes and virulence characteristic of O104:H4 isolates from different origins, sources and time periods were also obtained. The genomic 'IdentyPath Platform' of ANSES investigated by high throughput PCR the presence of 49 genes associated with enteropathogenic *E. coli* (EPEC), enteroaggregative *E. coli* (EAEC) and enterohemorrhagic *E. coli* (EHEC), while the BfR conducted Pulsed Field Gel Electrophoresis (PFGE) analyses. We showed that the EAEC virulence genes were only present in the STEC O104:H4 serotype but absent in other O104 serotypes (O104:H2, O104:H7 and O104:H21). The 2011 outbreak strains and the older O104:H4 strains from Germany (2001), Georgia and France (2009) clustered together at > 86.2 %. O104:H4 strains isolated between 2001 and 2009 differed for some plasmid encoded virulence genes compared to the outbreak strain from 2011. STEC O104:H21 and O104:H7 isolated in the US and Europe showed characteristic differences in their stx-type, virulence genes and PFGE profiles indicating that these have evolved separately. Sequencing the clustered regularly interspaced short palindromic repeats (CRISPR) locus of *E. coli* O104:H4 allowed the design of a $CRISPR_{O104:H4}$ real-time PCR test highly specific (99.06 %) and sensitive (100 %). This PCR assay did not cross react with *E. coli* O104 having H-types other than H4 and could be used for detecting STEC O104:H4 in complex matrices like foods. The collaborative work conducted jointly by ANSES and the BfR has been presented in particular at the Annual Meeting of IAFP (International Association for Food Protection) at Milwaukee, WI, USA in August 2011.

Following the O104:H4 outbreak, the genomic 'IdentyPath Platform' of ANSES and the BfR have reinforced their collaboration on *E. coli* to publish many common scientific papers dealing with 1) the molecular and virulence characterisation of other *E. coli* serotypes, 2) the CRISPR sequencing of various *E. coli* serotypes and pathotypes, 3) the design of a molecular approach for serotyping *E. coli* based on high throughput qPCR. In final, the "Molecular Risk Assessment" approach proposed by ANSES and the BfR resulted in the development of methods which can be used by the food industry to monitor pathogenic *E. coli*. The ongoing common research projects of BfR and ANSES on *E. coli* aim at anticipating outbreaks and crisis with new virulent strains of *E. coli* that can emerge in the future.

6.3 The fascinating world of analytical chemistry – a continuing story of contaminants in food

Prof. Dr Jørn Smedsgaard
Technical University of Denmark (DTU), National Food Institute, Lyngby, Denmark

Summary
The presentation will by a few examples from the last 10 years illustrating the fascinating challenge of the unexpected and/or unknown contaminants that may occur in food. While many harmful compounds are known, regulated and systematic monitored, the real challenge for the analytical chemist is the huge number of other potential harmful compounds that may occur in food and where knowledge and analytical methods is limited.

Abstract
Introduction of high resolution and accurate mass spectrometry some 20 years ago has over the last decade provided the analytical chemist with an amazing tool to identify and monitor a very wide range of compounds in food. Today, a skilled analytical chemist can easily find many hundreds of compounds in any type of food often many more. But even so, the chemical challenge is huge – a staggering number of more than 133 million unique chemical structures are reported in Chemical Abstracts, of these are several 100.000 natural products and in REACH more than 6.000 are registered with an additional 100.000 notified to as used by industry. Even the simplest organism will have more than 600 small compounds in their metabolism while several thousand compounds are found in complex organisms like plants and animals. And in complex combined and processed food we will find even more different compounds.

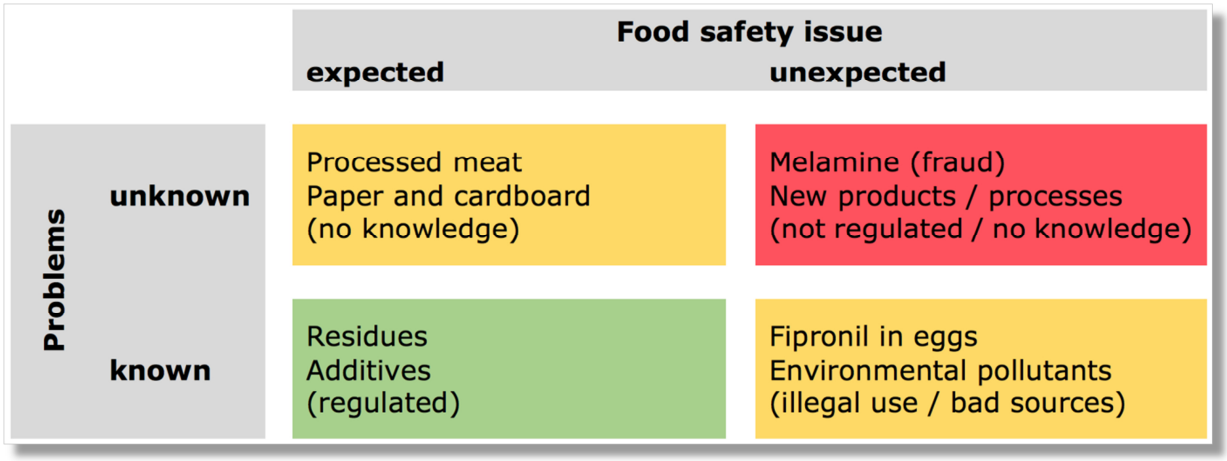
In this complex soup, we find the “good” natural occurring compounds (nutrients, vitamins, flavors etc.) we want but at the same time, we may find a huge number of compounds that may be of concern; whether those are natural occurring compounds or originate from processing, environment or other sources.

Many of these unwanted compounds are well-known and regulated by legislation and we have specific (target) analytical methods for food monitoring. However, the real challenge are all those compounds where toxicology has raised a concern, but where we lack data on their occurrence in food, hence the human exposure. Even worse are those compounds where we don’t have standards or may not know the chemical structure. If we focus on these latter groups of compounds and take the perspective of chemical food monitoring, we may divide the analytical challenge into two orthogonal domains:

- A concern is raised by toxicologist for specific compounds, therefore target monitoring is needed to find the occurrence to determine human exposure for a risk assessment – target monitoring.
- A concern raised by epidemiological studies, where the chemical risk factors (compounds) may not be known, therefore identification of these compounds is crucial to understand the problem – untargeted monitoring.

In the first case, the challenge is chemical food monitoring where we need to get authentic standards and develop methods to quantify in all relevant types of food. This in itself can be very challenging. However, the second case is far more complex as it may involve identification of chemical risk factors (compounds), including their chemical structure, the source and to quantify the occurrence.

The focus of the presentation will be on those compounds that are not regulated or where compounds may occur in unexpectedly, as illustrated by the yellow and red areas on the figure below.



Choosing a few examples from the last 10 years the discussion will focus on the chemical fascinating challenge for the analytical chemist:

Melamine– almost 10 years ago, the melamine scandal hit the news. Melamine was added to milk to give a high but false protein content. This case of fraud was driven by the methods used to sell milk to dairies. Similarly, new processes or new types of food may lead to new unexpected food safety issues whether intentionally or not.

Processed meat – epidemiological studies have shown that processed meat may increase the risk for colon cancer, however responsible the risk factors has not been found. One suggestion is the nitrosamines formed by the use of nitrite salts, however those known do not fit with the risk profile, therefore a hunt for other responsible compounds presently not known is on the way.

Natural compounds – huge number of fascinating natural occurring compounds are known in nature, many are definitely harmful, but in most case, we don't know their biological effects. New production and harvesting methods may lead to co-harvest of toxicogenic plants hence we introduce new chemical risks without knowing.

Fipronil – is a "nice" product that works well hence why not use it – but like doping it is banned for a reason. But as in doping a lot of efficient compounds are out there that can improve yield some are used deliberately (fraud) or due to lack of knowledge (mal-practices).

6.4 Antimicrobial resistance I: Situation and strategies in Europe

Dr Ana Sofia Ribeiro Duarte
Technical University of Denmark (DTU), Division of Genomic Epidemiology, Denmark

Antimicrobial resistance (AMR) is in the order of the day around the globe, and has received increased focus of public health and food safety authorities in recent years. Studies describing the occurrence of AMR pathogens and AMR determinants in humans, animals, foods or the environment appear at an astounding rate, representing a valuable data pool ready to be explored for the objective of AMR risk assessment. These studies result both from independent national initiatives and from international joint efforts to characterise the AMR situation globally, and on multiple fronts (human, animal, food, environment). Indeed, there seems to be general agreement on the fact that AMR needs to be tackled from a one health perspective.

Simultaneously, there are growing efforts for the development of AMR frameworks that can accommodate those data and assess the risk of AMR in humans exposed through different routes. Several challenges have been identified in this task – from the definition of hazard, to the use of new generation sequencing results, and missing links along the transmission pathway.

This talk reviews recent AMR-focused scientific work developed in Europe, both at national and international level, and introduces recent developments in the area of microbial risk assessment applied to AMR.

6.5 Antimicrobial resistance II: Situation and strategies in Korea

Dr Soohwan Suh
National Institute of Food and Drug Safety Evaluation (NIFDS), Food Microbiology division, Department of Food Safety Evaluation, Cheongju, Republic of Korea

The Korean government has been engaged in efforts to slow down the spread of antibiotic resistance by preparing national antibiotic resistance management measures. In 2003, the National Antimicrobial Resistance Management Program, which has been implementing monitoring, research, public campaigns and policies, was established to reduce antimicrobial resistance in both clinical as well as non-clinical areas. The outcomes of the management program include prohibition of antibiotics in formula feed (2011) and mandatory veterinary prescriptions for antibiotic uses. Tetracycline resistance rate in *E. coli* has been reduced in staple meats, beef, pork, and chicken due to the antibiotics reduction policy. In this presentation, we will not only show the changes of use/resistance rate of antibiotics in Korea over the past 15 years but also outline the national action plan that was established for combating antibiotic–resistant bacteria. In 2016, the Republic of Korea established a national action plan on antimicrobial resistance according to the WHO's global action plan and is pursuing one-health clinical and non-clinical national projects. As the control tower in the battle against antibiotic-resistance, the Korea Ministry of Food and Drug Safety will continue to strive to reduce antimicrobial resistance and champion the proper use of antibiotics.

6.6 Emerging pathogens: foodborne viruses

Prof. Dr Reimar Johne
German Federal Institute for Risk Assessment (BfR), Department of Biological Safety, Berlin, Germany

Foodborne viruses are increasingly recognised as causes of disease outbreaks in recent years. Their transmission mainly occurs by ingestion of food fecally contaminated during growing or handling, but may also involve consumption of meat products prepared from animals infected with zoonotic viruses. Besides the implementation of hygienic measures for prevention of food contamination, the further development of detection methods for viruses in food as well as the assessment of virus inactivation in food is of high priority.

Foodborne viruses contributed to several disease outbreaks during the last years. Prominent examples include a large gastroenteritis outbreak in Germany in 2012, in which nearly 11,000 children fell ill due to the consumption of norovirus-contaminated frozen strawberries. In another outbreak, about 1,500 patients diseased on hepatitis in several European countries after ingestion of a hepatitis A virus-contaminated frozen berry mix. Cases of hepatitis E are increasingly recognised in several European countries, which are suspected to be connected with the consumption of undercooked hepatitis E virus-contaminated pork products. In the latter case, a zoonotic virus transmission of the hepatitis E virus (HEV) with meat prepared from infected pigs is assumed. However, most of the other commonly recognised foodborne viruses, such as norovirus (NoV) and hepatitis A virus (HAV), are transmitted to food via fecal contamination of the environment, irrigation water, fertilizer or by direct contact with infected food handlers.

A major problem of foodborne viruses in risk assessment, food control and outbreak investigation is their detection in food. In contrast to most foodborne bacteria, the viruses cannot be propagated from food. Therefore, they have to be detected directly in the food matrix without any pre-amplification step. This challenges the sensitivity of the detection methods, which is often further decreased by the presence of PCR inhibitors in the food matrix. Only recently, standardised methods for NoV and HAV detection in several types of food are available (ISO15216). However, they are mostly laborious and their sensitivity should be increased in the future. New developments using inhibitor-removing columns are promising. In addition, novel techniques, e.g. Next Generation Sequencing, are in development.

In the last decade, HEV infections have been increasingly recognised in several industrialised countries. The HEV genotypes 3 and 4, which account for most of the infections in these countries, are zoonotic viruses with reservoirs in pigs and wild boars. In Germany, about 50 % of domestic pigs and 30 % of wild boars have HEV-specific antibodies. The HEV genome could also be detected in meat products containing liver or meat of pigs and wild boars. However, it is not known so far whether the contained virus is still infectious or has been inactivated due to heating, curing or salting during production of the respective meat products. The measurement of infectivity is difficult because of a lack of reliable and efficient cell culture systems for HEV. We isolated an HEV strain from a chronically infected patient and optimised the cell culture conditions. Using this system, we were able to investigate the long-term stability of HEV and its inactivation by short-term heating in a first set of experiments. Further analyses using this system should identify risk products for HEV transmission and provide strategies for inactivation of HEV in food products.

6.7 Microbial food safety in the age of whole genome sequencing

Maria Borowiak
German Federal Institute for Risk Assessment (BfR), Department Biological Safety, Berlin, Germany

Summary
Recent developments in Whole Genome Sequencing (WGS) technology play a significant role in the area of food safety by enabling real-time surveillance of foodborne pathogens. WGS has the potential to improve our ability to identify pathogens along the food chain, to detect outbreaks, to monitor virulence as well as antimicrobial resistance and to identify new resistance or virulence genes. Once implemented in food, veterinary and clinical laboratories, this technique allows continuous molecular surveillance of foodborne pathogens and improves consumer protection and food safety.

Abstract
According to the WHO one in ten people fall ill every year due to consumption of microbial contaminated food and 420,000 die as a result. In general four main species are known to be major cause of foodborne diseases: *Salmonella* spp, *Campylobacter* spp, *Listeria monocytogenes* and Shiga toxin-producing *Escherichia coli*. WGS technology provides the possibility for a rapid identification and characterisation of foodborne pathogens regardless to the species by following a universal workflow. Due to rapidly declining cost of this technology, WGS can be easily implemented in food safety, public and veterinary health laboratories. The applications of WGS in food safety ranges from classical molecular typing of pathogens to the prediction and surveillance of antimicrobial resistance, virulence and pathogenicity by identifying relevant genes to the ascertainment of similarity, relatedness and diversity of foodborne pathogens by whole genome or core genome single nucleotide polymorphism (wg/cgSNP) analysis and multilocus sequence typing (wg/cgMLST). Hence, WGS methods and bioinformatical pipelines to analyse WGS data consolidate the numerous different methodologies currently in use in food, veterinary and clinical laboratories including classical serotyping, phenotypical antimicrobial susceptibility testing, 7-gene MLST, pulsed-field gel electrophoresis (PFGE) and multi locus variable-number tandem repeat analysis (MLVA). By allowing the rapid exchange of comparable data between different laboratories on a national and international level, WGS is not only restricted to traceback investigations but has the potential to be used in real-time surveillance of foodborne outbreaks. As a result WGS is revolutionising microbial food safety worldwide.

With its advantages, WGS is on the way to be integrated into routine foodborne disease surveillance at the German Federal Institute for Risk Assessment (BfR). So far the BfR could actively contribute to determine the outbreak sources in two real-life case studies regarding a national *Listeria monocytogenes* outbreak in southern Germany (2012–2016) and a Europe-wide *Salmonella enterica* subsp. *enterica* serovar 11:z41:e,n,z15 outbreak (2016–2017). Moreover a new resistance gene conferring colistin resistance in *Salmonella* and *Escherichia coli* was identified using a WGS approach.

Through ongoing participation in national and international projects with focus on NGS, the BfR aims to build and enhance the use of Whole Genome Sequencing in microbial risk assessment, food safety and public health protection.

6.8 Contribution of whole genome sequencing to source attribution of campylobacteriosis in France

Amandine Thépault[1], Guillaume Méric[2], Leonardos Mageiros[3], Typhaine Poezevara[1], Ségolène Quesne[1], Valérie Rose[1], Véronique Béven[4], Fabrice Touzain[4], Edouard Hirchaud[4], Samuel K. Sheppard[2,5], Marianne Chemaly[1], Katell Rivoal[1]

[1] French Agency for Food, Environmental and Occupational Health & Safety (ANSES), Hygiene and Quality of Poultry and Pig Products Unit, Bretagne Loire University, Ploufragan, France.

[2] The Milner Centre for Evolution, Department of Biology and Biochemistry, University of Bath, Bath, United Kingdom

[3] Swansea University Medical School, Institute of Life Science, Singleton Campus, Swansea, United Kingdom

[4] French Agency for Food, Environmental and Occupational Health & Safety (ANSES), Viral Genetics & Biosafety Unit, Bretagne Loire University, Ploufragan, France.

[5] Department of Zoology, Oxford University, Oxford, United Kingdom.

Campylobacter is responsible for the most frequent bacterial foodborne gastroenteritis in Europe. This bacterium is part of the commensal microbiota of numerous host species, which constitute potential sources of human infection. Molecular genotyping approaches, especially multi-locus sequence typing (MLST), have been used to describe *Campylobacter* populations enhancing the understanding of their epidemiology and their genetic structure. In addition, MLST has been extensively used to identify the origin of human campylobacteriosis based on allelic variations at 7 MLST loci, and identified chicken as a major infection source in several countries. However, assignments of clinical isolates harbouring genotypes isolated from various animal or environmental reservoirs constitute one limitation of MLST. The increasing availability of bacterial genomes provides data on allelic variation at loci across the genome, providing potential to improve the accuracy of source attribution.

Using a reference pan-genome approach and a systematic gene-by-gene comparison of several hundreds of *C. jejuni* genomes, 15 loci were selected as potential markers for source attribution, since they allowed the segregation of isolates according to their host. Then, these 15 host-segregating markers were used in a source attribution study in comparison with MLST loci, to identify the most likely origin of campylobacteriosis from 2009 and 2015 in France. Simultaneously, to assess the accuracy of source attributions, self-attribution tests were performed in each population of *C. jejuni* isolates with the different genotyping data. For this purpose, a collection of 1067 *C. jejuni* from chicken, ruminant, pets, environmental waters and clinical cases was characterised using MLST and a sub-selection of 370 isolates was whole genome sequenced.

In contrast with previous studies, analyses performed using STRUCTURE software and MLST genotypes, identified ruminant as the first cause of campylobacteriosis in France in 2009, while chicken and ruminant were equally involved in 2015. Using the 15 host-segregating markers, ruminant and chicken appeared to be equally implicated in human infection by *Campylobacter* in 2009 while chicken was the first infection source in 2015. On another hand, environment and pets were slightly implicated using both techniques. Regarding self-attribution tests, the 15 host-segregating markers showed a higher accuracy in the assignment of chicken isolates than MLST, while their accuracy were equivalent for *C. jejuni* isolates from ruminant, pets and environment.

In conclusion, using the gold standard technique for source attribution in *C. jejuni*, ruminant reservoir appeared to be a significant transmission route for *C. jejuni* to humans in France, while the significant role of chicken in campylobacteriosis was reinforced. These findings illustrate a potential role for local/national variations in *C. jejuni* transmission dynamics, indicating a benefit for further national-scale attribution modelling to account for differences in production, behaviour and food consumption. Finally, the use of the 15 host-segregating markers in source attribution study for *Campylobacter* allowed a higher accuracy of chicken

isolates compared with MLST loci. This finding suggests that using MLST loci the importance of chicken in campylobacteriosis may be underestimated. Therefore, despite the numerous studies implicating chicken as the first source, its implication could be much more important than currently described.

6.9 Endocrine disruptors – EU criteria and guidance

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Summary
In the EU, based on the proposed criteria for the identification of endocrine disruptors in plant protection products and biocidal products a corresponding guidance document is currently developed by EFSA and ECHA. The BfR supports these activities by several activities including providing an annex of this guidance addressing practical issues of hormone measurements.

The European Commission (EC) has proposed scientific criteria to identify endocrine disruptors for pesticidal active substances and requested the European Food Safety Authority (EFSA) and the European Chemicals Agency (ECHA) to develop a common Guidance Document for the implementation of the hazard-based criteria to identify endocrine disruptors (ED) in the context of Regulations (EC) No 1107/2009 on plant protection products and (EU) No 528/2012 on Biocides. An EFSA/ECHA/JRC drafting team is coordinating this work and the BfR supports these activities.

The Guidance Document will support for the practical implementation of the scientific criteria concerning the hazard-based identification of EDs in the context of Regulations (EC) No 1107/2009 and (EU) No 528/2012. The Guidance is intended to be suitable for applicants and regulatory authorities and should also be applicable for the evaluation of EDs in other legislative areas und in the scientific world.

On behalf of the EFSA/ECHA/JRC drafting team, the German Federal Institute for Risk Assessment has undertaken an anonymous laboratory survey in academia, industry and contract research organisations as well as a literature search to gauge the applicability and practicability of currently employed and potentially new methods for the evaluation of the hormone status to support the assessment of ED potential of chemical substances within the EU regulatory framework. The survey consisted of two parts, one concerned with the measurement of hormones of different endocrine pathways in the blood and the other concerned with histochemical methods for measuring hormones in tissues/organs. The aim was to collect specific information regarding practical methodology.

The information garnered in this survey and the results of the literature search were discussed between experts from the participating laboratories and authorities at an expert hearing in the BfR in October. The resulting practical recommendations regarding measurements especially of thyroid and sex hormones were used to prepare an Annex to the ECHA/EFSA guidance document. It is expected that the draft Guidance Document will be released for public consultation in January 2018. Furthermore, the results of this expert hearing will be discussed and published to provide recommendations for an improved methodology and necessary research in the assessment of endocrine effects. These activities are closely related also to the activities of other scientific organisations and the OECD.

6.9 Endocrine disruptors - OECD

Dr. Philip Marx-Stölting
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At OECD level several testing guidelines have been or are currently updated or developed to better address endocrine related endpoints. This includes TG407 and TG408 for testing of short term toxicity but also the extended one generation reproductive toxicity study (TG443). Additionally new testing guidelines have been established to address specific endocrine modes of action, like the androgen receptor transactivation assay (TG458) or estrogen receptor transcriptional activation assay (TG455) *in vitro*. Furthermore several Adverse Outcome Pathways (AOP) have been proposed, e.g. for chemically induced adverse effects on the thyroid and guidance documents have been prepared facilitating the regulatory evaluation of potential endocrine disruptors (e.g. GD150). This presentation will give a brief overview on activities related to ED on OECD level.

6.10 Risk assessment of aflatoxins from food consumption in the Korean population

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The aflatoxins are a group of fungal metabolites that contaminate a variety of staple crops, including cereals, oil bearing seeds, spices and nuts, and cause an array of acute and chronic human health effects. These substances, aflatoxin B_1 in particular, have genotoxic carcinogenic effects, with no threshold, and are not set an acceptable daily intake by the appropriate international bodies. Most countries, including South Korea, manage to minimise the exposure of aflatoxin through food intake in accordance with the ALARA (as low as reasonably achievable) principle.

The intake of total aflatoxins (TAF, sum of aflatoxins B_1, B_2, G_1, and G_2) from food marketed in South Korea was estimated from TAF concentration and frequency data in 300 food commodities (10,443 samples) from a 4-year survey (2012–2015), and by food consumption data from the Korea National Health and Nutrition Examination Survey performed in 2011–2013. The TAF survey revealed that TAF was detected in 6.8 % (708/10,443) of food samples marketed across 16 cities in South Korea, using high-performance liquid chromatography coupled tandem mass spectrometry. The highest contamination level for TAF was found in angelica root consumed as health food and one millet sample contained TAF above the legally permitted level (15 μg/kg) in South Korea.

To assess the occurrence data, a lower bound (LB)–upper bound (UB) approach was used. For the average consumer in the total Korean population, the average dietary exposure to TAF was estimated to be 0.263 ng per kg body weight and day (ng/kg/day) (LB) and 1.105 ng/kg/day (UB). The age group with the highest TAF exposure was 1–2-year-old children at 0.614 (LB) to 3.049 (UB) ng/kg/day. Among foods, polished rice and glutinous rice were considered to be common contributors of TAF exposure in the Korean population. In 1–2-year-old children, polished rice, milk, and glutinous rice were the major contributors to dietary TAF exposure. For high consumers (95^{th} percentile consumption in the total population), the average dietary exposure to TAF was 0.777 ng/kg/day (LB) and 3.596 ng/kg/day (UB). Overall, these exposure levels are lower than those in other countries.

The margin of exposure (MOE) approach, which compares daily exposure with the benchmark dose lower confidence limit ($BMDL_{10}$) values of 0.170 μg/kg/day, was used to determine whether TAF exposure posed any risk to the Korean population. The derived MOE values for the average consumer ranged from 154 (UB) to 646 (LB) in the Korean population, and from 56 (UB) to 277 (LB) in 1–2-year-old children. By contrast, the respective derived MOE values for highly exposed consumers ranged from 47 (UB) to 219 (LB) in the Korean population and from 16 (UB) to 89 (LB) in 1–2-year-old children.

In conclusion, current dietary exposure to TAF has no appreciable effect on the Korean population. Nevertheless, because aflatoxins are carcinogenic and genotoxic substances, their levels in food should be continuously monitored and minimised following the ALARA principle.

6.11 Marine biotoxins: facing new facts

Dr Charlotte Grastilleur

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The very-well renown Fugu fish was properly processed by skillfull cooks in Asia for centuries, in order to avoid lethal poisonings, long before the structure of the tetrotoxin was elucidated.

Although food poisonings occurring through shellfish and fish consumption have been identified historically and confirmed with a non-specific approach by bioassays, it is only recently that analytical developments allowed the formal chemical identification of the toxins involved in those acute diseases.

Shellfish toxins show various properties and chemical profiles, from lipophilic to hydrophilic with a common tendency of being complex-structured molecules. Their toxicological profiles drastically differ depending on their mechanism of action that determines their toxicity.
The toxins involved are strongly active poisons triggering a large range of symptoms, due to their acute toxicity, from neurological to digestive, commonly known as amnesic, paralytic or diarrheic shellfish poisonings or syndromes (ASP, PSP, or DSP). They can be related to serious public health concerns. What is more, the question of the chronic adverse effects is also a pending issue. Apart from main toxins already assessed and even regulated at EU level (yessotoxins, okadaic acid, saxitoxins, domic acid …) and at the international level, new hazards are therefore not or only partially elucidated.

The continuous refinements of analytical methods in the mass spectrometry array make it possible to point out the presence of toxins in seafood (fish and shellfish) and to map production and fishing areas where their presence was not previously clearly proven. These new findings raise questions as to the emergence or reemergence of some biotoxins (and related harmful algae). The possible threat to public health also needs to be addressed with reliable toxicological data that are still lacking.

Considering globalised market and worldwide transportation systems, global warming and climate change, but also analytical capacities and toxicological studies, marine biotoxins are a challenge to scientists that illustrates the complexity to tackle emerging risks, from detection to interpretation.

How can we manage to gain data to perform complete risk assessment on these toxins, how can we learn from new discoveries about the possible new threats related to marine biotoxins and mitigate their heath impact through surveillance and early warning systems?

6.12 Analytical challenges for nanomaterials in risk assessment

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Summary
The talk will present the possibilities and challenges of detecting and characterising nanoparticles in food and biological samples in the context of risk assessment. Selected examples from 10 years of working with nanomaterials at the National Food Institute in Denmark will be presented including ongoing and future work.

Nanotechnology and more particularly nanotechnology-based products and materials have a huge potential for providing novel solutions to many of the current challenges facing society such as energy supply and resources efficiency, a clean environment, information and communication, mobility and security, and the efficiency of health-related products [1]. Current applications in the agri/feed/food sector are food additives and food contact materials, whereas potential future developments are expected in the field of nanoencapsulates and nanocomposites in applications such as novel foods, food/feed additives, biocides, pesticides and food contact materials [2].
Nanotechnology is considered to be a key enabling technology by the European Commission. As a consequence, the European Union's (EU) regulatory framework covers nanomaterials explicitly or implicitly [3]. For example, foods consisting of engineered nanomaterials (ENMs) and ENMs used in plastic food contact materials require specific risk assessment according to EU regulations [4,5]. In 2011, the European Food Safety Authority (EFSA) published a document which provides guidance on the risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain [6]. According to the document, the risk assessment paradigm, hazard identification and hazard characterisation followed by exposure assessment and risk characterisation, is also appropriate for nanomaterials. Adequate characterisation of ENMs is considered essential for establishing the ENM's identity and physico-chemical forms in food/feed products and under testing conditions. One major challenge related to ENMs is their dynamic behaviour, meaning that the physico-chemical properties can change in different environments. ENM characterisation is therefore recommended to be performed at five stages: 1) as manufactured (pristine state), 2) as delivered for use in food/feed products, 3) as present in the food/feed matrix, 4) as used in toxicity testing, and 5) as present in biological fluids and tissues [4]. Stage 3 (in food/feed) and 5 (in biological fluids and tissues) can be considered as the most challenging from analytical point of view due to the presence of a complex matrix. The characterisation of the ENM in food/feed and biological samples is, however, of high importance for exposure assessment and for hazard identification/characterisation, respectively.
The talk will present examples of analytical challenges and solutions based on DTU Food's work with NMs in food and biological samples throughout the last 10 years. The most frequently used analytical techniques asymmetric flow field flow fractionation (AF4) hyphenated with inductively coupled plasma mass spectrometry (ICP-MS), single particle (sp) ICP-MS and transmission electron microscopy (TEM) will be introduced and their potentials and limitations highlighted. Examples will cover ENM characterisation in food, food simulants, toxicity testing and biological tissues.

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6.13 Fighting unknown chemicals: analytical strategies for risk prioritisation

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In chemical risk assessment, we have always relied on an availability or attainability of exposure and hazard assessments. Although this never was easy, it has nowadays become nigh impossible because relevant data is rarely and scarcely available, while the number of known chemicals is merely the tip of the iceberg of total available chemicals. To investigate, elucidate, and assess the poorly-understood potential risk of unknown chemicals, we need novel analytical methodologies and a change in the mind-set of risk assessment.

Introduction
Risk assessment by its very nature has always been a compromise between what is attainable and what is needed. In public perception, acute hazards seem to be dominating several high-impact scandals. Even recently, the Fipronil scandal has reminded the public that food safety is not guaranteed. Scientists, risk assessors, and risk managers should remain ever vigilant in ensuring that food is and remains safe. Yet, among these high-impact scandals we often tend to side-track another persistent problem in chemical food safety: long term exposure to low doses of chemicals. Currently, food contains a cocktail of chemicals from origins never intended for consumption, present from a large variety of sources. The actual structure and exposure to these chemicals are often riddled with uncertainty, or regularly completely unknown. Moreover, we seem to know very little about long-term and low-dose chemicals and their fates in the environment or human body, especially in regards to mixtures. How can we ensure safe food if we do not know what and how much is hiding below our action thresholds?

One of the sources of intake chemicals are packaging materials for food (Food Contact Materials, FCM) such as plastics, metals, or paper and board. FCMs are known to transfer chemicals to food. The “cloud” of chemicals that migrates from FCM contains huge variety in the type and the levels of chemicals. In contrast, there is little specific data to perform proper risk assessments for each chemical and possible metabolite from the “cloud”. Often, no chemical data, toxicological data, or exposure data exists. Unsuccessfully, regulators or industry are required to perform risk assessment on thousands of possible chemicals without data: no exposure and no hazard. As a consequence, these substances can be unjustly combined into total migration limit rather than a specific migration limit. Hence, exposure to harmful chemicals via diet is likely, while we have extremely limited knowledge on the possible effects: it seems current risk assessment is inadequate in this matter (Muncke *et al.*, Environ. Health Perspect. 2017, *125* (9), pp. 1–9.). As resources in risk assessment are limited, we indeed struggle to understand the possible impact of this intake.

Methods
In our work, we decided to combat the lack of knowledge on the risk of unknown chemical substances. In order to achieve this, we designed and tested analytical methods capable of investigating unknown substances. Currently, when faced with either uncertain or lacking data we are unable to ensure lasting safety: a premise that is unacceptable. To alleviate this, we developed a series of novel explorative methods useful to map unknown parts of the chemical profile of a sample, whereas conventional methods look for targeted, known compounds. The goal of exploration is to get a better grasp on the knowledge gap between known and unknown chemical substituents by generating basic but tentative data. The data obtainable by exploration may not be used first-hand to perform or improve risk assessment, because exploration naturally contains uncertainty due to the defocusing effect of untargeted premises. Rather, it is used to bridge or lessen the knowledge gap. However, in order for

exploration to be useful for risk assessment, we need to find ways to work with preliminary data

Results
In this presentation, we report on the development of comprehensive analytical methodology to aids future risk assessment studies. As a case study, we decided to focus primarily on the possible migration components in paper and board FCM, since these are the least regulated, yet widely used in Europe. First, the journey from an unknown chemical to obtaining tentative exposure and hazard data is reconstructed. For exposure, we used semi-quantitative methodology in liquid chromatography mass spectrometry (LC-MS) to estimate the concentration of unknown chemicals in FCM extracts. Then, we processed semi-quantitative concentration data into a form of exposure by using an adaptation of the threshold of toxicological concern (TTC) approach. For identification of unknown substances, we used high resolution mass spectrometry (HRMS), fragmentation patterns, data-mining algorithms, and pre-existing data to reconstruct a possible chemical structure match. With the reconstructed chemical structure, we evaluated hazard by using computational Quantitative Structure-Activity Relationship (QSAR) models to estimate carcinogenicity, mutagenicity, and reproductive toxicology of identified chemical substituents.

Following, we combined the identification, hazard characterisation, and exposure estimates into an overall chemical picture of the sample, and investigated the applicability this data in the process of risk assessment. Here, it was clear that performing actual risk assessments was unviable due to the large degree of uncertainty in the data. Instead, we used the data to prioritise unknown chemicals which were most likely responsible for adverse effects: an application of risk prioritisation. In this sense, exploration is extremely well suited to prioritise risk rather than to quantify it, as it excels in cases where existing data is insufficient or non-existent by generating new information. By classifying newly discovered chemicals on their perceived risk, following risk assessments can prioritise the order of assessment based on available preliminary information.

Conclusion
The use of methods that emphasise the use of preliminary knowledge on unknown substances can greatly aid future risk assessments by allowing risk prioritisation, while not yet requiring a full data picture like needed for an actual risk assessment. Less time may be used assessing likely-safe chemicals and more time can be efficiently used towards assessing likely-risk chemicals. In addition, explorative data can contain findings that may lead to different risk assessment studies, for example burden of disease case studies, of which an example using endocrine disruptors is shown as a poster presentation.

6.14 Data challenges to improve dietary exposure assessment

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Summary
Dietary exposure is estimated by matching food consumption data and data describing concentration of substances in food. Different risk assessment agencies in the world have different approaches for collecting and combining data sources to perform the most pertinent dietary exposure assessments. The strategy of each agency to data collection and combining is built on guidance (best practices) documents but also on its own means. This presentation will describe different approaches in Denmark, France and Germany to improve data collection for both sources so as to better suit the needs of dietary risk assessments.

Content
Dietary exposure assessment is complex and highly data dependent. To ensure well-informed risk management decisions high quality data on food contamination and food consumption are needed. One example for challenges to collect sound data for exposure assessment is to cover a sufficient range of the inter- and intra-individual variability, including variability in the frequency and amount of consumption as well as variation of concentration of substances in food. Another challenging question is how to describe the foods as precise as possible without demanding too much from participants. But even if both data sources for consumption and concentration data are of high quality there is another challenge to find an appropriate match of both data sources.

Different approaches exist to match food consumption and concentration data to fit the needs of different regulations as for contaminants, food additives or pesticides. Dietary survey data need to be grouped/disaggregated up to different levels between raw agricultural commodity level and foods as consumed including complete recipes. Further information reported by respondents needs to be completed using secondary data by matching more information via the brand names, like food additive information from the labeling as done by the German database on the occurrence of food additives. The German nutrition survey for children aged 6 month to 5 years (BfR KiESEL study) intends to collect data not only suitable to assess nutrient intake but also a wide range of substances with potentially harmful effects. With this aim the dietary protocol was refined and high effort was done to support respondents by training, phone hotline and by additional investigations on the consumed foods.

For concentration of substances in food there exist two main data sources in Germany. Traditionally dietary exposure assessments of the BfR are based on the German food monitoring. Laboratories of the federal states analyses a variety of foods to get a representative picture of exceedances of maximum permitted values in Germany and to assess exposure. To complement the food monitoring data the BfR MEAL study was started as the first German Total Diet Study. The BfR MEAL study was designed to fit the specific needs of each group of substances grouped into separate modules. This will provide data on food categories that are highly consumed but do have only low concentrations and/or no maximum permitted levels. Further substances can be analysed where it is of importance to consider the increase or decrease of concentrations due to household processing. One advantage is to complement the list of substances of the food monitoring with data e.g. for processing contaminants, food additives or substances migrating from packaging material. For other substances measuring food as consumed will be a further level of refinement to reduce uncertainties related to data from food monitoring.

In Denmark, dietary exposure assessment is based on data from the Danish national survey of diet and physical activity (DANSDA). DANSDA is conducted to perform public health research on diet, physical activity and overweight, monitor intake of foods and nutrients to identify groups at risk for nutrient deficiency as well as excess and last, but not least, to estimate dietary exposure of contaminants, food additives, pesticides etc.

As the primary aim of DANSDA is public health nutrition, the nutrition division at the National Food Institute has been responsible for carrying out the survey. In the last decades, the aim of survey has also been to cover exposure assessment of contaminants, pesticide residues etc. This aim has been fulfilled by including new pre-coded foods but also by combining different data sources when calculating the intake of specific foods related to chemical or microbiological risk. The wishing list from food safety researchers of foods to assess by the survey is long. However, our experience is that, the more questions being asked in the survey, the bigger burden is laid upon participants. This influences the response rate of nutritional surveys. Moreover, it is important to consider to which extent participants are able to give valid and accurate answers to highly specific questions on intake of different foods, food preparation methods, and packaging material needed in chemical or microbiological risk assessment.

In the past, paper based questionnaires have been used in dietary surveys, which puts a natural limit on the number of pre-coded foods included. Different data sources have therefore been used in order to obtain detailed information on foods without raising the participant burden. Data from dietary surveys have been combined with sales statistics and data from household budget surveys which comprise thousands of foods with information on brand and package size.

Web based dietary survey methods make it possible to include more foods, thus reducing the need for combining different data sources. However, due to the interdisciplinary research in DANSDA we have special attention on which information it is possible to obtain from participants. Sociologists with knowledge in designing questionnaires challenge the level of details that chemists or toxicologists want to include in dietary surveys. In Denmark we use qualitative methods to examine the knowledge on foods by participants and also to examine feasibility of the dietary survey methods.

Currently, we conduct a comprehensive validation study with an interviewer based dietary assessment method (24 hour diet recall) with many detailed questions on foods fit for chemical/toxicological/microbiological risk assessment. By using data from the validation study, we can examine what participants are able to give valid and accurate answers for. These results will be used to plan the next Danish national dietary survey in 2018–2020 and balance the dual purposes of public health nutrition and chemical/microbiological risk assessment.

In France, data for dietary exposure assessment at the general population level, collected by the French Agency for Food, Environmental and Occupational Health & Safety (ANSES), is essentially based on two major studies: the individual national food consumption survey (INCA) combined with the total diet study results (EAT) for chemical substances. This is possible because, based on EFSA guidance and the facets of the FoodEx2 food classification and description system, the INCA survey goes beyond food consumption and integrates related information required for dietary exposure and risk assessment (like food preservation methods, food packaging material, etc.). Moreover, ANSES decided to further extend this survey to include specific information potentially useful for ANSES' different risk assessments panels. In particular, information needed to assess microbiological risks, like the fridge temperature and use-by dates of food in the fridge, were also collected in a secondary face-to-face questionnaire.

The recently published third INCA survey (INCA3, 2014–15)[1] was the first INCA study to adopt such a wide-reaching integrated approach to collecting dietary related risk assessment information. However, while such an integrated approach is very useful to be able to respond to a wide range of risk assessment issues, it also has a downside: a longer, more complicated survey can imply potentially lower participation rates and hence the need for greater dependence on statistical adjustment to ensure representative results. The difficulty is to find the right trade-off between the gain in precision in dietary risk assessments and the logistical and financial difficulties needed to overcome to carry out the all-encompassing food consumption survey.

Hence, based on the INCA3 data, a series of analyses will be carried out in the next year or two to confirm or challenge the usefulness of the all-encompassing approach of the survey. The results of this work will be particularly usefulness in the process of conceiving and designing the individual national food consumption survey that should most likely be carried out in the early 2020's.

The work presented is based on one of these analyses made on information related to food contact materials (FCM). This information was collected, as one of the many facets of EFSA's FoodEx2 classification system, during each of the three 24 h recalls. It is thus possible to link each of the about 285 000 food consumption events of the INCA3 survey to its specific packaging material. This analysis provides responses about a link between a consumer and the type of FCM to which his food is exposed. Typically we will be able to reply to questions like: what is the profile of consumers who preferentially eat canned foods? Or foods sold in glass containers? And what does this imply in terms of the associated potential risks?

A series of such analyses on the ancillary information collected as part of the INCA3 integrated survey will allow us to determine precisely which variables are directly linked to food consumption and hence necessary to obtain in parallel with direct consumption data to provide the most pertinent dietary risk assessments. These analyses will also confirm which of the INCA3 ancillary information is less related to dietary exposure and hence less important to include in a food consumption survey. This is vital information for ANSES in its twin role as dietary risk assessor and collector of national dietary information when dimensioning future national consumption surveys.

Thanks to the vast INCA3 database, this data challenge, finding the balance between risk assessment precision and optimally dimensioned very expensive consumption surveys, can be dealt with in the near future through such a series of analyses. However, many other data challenges exist and, in particular, the need to better capture consumption and contamination for sub-populations. While INCA and EAT surveys cover the general population in a satisfactory way, this global objective and approach does not provide adequate data for particularly sensitive sub-populations like very small infants or pregnant women. Similarly, on the contamination side, the challenge of reducing the analytical limits of detection and quantification for chemical substances still remains to be addressed. For example, in the recent infantile EAT study (EATi, 2011–2012)[2], ANSES was unable to exclude the health risk for a certain number of substances because the existing analytical limits did not allow a precise enough exposure assessment.

This presentation highlights different approaches used by three leading national European agencies to provide improved dietary exposure assessments. The common denominator here is a major data challenge: how to use, adapt or combine essentially nutrition-oriented

[1] https://www.anses.fr/fr/system/files/NUT2014SA0234Ra.pdf
[2] https://www.anses.fr/fr/system/files/PASER2006sa0361Ra1.pdf

food consumption surveys to the specific needs of risk assessment. While this remains the focus of ongoing work other data challenges must not be neglected: capturing the specific sub-populations generally underrepresented in national surveys, correctly capturing inter- and intra-individual variability or improving analytical methods. Moving forward on these issues will provide more precise dietary risk assessment evaluations for the whole population spectrum of health risk situations.

6.15 Mixtures prioritisation based on exposure and hazard

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Through their environment and diet, populations are daily exposed to mixtures of chemicals which can interact and cause health diseases. Due to the complexity of mixtures, the associated risk is difficult to characterise. Over the past decade, lots of efforts have been made to propose concepts, methods, guidance and applications for risk assessment of mixtures (EFSA 2007, Boobis *et al.* 2008, EFSA 2008, WHO 2008, Fox *et al.* 2017). Regarding the multitude of possible combinations, the question on which substances should be assessed together remains a big challenge. One solution is to perform risk assessments for chemicals belonging to a same chemical family and/or having same mode of action. In this way, EFSA proposed a hazard-wise method based on “common adverse outcome” to group pesticides in “cumulative assessment groups” (CAGs) (Nielsen *et al.* 2012, EFSA 2014). Four levels of criteria for grouping were defined with each higher level being more refined: targeted organs (level 1), specific phenotypic effects (level 2), mode of action (level 3) and mechanism of action (level 4). Currently, level 1 and 2 CAGs, restricted to pesticides, have been identified in the nervous system and the thyroid. Comprehensive preliminary work has been done on effects on the liver, adrenals, eye and developmental and reproductive system (EFSA 2012, RIVM *et al.* 2016). Dose addition is the default hypothesis to assess the risk of these CAGs, but the appropriateness of this assumption is hardly ever investigated experimentally. Moreover, grouping substance into a certain CAG can be based on a small number of observations, thereby introducing uncertainties regarding CAG membership and relative potency in comparison to other substances in a CAG. Also, understanding of the mode and mechanism of action is unknown for many pesticides, thus, there is a need to make efforts to study them. However, as a certain CAG can contain a high number of components, it is necessary to prioritise the substances to be assessed in mixture experiments. Finally, the main default of this approach is to not account of the reality of the mixtures. Therefore, it is essential to develop a strategy that considers real exposures to extract the most relevant mixtures to which the population is exposed (Crépet *et al.* 2013) as prioritisation tool for further studies.

This presentation proposes prioritisation methodologies based on exposure data. The first method is based only on exposure. The second method combines exposure and hazard information to identify the most relevant mixtures of chemicals belonging to any CAG to which populations are chronically and acutely exposed. It starts from the list of substances in a defined CAG and reduces this list by using risk-based identification of co-occurrent substances in diet for a given time frame. The two approaches are based on sparse non-negative matrix under approximation (SNMU) (Gillis and Plemmons 2013). The SNMU is a modified version of the non-negative matrix factorisation (NMF) (Lee and Seung 2001) recently used to identify principal mixtures connected with diet (Béchaux *et al.* 2013, Traoré *et al.* 2016). It aims to decompose the co-exposure matrix into two non-negative matrices to extract the main mixtures which are relevant to study. It is possible to combine the SNMU with a clustering method to associate mixtures to specific diet patterns.

The method based on exposure only will be illustrated by an example on chemical substances analysed in the second French total diet study. The second method was developed in the Euromix project (H2020-2015-2019) which aims to develop a strategy for mixture risk assessment. An example on the CAG level 2 liver steatosis using exposure data from several European countries will be presented.

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6.16 Lessons learned from food fraud issues in Korea – focusing on DNA based analysis

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Food fraud has been and continues to be an ongoing international issue and many fraud types are known from the reported cases. Most food fraud cases reported in Korea were EMA (Economically Motivated Adulteration). The definition of this term by US FDA is: 'fraudulent, intentional substitution or addition of a substance in a product for the purpose of increasing the apparent value of the product or reducing the cost of its production for economic gain'. It includes the false declaration of origin to evade tariffs/taxes, false declaration of geographic, species, botanical, or varietal origin, and false declaration regarding the production process. For example, fish commonly enjoyed as sashimi such as croaker or snapper were substituted with relatively cheap drum fish or tilapia. Another example is the red pepper powder largely used in the manufacture of Kimchi. It is sometimes counterfeited with mixed seasoning imported from China after the process of drying and mixing with pepper seed and spice.

Domestic EMA cases have repeatedly occurred whereby consumers have been misled or deceived with relatively low priced food materials intentionally for economic gain. Furthermore it is often difficult to distinguish between the substituted materials and the original ones because the final products eventually lose their original shape after being sliced, ground, or extracted. We have tried to set up identification methods for about 230 animal and plant species using Polymerase Chain Reaction using species-specific or group-specific primer sequences since the early 2010s. However, the number of species required to be identified is still increasing every year in relation to presumptive substitutes, and it is still challenging that various species ID methods with various purposes depend on the various types of approval of raw materials.

DNA Barcode is widely used in biological research with advanced sequencing technology these days. Our team launched the seafood barcode identification 5 year research project that will run from 2017 to 2021 that is focused on domestic and imported seafood species.

6.17 How to build a crystal ball – the art of emerging risk identification

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EFSA provides scientific advice to the risk manager, at both European and Member State level for the identification of risks present in the food chain. Through the identification of emerging risks, EFSA also intends to anticipate future risks derived from changes in current food/feed production practices or factors impinging on food/feed production or changes in human exposure through food consumption.

Preparing for the future can take a number of different approaches, but importantly one has to accept that the future cannot be systematically *predicted* with precision. Nevertheless a number of "Futures" methodologies are useful, such as extrapolation from past trends into the future, scenario building, analysing drivers for change, through to detection of precursor signals and early detection of events in their own right (horizon scanning).

Emergence (of a risk) is also subject to perception, at times being a function of its detection rather than its de-novo emergence, that is to say a risk may have existed for some time but was only recently detected or identified as such.

When designing a system for emerging risk identification, the use of the output of such a system needs to be defined in advance. In the case of EFSA, the use is related to EFSA's remit, that is, risk assessment, and therefore the output is used to inform on preparedness activities in this area. Typically this would mean data gathering, risk analysis method development, knowledge creation, for example through research programmes. Whilst EFSA has only limited funding capacities, it is looking to increase its influence on research programmes, in collaboration with its major partners in the Member States and Commission Services.

Since 2009, EFSA has been exploring a number of approaches and data sources for the identification of emerging risks. From this experience, an approach based around networking has been developed. Key to the process has been the establishment of networks of experts both from representatives of the European Member States, but also from Stakeholders (Industry, NGOs and Consumer organisations), in order to exchange on potential emerging issues, gather further adding data, and also opinions on the relevance and importance of issues discussed.

In support of this activity, a number of tools and processes for analysing specific data sets have been trialled. Data on trade, food prices and food safety alerts and tools for analysing them have been examined, but found to be difficult to interpret in the context of emerging risks identification. More promising is the use of data sources for chemical production, i.e. the REACH database, for which a schematic approach is being developed for identifying chemicals of high toxicological concern that may be reasonably expected to find their way into the food chain, and for which food chain risk assessments do not currently exist.

In addition, an approach is being developed for the identification of emerging biological risks for human, animal and plant health based on the identification and analysis of drivers (those factors that influence the emergence of new risks).

Effective networking has proven to be essential for exchanging methods, data and evaluations of emerging risks. The engagement with Member States and Stakeholders has been reinforced and extended to international partners. Overall, our experience confirms that emerging risks identification requires a high level of expertise and solid knowledge networks for sharing information. Next steps include the widening of our networks to include more international partners, and continued investigation into promising approaches such as whole food chain analysis and crowd sourcing.

6.18 Risk-benefit assessment of foods

Dr Maarten Nauta
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Summary
Risk-benefit assessment integrates chemical and microbiological risk assessment with risk and benefit assessment in nutrition. In this presentation, current developments, challenges and the suggested way forward are discussed.

Introduction
Risk-benefit assessment (RBA) of foods aims to assess the combined negative and positive health effects associated with food intake. It is common to use the risk analysis and risk assessment frameworks as the basis for the RBA methodology, by applying the established concepts to both risks and benefits. In the past decades, some European projects have been conducted in which methods and modelling frameworks were developed, among others leading to the development of the ”tiered approach” as a general framework for RBA (Hoekstra *et al.*, 2012). A number of case studies have been performed, the majority of them relating to the risks and benefits of fish consumption (Boué *et al.*, 2015). Yet, although significant progress has been made, several challenges remain. Some of these challenges relate to the differences between the underlying research disciplines, which have different use of terminology and different approaches for the assessment of health effects related to the consumption of food. Other challenges relate to the specific objective of RBAs, the scarcity of the required data, or the complexity of the characterisation of health effects.

The scope of RBA
As with risk assessment, setting the specific objective of the RBA is essential for identification of the data needs and the choice of the method. From the objective, it should for example be clear whether the RBA concerns a specific food compound that can have both negative and positive health effects, a food product that contains both hazardous and beneficial compounds, and a comparison of diets. Also, the scope should be defined as covering only the human health effects that are a direct consequence of food intake (the “traditional” RBA), or including for example economical aspects, sustainability, life style, indirect health effects or personal preferences. The latter will require the further development of methods and metrics, and integration with methods such as LCA (Life Cycle Assessment) and MCDA (Multi Criteria Decision Analysis).

Comparing risks and benefits
Interestingly, there may be an imbalance in RBA, as commonly the level of scientific evidence needed for identifying negative and/or positive health effects is not consistent (Boobis *et al.*, 2013). In general, the presence of benefits and the absence of risks need to be guaranteed. Due to this discrepancy in the level of scientific evidence needed for considering a food compound as a “hazard” or a “benefit”, risks are more likely to be included in an RBA than benefits, thus leading to a potential bias in the RBA (Tijhuis *et al.*, 2012). This imbalance demands a paradigm shift from RBA as a sum of risk and benefit assessment to RBA as a well-integrated risk-benefit assessment. Such a well-integrated RBA deals not so much with studying a hypothesis about the presence or absence of health effects, but predominantly with the size of the health effects. Stochastic modelling techniques, which include quantification of uncertainty and variability, allow an evaluation of potential health

effects, even if the effects themselves are not statistically significant. From this, one might conclude that the risk or benefit is not very large, even if the evidence would be convincing or the opposite, that a risk or benefit may be large, even if the level of evidence is low.

The benefit of quantification

Following the tiered approach, a qualitative assessment is sufficient if the evidence is clear enough to conclude that the overall risks related to a food compound, food product or diet are larger than the benefits or vice versa. In that case, one can identify the healthiest scenario and advise that this scenario should be used. However, quantification of risks and benefits may have an important added value as it addresses *how large* the expected health effect of a specific food intake or change in diet may actually be. Even if it is significant, a small beneficial health effect of a particular intake scenario may be ignored by some, if put in the context of taste, costs, sustainability, etc. Therefore, this information may be crucial for regulatory decision makers, food industry and consumers, with regards to health claims and dietary advice. It requires the use of one or more health metrics like DALY (Disability adjusted life years) and a clear risk-benefit communication. The latter is an important challenge, but it should not withhold us from further developing methods to quantify risks and benefits.

Discussion

Risk-benefit assessment is a developing research area in which significant progress has been made. However, various challenges remain and more case studies that apply existing and novel methods need to be performed to show the utility of the research area. Recently, international initiatives have been taken to take up the challenges, as e.g. an EFSA sponsored workshop held in Copenhagen, May 2017.

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6.19 Using 21st century science to improve risk-related evaluations[3]

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Summary
Scientific and technologic advances in exposure science, toxicology, and epidemiology have led to vast amounts of diverse data being generated in government, industry, and academic laboratories. There are challenges to using the data, but several application areas are ripe for exploration. This presentation will highlight some relevant scientific advances, discuss promising uses of the new science, describe a few case studies, and emphasize the challenges to integrating the new science into risk-related evaluations.

Advances in biology and related sciences and increases in computational power are enabling new approaches for assessing risks to exposure to chemicals and other stressors. The focus has shifted from observing apical responses to understanding the mechanisms behind the responses, and advances in exposure science, toxicology, and epidemiology are allowing this shift to become a possibility. Over the last decade, the quality and breadth of exposure measurements have been enhanced and expanded with developments in, for example, remote sensing, personal sensors, computational exposures tools, and analytical chemistry methods. Advances in –omics technologies, cell-culture methods, and alternative animal species, including development of transgenic and genetically diverse animal models, have allowed scientists to probe the molecular mechanisms of and susceptibility to adverse effects of chemical exposures. Scientific advances have also helped to propel epidemiology onto new paths, for example, with the emergence of molecular epidemiology, which focuses on the underlying biology rather than on empirical observation alone.

All the scientific advances have led to the generation of a plethora of diverse data, and the question becomes how the data can be used today or in the near future to improve the assessment of risk from chemical exposure. The recent report, *Using 21st Century Science to Improve Risk-Related Evaluations,* describes several areas that could benefit from incorporating the new science. A primary application of the new science is setting testing priorities for chemicals that have no toxicity or exposure data. Another promising application area is chemical assessment. In the case of data-rich chemicals, questions or uncertainties surrounding dose-response relationships, susceptible populations, mechanisms, and previously unrecognized outcomes could be addressed or reduced. In the case of data-poor chemicals, the new science could provide hazard information and help to predict risk. Site-specific assessment is another application area; scientific and technical advances could be used to identify chemicals at a site and rapidly assess chemical toxicity. Finally, chemical-product design could benefit from modern toxicology methods, which could help to identify molecular features associated with toxicity or chemicals that might affect biological pathways associated with toxicity or to estimate possible exposure levels associated with various pathways.

Many challenges remain for achieving the new paradigm for assessing risk and for applying the data that are being generated now and in the near future. Insufficient attention has been paid to analysis, interpretation, and integration of the diverse data streams that are being (and will be) generated in exposure science, toxicology, and epidemiology. The technologies are advancing far more rapidly than the approaches for using the data. Although Bradford-Hill casual guidelines could be extended to help to analyze and interpret the new data, a research agenda is needed to develop case studies that reflect various scenarios of decision-making and data availability, to test the case studies with multidisciplinary panels, to cata-

logue the evidence evaluations and decisions so that expert processes can be improved, and to determine how statistically based tools for combining data and integrating evidence can be incorporated in the risk-assessment process. Ultimately, the acceptance of the new science will require scientists to communicate the strengths and weaknesses of the new approaches in a transparent and understandable way.

[1] The abstract is based on a report of the National Academies of Sciences, Engineering, and Medicine authored by the Committee on Incorporating 21st Century Science into Risk-Based Evaluations. Committee members were Jonathan Samet (chair), Melvin Andersen, Jon Arnot, Esteban Burchard, George Daston, David Dunson, Nigel Greene, Heather Patisaul, Kristi Pullen Fedinick, Beate Ritz, Ivan Rusyn, Robert Tanguay, Justin Teeguarden, James Tiedje, Paolo Vineis, Michelle Williams, Fred Wright, and Lauren Zeise. Ellen Mantus was the study director.

6.20 Introduction of the data management and risk assessment program: its application and expected effects on risk assessment for the future

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Regulators in the area of human health protection remain under constant pressure to improve on their efforts with regard to risk management, assessment, and communication. We believe Big Data will become an integral part of risk analysis and complement the current system.

In the course of dealing with recent risk crises related to public health in our country, many assessors and regulators discovered that their data architecture and IT systems could not support the monitoring and management of a broad spectrum of risks. When a crisis is not managed effectively, the impact can be severe-either financially or in terms of damage to society. In our experience, competent agencies successfully anticipate risk and manage issues before they become crises. For this reason, regulators want more frequent reporting of a wide variety of risks and expect firms to be able to respond quickly to public requests. Risk assessors also want risks to be assessed in more effective ways. For this, they are requesting more sophisticated data analysis tools and scenario analysis modeling.

With regard to future plans, NIFDS considers the benefits of Big Data in risk analysis and evaluates the potential of Big Data in risk assessment and measurement. Historically, it has often been difficult to predict the degree of impact that potential risks could have on public health. Big data and analytical tools support the quantifying and assessing of risks and facilitate decision making to enhance effective risk management. Big data and analytics can be used to establish an understanding of the potential costs and overall public health impact of unknown risks.

Chemical measurement data from food are typically obtained from MFDS's market surveys and NIFDS's research programs regarding chemical residue levels in food. However, as a great deal of data from NIFDS and MFDS is being produced in a variety of formats and from a variety of sources, management for these data will require more time to make the various data sets consistent with each other. Therefore, it is imperative that data are submitted by utilising the same formats (MIMS/Note) which have been provided by the NIFDS. Then, a hard copy and electronic copy of the statistical descriptors (e.g., means, minimum, and maximum values) are received by MIMS/MAP.

MIMS is an information management system for NIFDS's risk assessment and MAP systemically converts monitoring data directly related to human exposure levels to enhance risk assessment. A major purpose of MIMS/MAP is to produce high-quality, consistent, and scientifically defensible risk assessment. Data are maintained in a web-accessible database that accepts data as they are validated and uploaded. The MIMS/MAP system consists of three basic elements: managing information, converting information to the system and communicating knowledge to regulators and stakeholders. The user can select data for evaluation and convert the data into knowledge regarding human health risks. Knowledge about risks is communicated using graphic and tabular formats.

The main software used in the MIMS/MAP system is SAS software. All data by MIMS must be documented within the SAS programs that are created specifically for the data setup process. Toxicity values (health based guidance value, reference concentrations, and slope factors for analytes) are provided to MAP. The toxicity values are received from NIFDS-approved sources: The toxicity values are documented in the SAS programs used to make the changes according to plans to establish the health based guidance values for contaminants, food additives and pesticides. The original version of the toxicity data sets is maintained by MAP.

NIFDS plans to upgrade its MIMS/MAP system based on big-data, which includes information from other organisations. It will not only lead to improving risk assessment capabilities in our agency but also allow the organisation to provide consistent risk assessment results to the public. Therefore, as this is directly linked to raising public confidence in food safety we may expect risk communication to be enhanced.

6.21 Risk Assessment Modelling and Knowledge Integration Platform

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Summary
Risk assessment is a scientific process comprising of integration, evaluation and application of previously generated knowledge and the generation of new knowledge. Therefore efficient knowledge exchange within the scientific community is of highest relevance for risk assessment authorities. In a joint trilateral effort, ANSES, BfR and DTU Food created new community resources that support knowledge integration and exchange within the Quantitative Microbial Risk Assessment (QMRA) and predictive microbial modelling domain. This talk illustrates the effectiveness of the developed strategy through selected examples and highlight where joint efforts are needed in the future.

Abstract
The food safety community is generating a variety of scientific knowledge, e.g. scientific publications, experimental data, databases, mathematical models and software tools for model generation and application. However, the access to this knowledge and the exchange of information between databases and software tools are currently difficult and time consuming. Therefore, three European institutions specialised in food safety risk assessment (ANSES, BfR and DTU Food) initiated a joint project (RAKIP) to establish new community resources facilitating the efficient knowledge integration and exchange into and between IT-based applications and resources. The envisaged “Risk Assessment Modelling and Knowledge Integration Platform” (RAKIP) is based on harmonised data formats and consistent rules for knowledge annotation.
The feasibility of this concept has been demonstrated by the established RAKIP Web Portal available at https://foodrisklabs.bfr.bund.de/rakip-web-portal/. This portal encompasses the first proof-of-concept implementation of a community QMRA model repository and provides supporting resources facilitating efficient knowledge exchange. The RAKIP Model Repository (https://foodrisklabs.bfr.bund.de/rakip-model-repository-web-services/) allows users to execute, access and download different models or parts thereof (e.g. a specific process model, a dose-response model, etc.) in the proposed harmonised file format. These files can then be imported and executed by other software tools supporting the Food Safety Knowledge Markup Language (FSK-ML). In this way RAKIP created the basis for efficient knowledge sharing within the QMRA and predictive microbial modelling community as models can now easily be adapted to specific needs and used as building blocks for new risk assessments. Nonetheless, in the future it will be beneficial to strengthen the creation of free and open resources that support information exchange in the food safety risk assessment domain. To reach this, the following tasks are important to address:

- To extend and maintain web-based ***infrastructures*** for organisation, storage, retrieval, exchange, interpretation, and application of risk assessment models (and data).
- To extend and maintain ***harmonised controlled vocabularies*** for terms and concepts relevant for risk assessment modelling.
- To define, implement and maintain a comprehensive concept for knowledge annotation and an ***open information exchange format***.

- To develop new ***open source software libraries*** **and** ***converter tools*** and to directly support the enhancement of existing tools/databases/resources facilitating the adoption of the proposed harmonised information exchange format.
- To ***engage with the global food safety risk assessment community*** and create broad support and compliance.

6.22 Linking risk and sustainability assessment to meet current and future challenges in circular economy, food safety, and consumer protection

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Summary
A viable circular economy that should be resource efficient and compliant with food and consumer protection needs to be both safe and sustainable. In the present talk, I lay out a roadmap to consistently combine risk and sustainability assessment to address and overcome current societal challenges of circular economy.

Abstract
Increasing the sustainability of a globalised economy is gaining wide attention in a world with limited resources and growing chemical pollution. The circular economy has emerged as an elegant way to reduce carbon and other emissions, while increasing resource efficiency over several product life cycles. However, a circular economy is only viable if it is both safe and sustainable. The dilemma for any product or technology is that sustainable does not necessarily imply safe and safe does not necessarily mean sustainable. When minimising exposure to harmful chemicals in consumer products (safe), we often use more energy-demanding alternative solutions (unsustainable). In contrast, when maximising resource use efficiency and reducing carbon and other emissions through recycling (sustainable), cross-contamination of recycled materials can increase direct consumer exposure (unsafe). In these examples, the circular economy currently fails to unite the required expertise to simultaneously increase sustainability and reduce exposure to chemicals in materials reused across life cycles of different products. Consequences are for example unwanted residues in recycled food packaging or increased exposure to hazardous flame retardants in recycled plastics.

These examples show that it is essential to assess exposure to harmful chemicals in consumer products during product use (often dominating total human exposure) and from emissions of chemicals along the life cycle of recycled materials. However, for chemical substitution, only little is known about the hazards of potential alternatives. In consequence, this leads to regrettable substitutions (using similarly harmful alternatives) or burden shifting (reducing one hazard while increasing another). Finding safe and yet more sustainable solutions for a circular use of materials, hence, is a challenge for policy makers and industry. For a way out of this dilemma, a paradigm shift is needed towards a comprehensive and quantitative assessment framework. In this framework, consumer, worker and population exposure is consistently coupled with life cycle impacts for materials used in consecutive product loops to identify sustainable and safe solutions for a viable, circular use of chemicals and materials. To facilitate this paradigm shift, advances in the science for chemical and material prioritisation and in screening of exposure and life cycle impacts will be required and can be structured along three main aspects:

(1) Chemical and material prioritisation following a function-based approach structuring chemical, material and product functions: occurrence and functions of chemicals and materials in products will have to be systematically mapped based on initial work to map functional relationships from chemical elements to market products. Adding information on the migration of chemicals from product to product through material recycling loops will help targeting and prioritising chemicals for substitution.

(2) Screening of exposure and life cycle impacts building on recently proposed exposure metrics, exposure quantification frameworks, and advances in quantifying life cycle impacts: models for missing exposure pathways like migration of chemicals from packaging to food will have to be developed and tested, addressing and overcoming existing barriers. Consumer, worker and population exposure will have to be aggregated and coupled with a full coverage of life cycle impacts as basis for ranking alternative solutions.
(3) Unifying cross-disciplinary expertise involving integration of chemical and material prioritisation with the screening of exposure and life cycle impacts into a consistent assessment framework: this will have to be supported by forming an international and interdisciplinary task force of scientists and practitioners from environmental chemistry, computational exposure and toxicity, life cycle and alternatives assessment, and material and product design. The task force will have to develop cross-sector guidance for identifying more sustainable and at the same time safer alternatives to harmful chemicals in products, providing the foundation for global science-based decision support to optimise the circular use of materials.

Expected outcome of such a paradigm shift and concerted and targeted effort would be a safer and more sustainable circular economy through a targeted and efficient use of chemicals and materials by product designers within this economy. Based on identifying viable alternatives to harmful chemicals along material life cycles, this economy will be able to ensure controlled material recycling and successfully avoid the dilemma of safe but unsustainable or sustainable but unsafe solutions. Ultimately, such outcome would support developing a safer and more sustainable consumption and production in Europe and elsewhere in line with the United Nations' Sustainable Development Goals, foster a versatile circular economy, integrating the principles of both green and sustainable chemistry as well as holistic life cycle thinking in policy making and industry, and finally building more trust by consumers and stakeholders.

6.23 Trust in science, interaction with stakeholders and risk communication

Prof. Dr Gérard Lasfargues
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Can the principles of transparency and openness to civil society (taking into account the knowledge and the queries of the stakeholders concerned) be compatible with impartiality and independence of risk assessment? Is such an approach likely to improve the quality of public decisions and ultimately their understanding by stakeholders and public opinion? How can it contribute to trust and a more “fit-for-purpose” communication approach? This presentation will focus on ANSES' experience regarding openness to society and the definition of strategic communication and the way it combines stakeholders' engagement, social sciences expertise along with classical communication tools.

6.24 Globalised markets – local risk assessment?

Prof. Dr Dr Andreas Hensel
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The globalisation of the world's food supply has brought about new challenges to food safety. All sold food must be safe. This also applies to imported products. Guaranteeing safe food is a complex task and there are increased risks of widely distributed food contamination crises.

Recent incidents in different countries worldwide highlight how the globalisation has opened the possibilities for food contamination on a much larger scale. This is because food is increasingly being traded at global level, new ingredients and products are developed, pathogens occur and consumers change their eating habits.

The food industry is challenged by its dynamic nature as well as by predictable trends. Developing technologies can result in new packaging materials and processes that may affect food safety. These new products and processes can hold previously unknown risks of new contaminants and food fraud through the constant production of new substances, additives, technical aids and process contaminants. Additionally, predictable trends affect food producers and suppliers, like climate change, population increase, demographic trends and evolving energy policies.

Against the background of the global food trade, we need effective strategies for precise risk assessment and for ultimately improving food safety as well as communication of the risks arising from food. As one important consequence of global trends, traceability along the whole food chain is indispensable to avoid food crises, to enable fast reaction in the case of a crisis, to protect regional markets and products and to help ensuring fair trade rules. By integrating traceability systems, regulatory agencies can verify geographic, production and species origin. Legally compliant monitoring of standards required by law is only possible, however, if reliable and - more important - globally harmonised analytical methods are available for such complex matrices as food and feed. These methods must allow the detection of even small quantities of undesirable contaminants and residues. Newly evolved analytical techniques are robust in the detection of both known and unknown components, which is not only an essential element of monitoring the food supply and keeping contaminants out of the food chain, but also plays a key role for safeguarding food authenticity. As a further solution, software programmes based on well-managed traceability data need to be developed, validated and finally applied as tools to analyse and simulate food supply chains.

Tackling the challenges arising from globalised food trade cannot be achieved anymore in an isolated approach of local risk assessment. International collaboration of risk assessment and management agencies becomes more and more crucial. International cooperation is not a one-way street. It requires an evident mutual benefit in order to maintain regular communication between partners. This applies especially to publicly funded authorities which are continuously held accountable by their customers from the field of politics. In the case of capacity building measures, the benefit for the receiving institution is obvious. However, also the providing partner may obtain advantages, such as (a) an increased visibility, (b) exerting a higher influence, (c) an improved access to information or (d) profiting from synergies and sharing work. The tools to achieve these goals usually comprise trainings, events and the exchange of experts. Offering such tools in turn requires certain preconditions and structures, because different levels have to be addressed: when the counterparts of capacity building efforts are governments, ministries or subunits thereof, political consulting is needed on the leadership level. In contrast, the main body of work is to be done on the second, viz. the working level between the actual experts. The third level of services, that a provider of

capacity building has to prepare, is the organisational competence. This includes physical meetings, conferences, workshops, provisions to host guest scientists - and to an increasing degree of importance also virtual meetings by using webinars, web conferences and online courses.

In conclusion, global quality assurance systems, harmonised risk assessment procedures and successful communication strategies of food-related risks are essential to ensure consumer protection in a changing world.

7 Poster Abstracts

7.1 Complete genome sequence of foodborne pathogen *Salmonella enterica* subsp. *enterica* serovar Thompson str. isolated from Korean foodborne outbreak

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Salmonella enterica subsp. *enterica* is a major cause of food-borne illnesses associated with a wide variety of foods, including meat, eggs, fruits, vegetables, nuts, and spices. Here, we presented the complete genome sequence of *Salmonella enterica* subsp. *enterica* serovar Thompson str. MFDS1004026

Salmonella enterica subsp. *enterica* is a major cause of foodborne illnesses associated with a wide variety of foods, including meat, eggs, fruits, vegetables, nuts, and spices. Based on the serologic identification of O (lipopolysaccharide) and H (flagellar) antigens*, S. enterica* subsp. *enterica* has been classified into a variety of groups and specific serovars. The genome of *Salmonella enterica* subsp. *enterica* serovar Thompson strain MFDS1004026 which was isolated from a human fecal sample in the wake of a foodborne illness outbreak was completely sequenced using the PacBio RS II platform. Genomic DNA was extracted by standard protocols and sheared into ~10- to 20-kb fragments for PacBio library preparation. P6-C4 sequencing was perfomed on one single-molecule real-time (SMRT) cell. The continuous long reads were assembled using the PacBio SMRT Analysis version 2.3.0, resulting in an assembly with single contig. Final assembly showed mean coverage of 242X. The genome consists of a circular chromosome of 4,742,942 bp with a GC content of 52 % and did not contain any plasmids. The chromosome contains 4,482 open reading frames, 84 tRNA genes, and 22 rRNA genes organised into seven rRNA operons. Whole-genome sequence based multilocus sequence typing (MLST) showed that this strain belongs to the sequence type 26 (ST26). *In silico* serotyping predicted an antigenic profile of this strain as 7:k:1,5 Thompson in the Kauffmann-White scheme. Functional categories based on COG and KEGG metabolic pathway analysis revealed that the genome of MFDS1004026 contains the 24 genes associated with salmonella infection and 19 genes related to beta-lactam resistance. Furthermore, this genome information will be useful for the development of a novel biocontrol approach to regulate the pathogenesis of food isolate *Salmonella* Thompson.

7.2 Health-based guidance values for food additives and contaminants in NIFDS

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National Institute of Food & Drug Safety Evaluation (NIFDS) performs risk assessment and develops a scientific risk management system. From 2006, NIFDS has been establishing Health-based Guidance Values (HbGVs) for food additives and contaminants.

Among current issues affecting the world, safety and security are attracting particular attention. Ensuring the safety of food has been also a major focus of the Korean government as well as a notable concern among the international community. As the nation's food supply becomes more complex, decisions about policies to prevent contamination and illness have become even more important to ensure public health. There are numerous hazards that may adversely affect the health of humans, including pathogenic microorganisms, and chemical substances. Exposure to these hazards can occur through various sources, but most importantly through food consumption. One of the main roles of NIFDS is to carry out assessments of the risks that humans may face, qualify those risks as far as possible, and where necessary, issue recommendations. HbGV is defined as an estimate of the intake of a substance over a lifetime that is considered to be without appreciable health risk. The aim of HbGV is to provide quantitative information from risk assessments for risk managers to enable them to make decisions concerning the protection of human health. NIFDS set up a strategic plan for establishing HbGVs for food additives and contaminants in 2012. The process of the establishment of HbGV such as data quality, adequacy of critical effects, and adequacy of uncertainty factors is verified by an expert committee included toxicologists, pathologists, and epidemiologists. NIFDS has selected major management substances in 300 food additives and 60 contaminants, and plans to evaluate these by 2020. NIFDS has currently evaluated 135 food additives and 28 contaminants. In the future, NIFDS will carry out the development of alternative methodologies for substances with insufficient toxicological information, the development of a PBPK model, and studies on the integrated risk management of individual hazardous substances.

7.3 A study on authentication of seven shrimp species using genetic marker

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Seven edible shrimp species were selected to develop an effective authentication method using end-point PCR. The specificity was checked among the seven shrimp species and each primer set amplified the marker genes corresponding each shrimp species without cross-reactivity.

Shrimp is one of major fishery resources traded internationally, and certain species are sold at high prices in the Republic of Korea. The main difficulty to discriminate shrimp species is likely due to phenotypic similarities and removal of external carapaces during processing. Therefore, the importance of a rapid authentication method to substitute morphological analysis is increased. In this study, seven edible shrimp species (*Fenneropenaeus chinensis, Marsupenaeus japonicus, Fenneropenaeus merguiensis, Penaeus monodon, Pandalus hypsinotus, Litopenaeus vannamei, Macrobrachium rosenbergii*) were selected to develop an effective authentication method using end-point PCR.

Our methods were developed using seven edible shrimps, fleshy prawn *(F. chinensis),* kuruma shrimp (*M. japonicus),* banana prawn (*F. merguiensis), g*iant tiger prawn (*P. monodon),* humpback shrimp (*P. hypsinotus),* white leg shrimp (*L. vannamei),* and giant freshwater prawn (*M. rosenbergii).* DNA was extracted using Dneasy® Blood & Tissue kit (Qiagen, Hilden, Germany) according to the manufacturer's recommendations. Species-specific primer pairs were designed based on cytochrome oxidase subunit I and cytochrome B genes retrieved from NCBI Genbank. PCR condition for each species was optimised with three criteria, annealing temperature (54 to 64°C), PCR cycles (30 to 40 cycles), and limit of detection (0.05 to 0.0005 ng). The specificity was checked among the seven shrimp species and each primer set amplified the marker genes corresponding each shrimp species without cross-reactivity. These results reveal that the developed method is a rapid and efficient tool to identify shrimp species.

7.4 Influence of processing on honey – new insights using NMR honey profiling™ to detect adulteration

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Adulteration has become an issue on the honey market in the past years and may occur unintentionally through feeding during nectar flow or by adding sugars or syrup to honey. To ensure quality and authenticity of honey it needs to be tested.

However, the availability of specific markers for processing, quality or especially for adulteration are crucial. The fructose/glucose ratio (F/G) of a unifloral honey can be specific for its botanical origin. An F/G < 1.0 is rare and typical for rape honey (*Brassica napus*, canola). Additionally it could be observed that rice syrups have similar F/G values as rape honey. One particular marker for adulteration with extraneous sugars in blossom honey is the monosaccharide mannose. All analysed natural blossom honeys showed no indication of mannose. Results indicate that mannose finds its way into blossom honey either through adulteration with high end syrups or through treatment with ion exchange resins as part of purifying processes. Either way the resulting product does not comply with the EU honey regulation (Council Directive 2001/110/EC of 20 December 2001 relating to honey) and cannot be marketed as honey.

7.5 The FoodAuthent project – steps forward harmonised analytical authentication: investigation of hard cheese, edible seed oils and spirits

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Identity and authenticity of products are current topics in food and feed science for both sides: on the one hand consumer protection authorities and on the other hand producers and dealers. Since the beginning of food trade, incidents concerning adulterations of relevant products are well known. However, detection of these adulterations is challenging to the analytical chemists concerning its identification because of increasing product diversity and the continuous development of new production technologies.

Therefore, the application of fingerprinting techniques obtained increasingly importance during the recent years. These procedures are usually based on non-targeted spectroscopic and spectrometric data, providing the capability for characterisation in form of a so called chemical fingerprint. The subsequent statistical data analysis (optionally multivariate data analysis) provides a general identification of many deviations from the expected product, such as proof of authenticity (e.g. botanical or geographical origin) or adulteration (addition of forbidden substances, e.g. melamine to milk products or methanol in vodka).

However, the routine use of fingerprinting approaches is currently restricted to certain products, e.g. juice, wine and honey, often in conjunction with commercial solutions. A number of basic requirements regarding the application in routine and official control have to be fulfilled, e.g. standardised protocols for sample analyses, concept for quality assurance of chemical analysis. Thus, with the aim to promote the implementation of non-targeted analytical approaches into routine analysis, the BMEL-funded project FoodAuthent inter alia focusses on standardisation/harmonisation analytical aspects.

7.6 ImproRisk: a rapid risk assessment tool

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Summary
ImproRisk, a user-friendly excel-based model, is a tool for conducting rapid exposure assessment analysis. It comprises a lot of features, the most important of all is the derivation of probability and cumulative distributions of exposure; therefore, it is a useful tool for risk assessors and risk managers. The model is fairly used at national and EU level and will be further upgraded in the near future to meet the needs of risk assessors within the EU, as well as for third countries.

Abstract
ImproRisk is a model for conducting dietary risk assessment analysis. It was developed for SGL by the IMPROVAST company (www.improvast.com). Based on MS Excel, it is an empirical distribution model using the deterministic method of dietary exposure assessment to contaminants.

The ImproRisk model combines food consumption data with occurrence data (concentrations of chemical substances) and calculates the exposure rate for the population. The model embeds the EFSA FoodEx system version 1 (FoodEx). The consumption dataset must be coded according to FoodEx Level 4 and the occurrence dataset according to FoodEx Level 2. Then the consumption is transformed to FoodEx Level 2 and the matching of both databases leads to the estimation of the intake level. It has the capacity to work with food consumption data at individual level; therefore, it supports exposure calculation at each food consumption instance. Every individual, at each food consumption instance, is exposed to a chemical. The exposure at that consumption instance is calculated by matching the consumption and occurrence. The individual's body weight is taken into account. Then, the results aggregation allows the calculation of the exposure rate of a given population; as well as, the percentage of the population above an established toxicological reference value for a given chemical.

The **current features** of the model include the following: a) Easy (a click of a button) load/update of the occurrence dataset and rapid exposure assessment of different chemicals. The loaded occurrence dataset must be in a specific format (according to EFSA guidelines) and it can be saved in a provided simple excel spreadsheet template. b) Easy upload/update of the consumption dataset at individual level and the same applies as above. c) Descriptive statistics of the exposure (mean, median, standard deviation, percentiles, etc.). d) Probability and cumulative distribution of the population exposure. e) Contribution rate of food categories (at FoodEx Level 1 & 2) to the total exposure. f) Statistical inference tests (i.e. t-test) for comparisons among exposure for men and women and other tests, such as Cohen's D, which quantifies the size of the difference between two population exposure estimates. g) ImproRisk has lately been updated to accommodate weighting coefficients to adjust the sample for non-representativeness of the population. h) The instruction manual is already written (in English) and updated on a regular basis, and is published-along with other important updates-in the ImproRisk website (www.improrisk.com).
There are several **benefits** of the ImproRisk model: it abridges the gap between screening and probabilistic models and is compatible to the approach applied by EFSA for exposure assessment. Also, it is employed in the field of exposure assessment for contaminants, since at EU Level only the Food Additives Intake Model (FAIM) for additives and the Pesticide Residue Intake Model (PRIMo) for pesticides exist. In addition to contaminants, the model can easily be applied to food additives and other chemicals. It is simple, totally straightforward and a user friendly model, which was validated by EFSA. It takes into account the individual's body weight, so that the exposure is calculated at individual level. The model derives distri-

butions of exposure; therefore it is a useful tool for risk assessors and risk managers to get a clear view on how the exposure is distributed over the population of interest. It is not a closed box model. All the calculations (in excel) are visible and there to inspect. All formulas are transparent; consequently, the model results can be validated easily.

In the future, the model will be upgraded; so that, it can be used at FoodEx level 3. Furthermore, it will be configured in order to be compatible to the EFSA FoodEx system version 2.

Up to now, **at national level**, ImproRisk has been used for the risk assessment of the Cypriot adolescent population to heavy metals (lead, cadmium, mercury), nitrates and aflatoxin B1 (AFB1). The work in progress includes the risk assessment of acrylamide, PAHs and dioxins.

Regarding the **impact of the model at EU level**, in 2016, there was a request from the Member States (MS) to be trained on the ImproRisk model. The training workshop was co-funded and co-organised between SGL and EFSA in Cyprus, with the participation of 18 MS and 4 pre-accession countries. Shortly after, ImproRisk was presented in quite a detail in a training course on risk assessment in Montenegro organised by EFSA. All pre-accession countries participated in this training. The same year, two trainings on the use of the model took place in Belgium and Estonia, and they were carried out by the Belgian and Estonian participant at the workshop in Cyprus, respectively. Recently, Croatia published an opinion on risk assessment of nitrates in vegetables using ImproRisk. Up to now, more than 60 risk assessors from Food Safety Authorities/Agencies in MS and pre-accession countries are registered users of ImproRisk, therefore the model is fairly used at EU level.

7.7 Occurrence and assessment of aflatoxins and fumonisins exposure in corn products in Serbia

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Cereals, particularly corn products (corn flakes, corn flour, popcorn, etc.) are common in everyday diet in Serbia and worldwide. Cereals are possible sources of mycotoxins. Most common mycotoxins in Serbia are fusariotoxins, but lately aflatoxins were found as well. The aim of this research was to report data on the occurrence of aflatoxins (AFs) and fumonisins (FUMs) in corn products marketed in Novi Sad, Serbia during March 2016, and to try to estimate dietary exposure. In total, 31 samples of corn product were analysed. The samples we grouped into four categories: maize flour (7), maize meal (10), popcorn kernel (6) and corn snack products (8). None of the analysed samples contained AFs above the LOQ. FUMs were present in 68 % of the samples, where one sample of popcorn kernel exceeded EU and Serbian regulations. Overall, FUMs contents were ranged from 28 to 1700 µg/kg. The highest FUMs levels were found in popcorn kernels (ranged 227 – 1700 µg/kg), followed by maize flour (119 – 371 µg/kg), while the lowest FUMs contents were found in maize meal (28 – 148 µg/kg) and maize snack products (39 – 87 µg/kg). By comparing recommended tolerable daily intake (TDI) of fumonisins (2 µg/kg body weight) with the data on exposure estimate in Serbian adults that we obtained, it can be concluded that there was no concern for the public health.

Key words
aflatoxins, fumonisins, exposure, corn products

7.8 Exposure assessment of adults in Croatia to patulin from apple juice

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Patulin is a mycotoxin produced by particular moulds species, like *Penicillium* (particular *P. expansum*), *Aspergillus* i *Byssochlamys* which can grow on fruits, cereals, cheese and some other food. The main source in human consumption is apple juice. Other juices mixed with apple juice can also contribute to the exposure. Apple juice consumption is the most frequent among other juices in Croatia, and juice production expanded with small family economy production. In this production, home grown apples are used and due to the lack of experience in it, higher juices patulin contamination was observed. The results from three-year monitoring included 122 apple juice samples were analysed. The food consumption data on apple juice are coming from National Food Consumption Survey (2011 – 2012). Regarding different types of apple juices on the Croatian market, in our scenario was assumed consumption of juice with 100 %, 50 % and 17 % of apple content, and in case when it was not known what type of juice was consumed, 56 % of apple content was used as an assumption that all three juices type can be equally randomly picked. According to result under limit of quantification (LOQ), lower bound (LB) – concentration equal to 0, middle bound (MB) – concentration equal to half LOQ, and upper bound (UB) – concentration equal LOQ, scenarios were used. The results were statistically analysed in the programming language "R" using the appropriate diagrams, while the conclusions were made regarding the results of the t-test and the MWU test. Exposure assessment was calculated for whole adult population, separately for male and female, age groups and geographic region. In the worst case scenario average exposure to patulin from apple juice was 0.07 µg/kg b.m., what is five time less than the actual PMTDI.

In comparison with men, women are more exposed to patulin, also the population living in the Dalmatia region compared to other regions and persons between 18 and 30 years compared with other age groups, but exposure was not above PMTDI value.

It can be concluded that the health risk from patulin from apple juice is negligible for adult population in Croatia.

7.9 Occurrence of mycotoxins in beer and coffee from the Czech market

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Mycotoxins belong to the most frequent contaminants of various food crops and products thereof. The determination of these toxins often represents a challenging task, especially when present at low content or in specific mycotoxin-matrix combinations, e.g. aflatoxin M1 in milk, ochratoxin A (OTA) in coffee, etc. Extract purification and pre-concentration is often employed in such cases to achieve sufficiently low detection limits which are in accordance with legislative regulations. Nevertheless, generic isolation approaches mainly followed by liquid chromatography separation and mass spectrometric detection (LC-MS) enabling simultaneous determination of tens up to hundreds of analytes in a single run represents the modern trend.

Within this work, an extensive monitoring study focused on evaluation of the mycotoxin contamination of popular commodities, coffee and beer, was conducted. Altogether, 119 samples of coffee (soluble, roasted and green) and 129 samples of beer (non-alcoholic, ales, lagers and specials) from the Czech market were analysed using and ISO 17025 multi-toxin method. Wide range of 57 mycotoxins of the *Fusarium*, *Aspergillus*, *Penicillium*, *Alternaria*, *Stachybotrys*, *Claviceps* and *Phomopsis* genera were determined in beers while only predominant ochratoxin A was analysed in coffee using highly-specific extract clean-up enabled by immunoaffinity columns. For analytical determination, ultra-high performance liquid chromatography coupled to tandem mass spectrometry (U-HPLC-MS/MS) was utilised.

The majority coffee samples (n = 94; 79 %) contained detectable OTA of which 2 samples of soluble coffee exceeded the current EU legislation limit of 5 µg/kg. Contrary to roasted coffee, soluble coffee showed higher contamination in average, most probably due to the matrix pre-concentration within its production while green coffee contained higher OTA content which is subsequently reduced by coffee roasting. As regards mycotoxin contamination of beer, only deoxynivalenol (DON) and its conjugate, deoxynivalenol-3-glucoside (DON-3-Glc), were detected. In some beers, levels exceeding 100 µg/L of DON and DON-3-Glc were determined. Currently, there are no maximum limits set for beer, however, our results might indicate the need for some regulation. It should be noted that for some highly contaminated beers, TDI for DON (1 µg/kg bw.) could be even exceeded by some consumers. Interestingly, beers with higher alcohol content showed the highest contamination, most probably due to the use of more malt extract for their production.

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Keywords
Mycotoxins; beer; coffee; ultra-high performance liquid chromatography; tandem mass spectrometry.

7.10 Risk assessment of formaldehyde in food and drinking water

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The critical effects of formaldehyde following oral exposure are considered to be the non-neoplastic histopathological changes observed in the forestomach and stomach in the repeated dose toxicity studies with Wistar rats. No risk for adverse effects following intake of formaldehyde occurring naturally in drinking water was identified. The risk for adverse effects following intake of formaldehyde in beverages and foods could not be evaluated.

Formaldehyde is ubiquitous in the environment and occurs naturally in the environment. Formaldehyde in drinking water arises mainly from the oxidation of natural organic (humic) matter. In water, formaldehyde is rapidly hydrated and is found largely in the form of methylene glycol and its oligomers. Equilibrium favours the glycol and less than 0.04 % by weight of unhydrated formaldehyde is found in highly concentrated solutions.
Formaldehyde occurs naturally in food. Reported background levels are very variable with values around 0.1 – 0.3 mg/kg in milk, 6 and 35 mg/kg in fruit and vegetables, and 6.4 – 293 mg/kg in fish. Formaldehyde can also occur in food if released from melamine resin food contact materials. Owing to its chemical reactivity, formaldehyde is essentially present in reversibly bound forms and irreversibly bound forms. The degree to which formaldehyde in various foods is bioavailable following ingestion is not known.

The general population is exposed to formaldehyde from many sources. The contribution of formaldehyde from food has been assessed by EFSA not to exceed 100 mg/person. Drinking water will only be a minor source of exposure.

Formaldehyde occurs in most organisms, tissues and cells at very low concentrations. In humans, as in other animals, formaldehyde is an essential metabolic intermediate in the physiological one-carbon pool (central to many biological processes).
Owing to its chemical reactivity, formaldehyde is essentially present in reversibly and irreversibly bound forms. Formaldehyde can be reversibly bound to some amino acids or to proteins to form protein adducts. Irreversible reactions result from reaction of formaldehyde with two proteins (protein-protein crosslinks) or from reaction of formaldehyde with protein and DNA (DNA-protein crosslinks [DPX]).

Ingestion of formaldehyde may cause burning in the mouth and oesophagus, nausea and vomiting. The fatal dose in humans has been reported to be about 60 – 90 ml. No human data regarding effects after repeated oral exposure to formaldehyde have been located.

Oral repeated dose toxicity studies in experimental animals include one sub-acute study in rats, two sub-chronic studies in rats and dogs, and three chronic studies in rats.

The principal non-neoplastic effects observed are histopathological changes in the forestomach and glandular stomach, such as erosion, ulceration, inflammation and hyperplasia. These effects were seen when formaldehyde was administered in the drinking water to Wistar rats at high concentrations. In contrast, no gastrointestinal effects were reported in Sprague-Dawley rats or Beagles dogs. Whether the histopathological changes observed in Wistar rats but not in Sprague-Dawley rats and Beagle dogs are due to a strain-specific sensitivity cannot be evaluated. Therefore, it is considered that humans are at least as sensitive as the Wistar rat regarding effects locally in the stomach.

Based on the most valid study, a NOAEL of 260 mg/l is considered. The local effects induced in the stomach are likely due to the irritative potential of formaldehyde.

Formaldehyde is genotoxic, with effects observed *in vivo* in cells from tissues with which formaldehyde first comes into contact, i.e. nasal tissue.

Three oral carcinogenicity drinking water studies have been performed with rats.
In two studies with Wistar rats, the incidences of tumours did not vary markedly between groups following administration up to 1900 mg/l.

In contrast to these two studies, an increase in the total incidence of leukaemias and lymphomas was reported in Sprague-Dawley rats groups at 500 mg/l and above. In addition, the incidence of adenomas/adenocarcinomas in the stomach gland (males) and of tumours in the intestine (females) was reported as being slightly increased at 1500 mg/l. However, this study has several serious limitations and has been heavily criticised.

The weight of evidence indicates that formaldehyde is not carcinogenic by the oral route; however, it cannot be fully excluded that formaldehyde could have the potential to induce tumours locally in the gastrointestinal tract following oral intake of high concentrations for a prolonged period – concentrations exceeding those that humans can be exposed to from drinking water and food. Formaldehyde-induced cytotoxicity is thought to be the initial lesion that precedes the proliferation of target tissues and therefore, it is considered that there would be a threshold for the potential carcinogenicity locally in the gastrointestinal tract. Based on the most valid study, a NOAEL of 1900 mg/l is considered for neoplastic effects. Consequently, the NOAEL of 260 mg/l for non-neoplastic changes is considered also to take into account a potential carcinogenic effect of formaldehyde following oral ingestion.

A tolerable concentration of formaldehyde in drinking water is estimated to 30 mg/l (rounded value) based on the NOAEL of 260 mg/l and assessment factors of 2.5 and 3.2 to account for interspecies and inter-individual variability, respectively, in toxicodynamics.

Based on the tolerable concentration of formaldehyde in drinking water of 30 mg/l and an estimated concentration of formaldehyde in drinking water of 30 µg/l (worst-case scenario), no risk for adverse effects from intake of formaldehyde in drinking water was identified.

Based on the available data, a tolerable concentration of formaldehyde in food cannot be estimated. Therefore, the risk for adverse effects from intake of formaldehyde in beverages and foods could not be evaluated. However, due to the low levels of naturally occurring formaldehyde in beverages and foods a risk for adverse effects is not considered likely.

Formaldehyde can also occur in beverages and food if released from melamine resin food contact materials. Based on the few available studies on migration of formaldehyde from melamine resin food contact materials, a risk for adverse effects following oral intake of formaldehyde is not considered likely. However, there is an uncertainty regarding the actual migration of formaldehyde from melamine resin food contact materials.

7.11 Cumulative risk assessment of chemical exposure of children/unborn children to endocrine disruptors and neurotoxic substances

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Unborn children/small children are considered particularly vulnerable when it comes to exposure to endocrine disrupters and neurotoxic substances. In a recent risk assessment report prepared for the Danish Environmental Protection Agency, 37 endocrine disruptors and 39 neurotoxic substances (with some overlap) were identified. From the scientific literature (preferably scientific opinions from the EU Scientific Committees, from EFSA or from RAC) exposure to children below 3 years and unborn children/pregnant women were assessed for all substances. Further, the estimated exposures were compared to exposure levels based on human biomonitoring studies. DNEL values were established for all substances for either endocrine disruption or chronic neurotoxic effects.

For all the assessed substances, the main source of exposure was typically found to be related to food. For some substances, other important sources of exposure were the indoor environment (such as dust), the outdoor environment (soil), cosmetics and consumer products, including toys.

The highest risk estimates (i.e. RCR >1) from endocrine disruptors were found in relation to exposure to paracetamol, dioxins/PCBs, phthalates (DEHP, DBP, DiBP), bisphenol A, as well as BHA and BHT. Therapeutic use of paracetamol by pregnant women resulted in a RCR value of 100. The highest risk estimates for chronic neurotoxic effects were found for: lead, dioxins/PCBs, mercury/methyl mercury, bisphenol A and acrylamide. Exposure to lead constitutes by far the highest risk as the current exposure of children exceeded the tolerable daily intake with a factor of more than 50.

For the majority of the substances with available biomonitoring data, it was observed that the detected measurements in general resulted in comparable or lower exposure estimates than the exposure estimates based on the modelled calculations from the different sources. Data on chemical levels in breast milk resulted in risk estimates for dioxin/ PCBs and PFOS that were much higher for breast fed infants compared to risk estimates for non-breast fed infants, indicating breastfeeding as a possible significant source of exposure.

To our knowledge, this is the first comprehensive overview of risk of endocrine disrupting and neurotoxic effects of the many chemicals that these specific vulnerable groups are exposed to.

The report “Exposure of children and unborn children to selected chemical substances” (1) has been prepared by DHI; DTU Food, National Food Institute; and Force Technology for the Danish EPA.

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(1) https://www2.mst.dk/Udgiv/publications/2017/04/978-87-93529-84-7.pdf

7.12 New challenges for risk assessment: targeting odors of toys and articles of daily use on a molecular basis

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Summary
Several toys available on the market exhibit offensive and irritating smells. Targeted odorant analyses revealed that many of the causative substances have critical toxicological properties and affected products are often additionally contaminated with other odorless, yet hazardous substances. The assessment of risks that such products pose to the health of children requires advanced analytical techniques.

Abstract
Global toy sales have experienced continued growth in recent years, with an increase by 11.6 % to $ 87.4 billion between 2011 and 2015 [1]. Several toys available on the market exhibit strong, offensive smells that have hitherto been rarely investigated on a molecular basis. Accordingly, in most cases neither the identity of the causative substances nor the exposure of children to them is known. Nevertheless, previous studies indicate that children are more sensitive to certain odorants than adults [2, 3], and the odor of a toy has been observed to change a child's playing behavior significantly [4, 5]. Accordingly, odors might not only impact the health of children, but also affect their behavior or wellbeing.

One reason why odors of toys and articles of daily use have not been addressed before might be that targeted analysis of odorous contaminants requires a complex and advanced analytical infrastructure. To address this odor issue, our research group employs sensory evaluation and modern odorant analytical tools – as routinely used in food science – to identify the odorants responsible for the intense smell of such products. Using these techniques, we analysed selected products such as plastic toy swords, fancy dress handbags for children, and several aquatic toys and swimming aids, amongst other products.

Sensory evaluation revealed that the smell of all samples was generally perceived as being unpleasant (except for the aquatic toys for single panelists). The odor profiles of the handbag and the sword were dominated by smell attributes associated with rubber, leather and gasoline, whereas the aquatic toys exhibited almond and solvent-like smells. Panelists also perceived the smell of all samples as being pungent; some even associated exposure with subsequent headaches.

A wide variety of odorants was successfully identified in the handbag and the sword. Amongst them were naphthalene and its methyl and dimethyl derivatives, as well as diverse alkylated phenols, all contributing to the unpleasant overall odor [6, 7]. In contrast, the overall odor of the inflatable beach toys and swimming aids could be traced back to residual solvents, namely cyclohexanone, isophorone and phenol [8].

Many of the odorants identified in our studies are classified as irritants, some even as toxic or suspected mutagens or carcinogens (e.g. naphthalene or isophorone) [6, 8, 7]. Accordingly, the toxicological properties of the odorants, as well as the strong physiological responses observed during sensory evaluation, demonstrate the urgent need for a detailed risk assessment followed by changes in legislation, if necessary.

Consequently, quantitative data about the emission or migration of the hazardous substances is required to estimate the exposition of consumers. Using proton-transfer-reaction mass spectrometry (PTR-MS), emission rates of odorants can be determined in real-time without complex sample preparation [9]. First application studies on toys already revealed promising results. In addition to studies assessing the risks for children, future research should also establish exposure scenarios of those people who are required to handle such products in their professional life, during production, distribution, or in retail.

Acknowledgements
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7.13 Tracing the source of foodborne disease outbreaks using FoodChain-Lab

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Short Summary
The free and open source software FoodChain-Lab was developed to trace sources of food contamination during foodborne disease outbreaks. It provides trace back and forward analyses for food items along food supply chains and was successfully applied by investigation teams in several national and EU-wide foodborne disease outbreaks.

Abstract
Food chains are complex and contain many items and stations. In the past years outbreaks on national and EU level demonstrated that there is a need for an expert software system handling the large amount of different food ingredient deliveries to support investigations on supply chains as well as exposure assessments in crisis situations.

To approach these needs, a free and open source software called FoodChain-Lab has been developed to help outbreak examination teams trace sources of food contamination. FoodChain-Lab was developed as a plug-in for the open source data analytics platform Konstanz Information Miner (KNIME) and can be downloaded via http://foodrisklabs.bfr.bund.de. FoodChain-Lab was applied during the EHEC outbreak in Germany in 2011 and has been used and tested in other outbreak investigations like the norovirus outbreak in Germany in 2012 or the hepatitis A outbreak in Europe. During these investigations the software evolved from a data visualisation and analyses tool into a tool box for data management, data enrichment, visualisation, data analysis and interactive reasoning. Data on food or feed deliveries can be imported via Excel sheets. An integrated database enables the user to store all relevant information in a structured way on the basis of stations, products, lots and deliveries. Plausibility checks are implemented to ensure high data quality, which is a major challenge in most outbreak situations. The flow of goods can be analysed and visualised as a network graph for the focus on delivery chains and also on a geographical map to show spatial dimensions between outbreak clusters and food deliveries.

7.14 Refinement of dietary exposure assessment in the context of global food supply – case study: aluminium in kiwi fruits

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Summary
The influence of origin-related substance concentrations in deterministic dietary exposure assessment has been considered using data for aluminium in kiwi fruits from German Food Monitoring 2010 and consumption data from German National Nutrition Survey II.

Background
Food supply is becoming more global. Agricultural products are available from different countries of origin for the consumer and for further processing in food industry. In connection with dietary exposure assessment, as an important base for risk assessment in food safety and consumer protection, the relation between substance concentration and geographical origin of food is of special interest. In the food supply chain there are different influences on substances and finally on dietary exposure possible. On one hand limited obligation to label the country of origin especially for ingredients in processed foods is a challenge while connecting food origin with substance concentrations (contaminants or residues) in a refined dietary exposure assessment. On the other hand more comprehensive information is expected from activities to better describe the global food chain in terms to prevent and to be prepared for food crisis. The influence of origin-related substance concentrations in deterministic dietary exposure assessment has been considered using data for aluminium in kiwi fruits from German Food Monitoring 2010 and consumption data from German National Nutrition Survey II (NVSII).

Methods
Data from the German Food Monitoring 2010 was used to obtain aluminium concentrations in kiwi fruits in connection with information on origin (Sieke *et al.*, 2008). A modified lower bound approach was applied for the determination of mean, standard deviation and percentile 95 replacing non-detects with zero and non-quantified values with the limit of detection (LOD) (WHO & FAO, 2009). Aluminium concentrations were grouped origin-related and examined for significant differences to compare all samples with samples from origins having higher aluminium concentrations. To obtain consumption data the dietary history interview (DISHES) of NVS II was used (Krems *et al.*, 2006). Recipe codes xy were decoded previously by the German Federal Institute for Risk Assessment (BfR) using Bundeslebensmittelschlüssel (BLS) recipes (version II.4) to derive consumption amounts of unprocessed food items which were used in household recipes. Typically applied standard scenarios of deterministic dietary exposure assessments were calculated by combining different distribution parameters of substance concentration and food consumption (Sarvan *et al.*, 2017). Statistical analyses were carried out using SPSS version 21 and Microsoft Excel 2010.

Results
For aluminium in kiwi fruits the mean concentration of 2.875 mg/kg from Non-EU region is 2.9-fold and therefore significant higher than 0.990 mg/kg from all samples. The chronic dietary aluminium exposure for consumers of kiwi fruits for average consumption and mean concentration considering all samples without distinction of origin is 0.002 mg/week/kg bw and the most conservative standard scenario (95th percentile consumption and concentration) results in intake estimates of 0.024 mg/week/kg bw. When using the mean concentration of that origin with highest concentrations aluminium exposure of 0.014 mg/week/kg bw is calculated. The highest calculated exposure represents 2.4 % of the tolerable weekly intake (TWI) of 1 mg/week/kg bw.

Conclusions
The most conservative standard scenario results in the highest exposure value and covers the origin influence on aluminium concentrations in kiwi fruits. For chronic aluminium exposure from kiwi fruits origin-specific scenarios do not have to be performed if all standard scenarios are considered. However, origin-specific scenarios provide more detailed information on possible origin influences.

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7.15 The Risk Assessment Modelling & Knowledge Integration Platform (RAKIP) project

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Summary
The RAKIP project is a joint ANSES, BfR and DTU Food initiative aiming to facilitate the generation and exchange of models (and data) in the food safety risk assessment community. A first challenge solved by the RAKIP partners was a harmonised understanding of terms and concepts used within this domain spanning from high level concepts as e.g. defined by Codex Alimentarius up to terms generally used in statistics, data or software science. Project results as well as a demonstrator RAKIP model repository are online available as community resources: https://foodrisklabs.bfr.bund.de/rakip-web-portal/

Abstract
The food safety community is generating a variety of scientific knowledge (e.g. mathematical models, experimental data and scientific publications) and resources (e.g. databases and software tools for model generation and application) in the areas of predictive microbiology (PM) and risk assessment (RA). However, the access to this knowledge and the exchange of information between resources are currently difficult and time consuming. This problem has increased over time due to the lack of harmonised data formats and rules for knowledge annotation. This includes the lack of a common understanding of basic terms and concepts in risk assessment and the non-existence of harmonised controlled vocabularies for metadata description.

Experts from ANSES, BfR and DTU Food were working together since January 2017 to establish a new initiative in the food safety community called Risk Assessment Modelling and Knowledge Integration Platform (RAKIP). The objective of the RAKIP Initiative is to create open resources that support the exchange of knowledge between existing and future software tools and databases in the food safety domain. Among these envisaged resources are an open information exchange format called Food Safety Knowledge Markup Language (FSK-ML) and a web portal to share models encoded in the harmonised data format. To reach these objectives, RAKIP project partners worked on the establishment of a joint understanding of general terms and concepts relevant in PM and RA modelling. In this context, a harmonised vocabulary for describing information relevant in PM and RA modelling has been generated.

The alignment of terms and concepts was carried out through expert workshops complemented by joined work on a white paper entitled: “RAKIP– terms and concepts”. This paper includes the generation of several schemata detailing steps that are crucial for performing risk assessments. These graphical schemata were necessary to clearly communicate and discuss the underlying modelling processes. Terms and concepts were finally defined in a glossary. In addition, an exhaustive list of metadata for describing data and models in the risk assessment domain, associated to different list of controlled vocabularies, were developed. All these generated resources can be accessed and updated online.

The newly developed RAKIP resources are designed to support the whole risk assessment community including national and international risk assessment agencies, food business operators and academic institutions. Modellers, risk assessors and risk managers will benefit

most from the envisaged RAKIP web portal. Other users like research scientists can also make use of the RAKIP resources, e.g. share their experimental data or apply improved modelling tools in the future. To accomplish this, the open information exchange format FSK-ML formalise the description of models and data using the terms and concepts framework. In this way a foundation for the harmonised annotation of risk assessment models and model components is provided. In addition, open source software tools and software libraries promote the adoption of FSK-ML by the research community and serve as an important resource for future software developments and efficient knowledge exchange within the PM and RA modelling community.

7.16 Food safety research for development in sub-Saharan Africa: tapping the expertise of German partners

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According to recent estimates by the World Health Organization, the global burden of foodborne diseases is comparable to that of HIV/Aids or tuberculosis or malaria. Up to 90 % of foodborne disease is caused by microbes in perishable foods of which more than 80 % are sold in the informal agri-food system. Informal markets, also referred to as wet or traditional markets, are characterised by local products, prices, and marketing channels where actors are often not trained, not licensed, and not paying taxes. However, these markets provide food and jobs to millions of people in sub-Saharan Africa. They are also the major markets for most smallholder producers of fresh foods. Lack of evidence on attribution data and limited understanding of risk-based approaches in food safety management only worsen the problem.

The Safe Food, Fair Food project, funded by GIZ and led by the International Livestock Research Institute, aims to improve the livelihoods of poor producers and consumers by reducing the health risks and increasing the livelihood benefits associated with meat, milk and fish value chains in sub-Saharan Africa. From 2008 – 2015 the project was implemented in ten countries south of the Sahara with partners from Africa, Germany and Japan.

Key findings include:

- Informal markets are integral to food, nutrition and job security in sub-Saharan Africa;
- Although hazards are often common in informal markets risk to human health is not necessarily high;
- Risks in the informal food chains have been under-researched and need attention;
- Risks vary and may not be as serious as perceived: food safety policy should be based on evidence not perceptions;
- Participatory methods are useful in studying food safety risks in informal food chains;
- Simple interventions could lead to substantial improvements: potable water, electricity, training, standards, appropriate hygienic supervision etc.;
- Food safety needs a multi-disciplinary (OneHealth) and multi-sectoral approach;
- Comprehensive, jointly developed and implemented policies are prerequisites for food safety assurance.

German partner institutions engaged were the German Federal Institute for Risk Assessment (BfR), Freie Universität Berlin, Friedrich-Löffler-Institute, and University of Stuttgart-Hohenheim. More than 30 food safety practitioners, students and scientists were trained in specific laboratory methods for hazard identification (i.e. *Listeria monocytogenes*, *Salmonella* spp., *Toxoplasma gondii* or *Trichinella* spp.) at German partner institutes or in their home countries, and field isolates were archived at German partner institutes. More than 200 key stakeholders at over 35 institutions in 12 countries were trained on the concepts of risk-based approaches and (participatory) risk assessment. Joint risk assessments and pilot interventions for improving food safety have been disseminated in 15 peer-reviewed journal publications and more than 200 other outputs.

7.17 The Federal Institute for Risk Assessment as an EFSA Focal Point

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The European Food Safety Authority (EFSA) has initiated the set-up of national contact points in the Member States to act as an interface between the EFSA and the various national authorities for food and feed safety, animal and plant health, as well as research institutes, consumers and other interest groups connected with the EFSA.

As the coordination point, the BfR ensures that the exchange of scientific information about initiatives, current processes, research projects and the results of risk assessments of foods and feeds takes place directly. Every year, the EFSA organises several joint meetings with representatives of the European Focal Points. The contact points report regularly to the EFSA about their activities which are summarised in an annual report (Focal Point Activities) published by the EFSA. The EFSA Focal Point coordinates the requests for scientific opinions from Germany and forwards them to the EFSA. In cases in which the EFSA holds a different opinion in the assessment of a risk than the responsible institutions in Germany, it is the task of the Focal Point to contribute towards the clarification of divergences of this kind. As the coordination point, the BfR has built up a network of representatives from public institutions, science, trade and industry, politics and consumer associations in Germany which supports the EFSA in the tasks it performs for the EU. The goal of these activities is to make even more intensive use of the existing European knowledge of the health risks of food, thereby ensuring food safety in Europe on the highest possible scientific level.

7.18 Assessing the public health risk associated with use of pleuromutilin in pigs in Denmark

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The Danish Veterinary and Food Administration are designing new antimicrobial treatment guidelines for antibiotic usage in pigs. The purpose is to assist veterinarians in choosing antimicrobial drugs that provide the best effect and have the lowest probability of developing resistance of importance for public health. The guidelines will be based on risk assessments. This poster presents the assessment of the public health risk posed by use of pleuromutilins in pigs carried out using a slightly modified OIE framework and to some degree EMA's guidelines[1].

Staphylococci, including livestock-associated methicillin resistant *Staphylococcus aureus* (LA-MRSA) and enterococci were identified as the relevant hazards. For LA-MRSA, the release assessment showed that the probability of development of pleuromutilin resistance was high. At the time of the assessment, the relevant exposure pathway was primarily occupational, which only exposed a small proportion of Danes. The consequences of exposure were assessed as high for vulnerable groups (severely ill patients at hospitals) and low for the general public, due to low transmission potential of LA-MRSA between people and current screening programmes in hospitals of patients with daily contact to pigs. For LA-MRSA, the overall risk was estimated as low (low uncertainty).

For enterococci, the probability of pleuromutilin resistance and cross-resistance to linezolid was low. Exposure pathways included both occupational and foodborne. The consequences were considered low to the general public due to low virulence in humans and high for vulnerable groups. There exist for the time being no national control measures, and enterococci have a wide resistance profile. The overall risk for enterococci was assessed as low but with high uncertainty and with potential for increasing consequences in the future if linezolid resistance emerges.

The risk assessment applies to the current situation in Denmark and it is recommended to reassess the risk, if the situation in humans or pigs changes.

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7.19 Development of a support system for the reduction of antibiotic resistant bacteria in the broiler production (EsRAM-Project)

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In the context of the EsRAM project we want to develop an electronical databased tool for the documentation and assessment of individual and multiple-sequential intervention strategies against ESBL-producing *Enterobacteriaceae* in the broiler production chain.

Extended beta-lactamase (ESBL-) producing *Escherichia coli* are of major concern in human and veterinary medicine due to their resistance against a variety of beta-lactam antibiotics. Farm animals, especially broiler chickens are frequently colonised with these resistant bacteria. Furthermore, chicken retail meat was found to be contaminated with different types of ESBL-*E. coli* in the recent years and is considered as a potential source for the exposure to humans. Therefore, intervention strategies on all levels of the broiler production chain are needed to prevent the spread and the transmission of ESBL-producing *Enterobacteriaceae*. In the project we use a literature based approach as well as experimental data from other involved partners to develop a documentation and assessment tool for possible interventions on the respective production levels, like broiler fattening farms and slaughterhouses.

First of all, possible procedures to reduce ESBL-producing *Enterobacteriaceae* were collected from the literature or from respective guidelines and German or European degrees concerning hygiene and animal health. These procedures are then going to be evaluated based on their efficiency to reduce the occurrence/amount of the resistant bacteria during the fattening period as well as on the slaughterhouse level. Therefore, we further develop a mathematical model for the broiler processing line and the quantitative transmissions of ESBL-producing *E. coli* to the chicken meat. Furthermore, certain strategies concerning the reduction of the use of antibiotics and the animal welfare are assessed in this project.

The developed tool can then be used by various stakeholders to improve their quality systems and operational procedures to prevent the occurrence, spread and transmission of ESBL-producing *Enterobacteriaceae* in the broiler production chain.

7.20 Modernisation of meat inspection of pigs by use of risk assessments

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The former EU Meat Inspection Regulation 854/2004 opened up for use of risk assessment to address what would happen, if meat inspection was changed for finishing pigs, raised under controlled housing conditions. Focus has been on assessing the effect of going from traditional inspection– involving palpation and incisions of various organs – to a visual-only inspection as well as replacing post mortem inspection with other assurance systems.

In Denmark, such risk assessments have been undertaken using the OIE approach to risk assessment involving hazard identification plus an assessment of release, exposure, and consequences, integrated into a risk estimate. To address these elements, we collected samples from abattoirs and subjected them to laboratory investigation, and we used slaughterhouse statistics, literature and expert opinion. The work was undertaken in collaboration between academia, industry, and veterinary authorities.

The first assessment dealt with the mandibular lymph nodes and the heart (Alban *et al.*, 2008), the second with the intestinal lymph nodes (Alban *et al.*, 2010), and the third with the lungs and the liver (Pacheco *et al.*, 2013). For each of these organs, we looked at what would happen if routine incisions and palpations would no longer be undertaken. This included addressing what we would miss, how often and what the consequences of this might be. This approach enabled us to introduce a gradual shift in inspection from traditional inspection to visual-only. In this way, we were able to document the safety of the new system to authorities, trade partners and meat inspectors.

Next, focus was directed to carcasses with embolic pneumonia. They may be missed, if the lungs are not palpated routinely, and lesions are not detected in other organs. In this study, 19 finishing pigs with embolic pneumonia were identified. Samples were taken from heart, liver, spleen, kidney, lungs, joints and muscles. The samples were subjected to standard microbiological investigation. This study showed that bacteria were only seldom present in muscles, and if they were, the numbers were low. A comparison of results from the different kinds of samples showed that the body in most cases had cleared itself from the original infection and that the bacteria present were not meat-borne (Kruse *et al.*, 2015).

Then, focus was broadened to cover purulent lesions indicative of prior septicaemia. These lesions may have been caused by a tail bite months earlier. According to the Danish meat inspection circular, acute cases should be condemned whereas chronic cases should be subjected to de-boning. Use of de-boning was introduced in Denmark in 1994 to ensure detection of osteomyelitis, not found in the rework area. Currently, 40,000 finishing pigs and 5,000 sows are subjected to de-boning in Denmark per year due to such lesions. The associated costs amount to approx. €3 million. Some of the questions we wanted to address were: 1) is meat from these pigs fit for human consumption? 2) Are meat inspectors able to find what they should find in the rework area, if the know that de-boning is not taking place? And 3) which alternative practices could replace de-boning?

The studies involved samples from 102 finisher pigs and 105 sows with purulent lesions indicative of prior septicaemia. For each case, samples were taken from abscesses present and muscle on the distal part of the right foreleg. As a control group, we collected muscle samples from the right foreleg from 60 finishers and 60 sows, which were fully approved at meat inspection. In general, deboning was not leading to finding of additional abscesses. The bacteria present in abscesses were not considered food-borne hazards in fresh meat, and if bacteria were present in meat then it was in very low numbers. There was no association between presence of bacteria in abscesses and in meat (Bækbo *et al.*, 2016; Pedersen *et al.*, 2017). At current, the Danish veterinary authorities are considering whether the mandatory requirement for deboning of carcasses with purulent lesions indicative of prior septicaemia should be replaced by intensive inspection at the rework area involving focus on predilection sites for abscesses and targeted local condemnation during ordinary cutting.

In 2011, EFSA published an opinion addressing the hazards which should be covered by meat inspection for swine. In that opinion, EFSA stated that traditional meat inspection in swine could safely be replaced by visual-only inspection (EFSA, 2011). And in June 2014, the EU Commission's new EU Meat Inspection Regulation came into force stipulating that meat inspection of all swine – irrespective of age or production system – should be undertaken using a visual-only approach unless food chain information or other information from *ante* and *post mortem* indicated otherwise.

Development of national risk assessments in parallel with EFSA may be seen as a complimentary work addressing specific needs in a Member State– in this case due to negotiations of acceptance of equivalence with trade partners outside the EU. The next step in Denmark will be to undertake a risk assessment for meat inspection of finishing pigs raised under non-controlled housing conditions, because the current trade agreements are based upon Regulation 854/2004 and, therefore, only dealing with finishing pigs from controlled-housing. And the EFSA Opinion is not considered as sufficiently detailed for addressing this question in the coming trade negotiations.

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7.21 Use of mathematical optimisation models to derive healthy and safe fish intake

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This study presents a method to model personalised food recommendations that requires the smallest possible diet change. The study is both methodological, describing the quadratic programming model used, and a case study on fish intake in Denmark.

Background
Recommended fish intake differs substantially from observed fish intake. In Denmark, around 15 % of the population meets the Danish recommendation on fish intake. How much fish individuals eat varies greatly. There are so many different patterns of fish intake that the fish intake of the average population cannot reflect this.

Objective
We developed a method that may provide realistic and achievable personalised dietary recommendations based on an individual's body weight and current fish intake. The objective of the study was to propose specific fish intake levels for individuals that meet the recommendations for eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and vitamin D without violating the tolerable intake recommendations for methyl mercury, dioxins, and polychlorinated biphenyls (dl-PCBs).

Methods
Two mathematical optimisation models were developed that apply quadratic programming to model personalised recommended fish intake, fulfilling criteria on nutrients and contaminants, while simultaneously deviating as little as possible from observed individual intake. A recommended intake for eight fish species was generated for each individual in a group of 3,016 Danes (1,552 women and 1,464 men, ages 18 – 75), whose fish intakes and body weights were known from a national dietary survey.

Results
Individual, personal dietary recommendations were successfully modeled. Modeled fish intake levels were compared with observed fish intakes. For women, the average proposed increase in fish intake was 14 g/wk for lean fish and 63 g/wk for fatty fish; and for men these numbers were 12 g/wk and 55 g/wk, respectively.

Conclusions
Using fish intake as an example, we show how quadratic programming models may be used to advise individual consumers on the optimisation of their diet, taking both benefits and risks into account. This approach has the potential to increase compliance with dietary guidelines by targeting the individual consumers and minimising the need for large and eventually unrealistic behaviour changes.

7.22 Prediction by the Danish (Q)SAR Database of genotoxicity of αβ-unsaturated carbonyls (structural alert for genotoxicity) evaluated as flavouring substances

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On the Union List of the chemically defined flavouring substances (Commission implementing regulation (EU) No 872/2012), a group of nearly 400 αβ-unsaturated carbonyls were included. As the αβ-unsaturated carbonyl structure elicits an alert for genotoxicity further data were requested to rule out the concern. Those of the αβ-unsaturated carbonyls for which EFSA now has reached a final conclusion for genotoxicity have been predicted using the Danish (Q)SAR Database*.

The Union List of chemically defined flavouring substances was published in 2012 (Commission implementing regulation (EU) No 872/2012). A group of nearly 400 αβ-unsaturated carbonyls (aldehydes, ketones and precursors for such carbonyls) were included in the list. As the αβ-unsaturated carbonyl structure is considered an alert for genotoxicity these substances were added a footnote pointing out that they cannot be finally included in the list until a possible safety concern has been ruled out.

The αβ-unsaturated substances were subdivided into structurally related subgroups and for each subgroup one or more representatives were chosen for genotoxicity testing. Adequate new genotoxicity data provided for the representative substances would then in theory cover the substances in the subgroup for which they was representatives. A list of the representative substances was published by EFSA.

As of October 2017, 23 subgroups have been evaluated based on new genotoxicity data and opinions for each subgroup have been published by EFSA.

The representative αβ-unsaturated carbonyls for which EFSA has either ruled out or confirmed the concern for genotoxicity have been identified in the opinions and the outcome of the evaluation of the new genotoxicity data collected and presented. In parallel, Those of the αβ-unsaturated carbonyls for which EFSA has reached a final conclusion for genotoxicity have been analysed by the free online Danish (Q)SAR Database*. The outcome of the evaluation of experimental genotoxicity data and the analysis of the substances in the QSAR database are presented.

*Danish (Q)SAR Database, Division of Diet, Disease Prevention and Toxicology, National Food Institute, Technical University of Denmark, http://qsar.food.dtu.dk/
The Danish (Q)SAR Database includes estimates from more than 200 (Q)SARs from free and commercial platforms and related to physicochemical properties, ecotoxicity, environmental fate, ADME and toxicity. (Q)SAR predictions for more than 600,000 chemical substances can be searched, sorting can be made on chemical similarity, and profiles for individual substances can be downloaded. The database is developed by the National Food Institute, Technical University of Denmark, with support from the Danish Environmental Protection Agency, the Nordic Council of Ministers and the European Chemicals Agency.

7.23 Burden of disease of exposure to endocrine-disrupting chemicals in recycled paper used for food packaging in Denmark: a case-study

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Background

The high molecular weight phthalate DEHP (1,2-bis(2-ethylhexyl) benzene-1,2-dicarboxylate) is a plasticiser with ubiquitous presence in the environment due to its extensive use in diverse articles. DEHP is in the Candidate List for authorisation (REACH [Registration, Evaluation, Authorisation and Restriction of Chemicals])[I] and is of high concern because it has serious and probably irreversible effects on human health and the environment[II]. Potential adverse effects of DEHP in humans include impact on male reproductive health due to DEHP´s endocrine disrupting properties. DEHP is one of the phthalates that can cause "testicular dysgenesis syndrome"[III], which includes the presence of malformations of the male reproductive organs including hypospadias, cryptorchidism, poor semen quality and testicular cancer[IV].DEHP is nowadays not permitted in toys, childcare articles, and cosmetics; yet, it is still used for other articles, e.g. medical tubing and blood storage bags, indoor furniture, cables printing, ink formulations, dispersion glues preparations[V]. France has recently banned the use of DEHP in pediatrics neonatology and maternity. Moreover, DEHP has been detected in recycled papers, probably resulting from its previous use with ink formulations and adhesive preparations. Semi-quantitative analytical experimental studies[VI] applied to food contact materials have shown presence of DEHP in pizza boxes made from recycled paper, and proved that DEHP is capable of migrating from the recycled carton box into the food, i.e. from the pizza box into the pizza. Therefore, the consumption of (take-away) pizza is a probable source of exposure to DEHP from food which could lead to adverse health effects.
Purpose: The aim of this study is to estimate the burden of disease due to exposure to DEHP from the consumption of commercially prepared (take-away) pizza in Denmark in terms of disability adjusted life years, DALY[VII-VIII]. We present the applied methodology, highlight some preliminary results, and discuss the possible link between this study and a life cycle assessment of pizza boxes made from recycled paper.

Methodology

We applied a burden of disease model consisting of three submodules (Fig1): the exposure module, the health outcome module, and the DALY module. In the exposure module, we estimate the DEHP exposure of women in fertile age in Denmark (ages 18 – 45) through consumption of take-away pizza and semi-quantitative analytical data of DEHP migrating from the pizza box. In the health outcome module, we estimate the probability of occurrence of the selected health outcomes in the newborn male child following the exposure of a pregnant woman to the hazard (based on dose response models). We estimate the probabilities of health outcomes from DEHP contribution using recent toxicological human data that correlates anogenital distance (AGD) in newborns (used as a bio-marker)[IX] and exposure of DEHP in the first trimester of pregnancy. In the DALY module, we integrate the incidence of the health outcomes with disease duration and disability weights, considering malformations as cryptorchidism and hypospadias, potential correction of these malformations, and other sequelae that may lead to infertility[X].

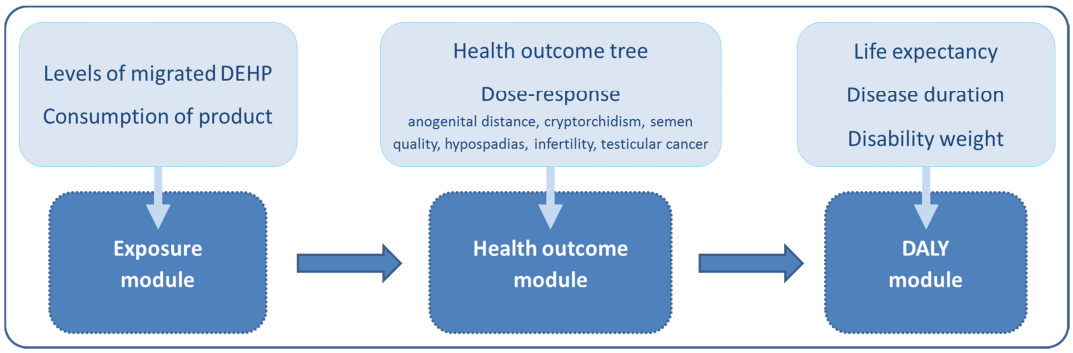

Fig 1: The three modules of the burden of disease model

Expected outcomes

Our estimates will:

- Provide evidence on the health impact of DEHP in male children since birth in Denmark through consumption of contaminated pizza by the mothers during pregnancy.
- Allow for the integration of health impact assessment of a food contact material with the environmental impact of this contact material in the same population by linking with life-cycle assessment.
- Facilitate the evaluation and comparison of different packaging alternatives by taking into account both human health and environmental impact of the material.
- Furthermore, the developed approach can be applied to estimate the disease burden of other endocrine-disruptor chemicals, filling in a knowledge gap at national and international levels.

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7.24 Korean regulations and current issues regarding food contact materials

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Korean standards and specifications including labelling for utensils, containers and food packaging are hereby introduced. Major amendments regarding food contact materials (FCMs) related regulations, recent trends, and related researches are also presented.

Food Additives and Packaging Division has been playing an important role in regulating and conducting research on FCMs through monitoring and risk assessment since 1998. Based on the Korean food sanitation act and relevant laws of FCMs, the division has been conducting tasks to protect and improve public health through scientific knowledge included safety assessment.

First, Korean standards and specifications regarding FCMs consist of general rules which describe purpose, scope and structure. The common specification standards describe manufacturing process and usage, application of the rules, suitability determination, sampling and handling methods, storage and distribution standards. The specifications for individual materials include thirty-seven synthetic resins such as PVC, PE/PP, PS, etc., regenerated cellulose, rubber, paper, metal, wood, glass, ceramic, porcelain enamel and pottery and starch. The test methods include general principles and fifty-seven test methods in relation to lead, cadmium, mercury, formaldehyde, melamine and bispheol A, etc. Second, the labelling standards of FCMs require the marking on all the food contact articles regarding the names and addresses of businesses, material names (limited to synthetic resin or rubber), the words ‘For food’ or labelling of ‘Utensils design for food’ (limited to utensils), precautions (limited to the corresponding cases). The other labelling requirements are related to plastic cling wraps for food packaging, starch utensils, containers and packages for non-waterproofing, pressure cookers, glass utensils for heating and for cooking and synthetic resin utensils, containers and packages used in a microwave.

Recently, the Korean regulations regarding FCMs were revised to include formaldehyde limits to polyethyleneterepthalate (PET), principles for the application of test methods and standards and specifications regarding porcelain enamel and pottery, raw food contact materials, migration test conditions of utensils for specific usage, and items were also newly established for biodegradable polymers such as 3-hydroxybutyric acid, butylenesuccinate-adipate copolymer (PBSA) and hydroxyl benzoic polyester.

With technological advances, many novel materials have been developed for food contact articles. In this field, the application of new technology can greatly improve thermal resistance, barrier function and anti-gas permeability etc. However, some well-known or unknown compounds inside food packaging might leach/migrate into food or beverage. Nowdays, since the database concerning these leached/migrated compounds is still inadequate and doubts and anxiety continue to persist in the public imagination, safety assessment related research works need to continously carried out.

Accordingly, we have been engaged in numerous research projects to secure the safety of food packagings in recent years. Some major projects are as follows: development of analytical methods for the monitoring of anthraquinone in paper packaging, study of nanomaterial-applied food containers and packaging, development of analytical methods regarding perfluorinated compounds that can migrate from utensils and packaging materials coated with fluorocarbon resin, study on standards and regulations for biodegradable polymers in food packaging, assessment of plasticiser migrating from plastic wraps into foods, study on analytical methods regarding antioxidants that can migrate from polyethylene and polypropylene, A study on migration of materials in repeatedly used kitchen utensils, study on analytical method of UV absorbers that migrate from polyethylene and polypropylene, studies on the improvement of migration testing methods for food contract materials, determination of bisphenol analogues that migrate from food packaging into food simulants, development of analytical methods regarding mineral oils from utensils and packaging materials.

NIAS (non-intentionally added substances), nano materials, plastic colorants, mineral oils and volatile organic compounds in food packaging will continue to be very challenging topics in the present and near future. Therefore, we are planning long-term research schedules for topics related to FCMs including safety assessments and hope to conduct studies in collaboration with international bodies to solve these global issues.

7.25 Review of the chemical composition and the toxicity of mineral oil compounds migrating into food from recycled paper and cardboard packaging

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Mineral oils (mineral oil hydrocarbons – MOHs) are complex mixtures derived from crude oil consisting of mineral oil saturated hydrocarbons (MOSHs) and mineral oil aromatic hydrocarbons (MOAHs). Because they are found in the inks or adhesives of paper and cardboard food packaging, these mineral oils can migrate into food. ANSES was formally asked to conduct an expert appraisal on the risks due to the migration of mineral oils into food from packaging. In this work, an up to date review of the literature was performed in order to review the chemical composition and toxicity of MOH migrating into food from recycled paper and cardboard packaging.

The conclusions of this expert appraisal led the agency to recommend better characterisation of the composition of MOH mixtures. Moreover, given the genotoxic and mutagenic nature demonstrated for certain MOAHs, ANSES believes that priority should be given to reducing the contamination of food by these compounds, and proposed some suitable measures.

The agency recommended to validate a specific and robust analytical method for determining the composition of mineral oil mixtures. ANSES considered that better knowledge of the composition of the mixtures is a prerequisite for making toxicological recommendations. ANSES also recommended to carry out additional toxicity studies on representative mixtures of the MOSHs to which the consumer is exposed. Furthermore, research on the influence of the chemical structure of the MOSHs on their bioaccumulation potential and toxicity should be pursued. Given the genotoxic and mutagenic nature demonstrated for certain MOAHs, ANSES believes that priority should be given to reducing the contamination of food by these compounds.

7.26 New strategies of NIFDS for risk assessments to ensure public health

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The mission of the National Institute of Food and Drug Safety Evaluation (NIFDS) and new strategies for an advanced risk assessment system are hereby presented. The new system includes aggregated risk assessment and effective cooperation among experts inside and outside the institute.

The Ministry of Food and Drug Safety (MFDS) of Korea is the administrative authority with the vision of “Safe food and drugs, healthy people, and happy society”. National Institute of Food and Drug Safety (NIFDS), an affiliated organisation of MFDS, supports the ministry’s mission with scientific and expert evaluations and research studies. In response to increased public concerns caused by repeated chemical crises exposed from food and consumer products, NIFDS is in an attempt to establish an advanced risk assessment system that will enable it to predict actual risks to consumers and ensure scientific reliability and public health, with looking back over its 30-year history.

NIFDS has evaluated chemical and microbial risks in food, food packaging materials, medicinal ingredients, cosmetics, or medical products. NIFDS normally establishes safety standards for individual items based on evaluated risks. However, the health risks to humans can be underestimated if only a single exposure source is considered because risk to a person can accumulate from a variety of sources. In this regard, NIFDS plans to establish an aggregated risk assessment framework that will cover the whole exposure potential of certain substances to humans from a wide range of exposure sources; diet, food packaging materials, consumer products, and so on. This aggregated exposure level also can be assessed through the bio-monitoring of the chemicals and related metabolites. Based on this overall assessment of health risks from chemicals to human receptor, management and communication strategies can be developed.

Toxicity and exposure data have been produced through research projects conducted by NIFDS and monitoring carried out by MFDS. NIFDS is currently developing a new data management program that organises all the data produced by MFDS and NIFDS and converts them into a data format suitable for risk assessment. In this context, NIFDS will emphasise cooperation between its data producing departments and utilising departments. NIFDS will also seek to reinforce cooperation between experts inside and outside the institute. Every assessment result will be thoroughly reviewed by an expert committee that consists of the experts from outside the institute.

Within the new system, NIFDS is going to initiate risk assessments of prevalent chemicals that the Korean population is exposed to in everyday life. Prioritising potential candidates for risk assessment and finalising the advanced system will be harmonised according to international standards and trends. In this context, current and future international cooperation with BfR, ANSES, and other risk assessment agencies from around the world will be vital. NIFDS is confident that this approach will ensure the health of consumers through the strengthening of safety standards for primarily responsible products by considering the whole risks from various exposure sources.

7.27 Source attribution of foodborne diseases: review of methods and inventory of data available in France

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[2] ANSES Working group on "source attribution of foodborne diseases"

Food safety management requires the identification of the most important hazards, routes for transmission, food sources and practices causing disease.

Source attribution of foodborne disease is an important public health tool which allows the estimation of the relative contributions of different sources to the human disease burden. Source attribution results are needed to set priorities for food safety interventions and to measure the impact of such interventions.

In September 2017, ANSES published an opinion and an extensive report on the currently available methods (based on literature review) and data types for source attribution of food-borne pathogens, discussing their main strengths and weaknesses.

A variety of approaches have been developed for source attribution of foodborne pathogens: epidemiological methods (analysis of outbreak investigations, case-control/cohort studies), microbial subtyping approach (frequency-matching and population genetics models), comparative exposure/risk assessment and expert elicitations. The report provides guidance for the choice of the source attribution methods based on the public health question, on the data available and on the epidemiological and microbiological characteristics of the pathogens.

The report describes the data available in France for 16 foodborne pathogens (bacteria, viruses and parasites) (surveillance data on humans, foods, and animals, epidemiological studies, etc.) and provides recommendations on the most appropriate methods to attribute human disease caused by different foodborne hazards. It was concluded that one or more of the source attribution methods could be applied in France for the majority of these hazards depending on the availability and the quality of the data. At short-term, epidemiological approaches and comparative exposure/risk assessment could be used to identify the most important food items, transmission routes, and practices related to these foodborne hazards. Microbial subtyping approach is conditional to the application of harmonised or standardised subtyping methods that are sufficiently discriminating for human and source strains.

In addition, this report provides recommendations for data collection for purposes of source attribution. The report is available on ANSES website:
https://www.anses.fr/fr/system/files/BIORISK2015SA0162Ra.pdf

7.28 Concern for adverse effects of huperzine A when sold as an ingredient in food supplements

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Huperzine A, when sold as an ingredient in food supplements, is marketed as a cognitive enhancer for healthy individuals. Huperzine A is an AChE inhibitor with potential for serious adverse health effects if administered in the doses recommended for food supplement use.

Huperzine A is a chemical substance found in a concentration of approximately 0.007 % in the Chinese club moss (*Huperzia serrata*). It is under investigation for use as a drug against Alzheimer's disease in China. Huperzine A is, however, also available in food supplements marketed as cognitive enhancers for healthy individuals. The recommended daily doses for food supplement use ranges from 50 to 900 µg huperzine A. Huperzine A acts by inhibiting acetylcholinesterase (AChE), thus preventing the degradation of endogenous acetylcholine, and is capable of crossing the blood-brain barrier. Symptoms associated with inhibition of AChE are: salivation, lacrimation, urination and defecation, muscle fasciculation, convulsions and death.

The aim of this study was to make a risk assessment of huperzine A from food supplements based on the available literature. A review of the literature covering the bibliographic databases SciFinder (encompassing the databases CAplus and Medline) and PubMed was performed to search for toxicological data on huperzine A. Very few toxicological studies were identified in the literature search. Most of them were found in articles citing unpublished studies or in papers written in Chinese with only an English abstract available. A No Observed Adverse Effect Level (NOAEL) of 0.1 mg/kg/bw/day for huperzine A has been suggested in unpublished studies sponsored by the National Institute of ageing (USA) based on increased lacrimation in female dogs after 30 days of oral administration. When the doses recommended by vendors of food supplements are used as exposure levels, the margin of safety (MOS) ranges from 8 to 143. The MOS is the reference dose (e.g. NOAEL) divided by the actual exposure of a chemical substance. Considering the lack of available long term toxicity studies the MOS should not be less than 200. The recommended doses are therefore a cause for safety concern based on the MOS. Human clinical trials after huperzine A treatment in patients with Alzheimer's disease generally report mild side effects when comparing it with other cholinergic drugs. They have, however, generally investigated doses half of the highest dose recommended by vendors of food supplements. Adverse effects like diarrhoea, nausea and vomiting, insomnolence and bradycardia have been reported in these studies. Whereas, a certain degree of side effects is accepted for drugs, the same effects may be unacceptable from food supplements intended for healthy individuals.

7.29 Hydroxycitric acid (HCA) in dietary supplements intended to promote weight loss: risk assessment of toxic effects on reproduction

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Summary
Certain dietary supplements that are intended to promote weight loss contain hydroxycitric acid (HCA), which is often added in form of *Garcinia cambogia*-extracts. In the current risk assessment, possible health risks associated with consumption of dietary supplements containing HCA were evaluated. In view of serious effects on the testes observed with certain HCA-containing (*Garcinia cambogia)* preparations in several animal studies and considering the available information from human studies, it is concluded that substantial knowledge gaps and uncertainties exist with respect to the safety of high doses of HCA or specific HCA-containing preparations found in a number of commercially available food supplements, particularly with regard to the human male reproductive system and long-term use.

Abstract
Hydroxycitric acid (HCA) is a fruit acid that occurs naturally in fruits of the tropical plant *Garcinia cambogia*. Certain dietary supplements that are intended to promote weight loss contain HCA, which is added in form of *G. cambogia* extracts. In many cases, the composition of the HCA-containing preparation in the respective product is not clearly specified. In the current risk assessment, possible health risks associated with consumption of HCA-containing dietary supplements (with HCA doses of up to 3000 mg per day) were evaluated, based on published animal and human studies, with a particular focus on possible effects on reproduction. In several animal studies, long-term application of certain HCA-preparations (*G. cambogia*-extract or Ca^{2+}-HCA salt) led to testicular atrophy (i. e. atrophy of seminiferous tubules and degenerative changes of Sertoli cells) and impaired spermatogenesis (i. e. decreased sperm counts) in male rats at high doses (lowest NOAEL and LOAEL observed with a specific extract of 389 and 778 mg HCA/kg body weight & day, respectively). Animal studies with other HCA-preparations (Ca^{2+}/K^{+}-HCA salt) found no such effects at the highest HCA-doses tested (NOAEL: 610,8 mg HCA/kg body weight & day). It remains to be clarified to which extent the adverse effects observed in some animal studies may be ascribed to certain HCA-containing preparations or to constituents thereof, including HCA itself. In human intervention studies which addressed the safety of HCA in healthy volunteers no substance-specific adverse effects after ingestion of HCA doses of up to 3000 mg per day over a period of up to 12 weeks were reported. However, the question of possible adverse effects of HCA on the human testes was not adequately addressed in these studies. In a single clinical study with 24 male test subjects, no significant changes in endocrinologically relevant parameters such as serum inhibin B or FSH were observed after consumption of 3000 mg of HCA for 12 weeks. However, no investigation of direct parameters that might inform on potential effects on spermatogenesis, such as sperm quality and sperm count, were conducted in this study. In view of the serious adverse effects on the testes observed in animal studies conducted with certain HCA-containing preparations and considering the lack of adequate human data on safety of the long-term use of HCA-preparations, it is concluded that knowledge gaps and substantial uncertainties exist with respect to the safety of HCA or certain HCA-containing preparations found in a number of commercially available food supplements, particularly with regard to the human male reproductive system and long-term use.

7.30 Human health risks related to the consumption of foodstuffs of plant and animal origin produced on a site polluted by chemical munitions of the First World War

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In this article, we developed a specific methodology to assess the health risks related to the consumption of foodstuffs produced on a former chemical munitions dismantling site polluted by poorly known chemical contaminants such as TNT, 2,4-DNT, 2,6-DNT and diphenylarsinic acid.

Shells fired during World War I exhibited different explosive compounds and some of these weapons also contained a wide variety of chemical warfare agents. At the end of the war, for safety purposes, the large quantity of weapons remaining on the former front needed to be dismantled and destroyed. A large amount of the remaining shells was destroyed in specific sites which led to the contamination of the surroundings in Belgium and France.

In the 1920s, 1.5 million chemical shells and 30,000 explosive shells were destroyed in a place close to the city of Verdun, in the east of France. In this paper, the risk for human health related to the consumption of foodstuffs produced on this site was assessed. To this end, food products of plant and animal origin were sampled in 2015 – 2016 and contaminant analyses were conducted. Human exposure was assessed using a specifically built methodology. The contaminants considered in this study were trace elements (TEs– primarily Zn, As, Pb and Cd), nitroaromatic explosives (trinitrotoluene, 2,4-dinitrotoluene, 2,6-dinitrotoluene, 2-amino-4,6-dinitroluene and 4-amino-2,6-dinitrotoluene), phenylarsenic compounds including diphenylarsinic acid and triphenylarsine, perchlorate, tetrabromoethane and vinyl bromide. Depending on the compound, different approaches were used to assess the risk for both adults and children.

Exposure to these contaminants through the consumption of foodstuffs produced locally on the considered site was unlikely to be a health concern. However, as for inorganic arsenic, given the presence of highly contaminated zones, it was suggested that cereals should not be grown on certain plots.

7.31 Biotoxins as threat agents - assessing risks

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Biological threat agents are usually considered as organisms like bacteria or viruses that can be used to harm people, animals or plants. But these agents also include a very special group of agents which are not infectious and combine “biological” as well as “chemical” characteristics: biotoxins. These molecules are at a hermaphroditic position, on the borderline between “synthetic” and “natural”.

Biotoxins are neither distinct biological nor chemical agents in a common understanding but can be considered as “mid-spectrum agents”. As a matter of fact, they deserve special attention as a group of threat agents of biological origin with great potential to harm people. There is a broad spectrum of biotoxins which can be employed in biological warfare and in bioterrorist attacks. The spectrum of biotoxins ranges from peptides and proteins to alkaloids and other bioactive small molecules.

On the one hand biotoxins differ from chemical threat agents since they are almost never produced synthetically, volatile gases or able to be absorbed through the skin. On the other side biotoxins differ from classical biological threat agents due to the fact that they do not carry any genetic information like bacteria or viruses. Nevertheless, some biotoxins are extremely toxic threat agents which can be dispersed as aerosols, liquids or as powders and consequently have the potential to create casualties, alteration or breakdown of social life, or economic loss if used in warfare or a terrorist attack. That in combination with the often existing lack of antidotes for post-exposure prophylaxis and treatment, vaccines for pre-exposure prophylaxis or detection methods makes these molecules critical.

Special attention must be paid to “mid-spectrum agents” that pose a serious risk as threat agents or weapons. Besides biotoxins several other mid-spectrum agents are known. Bioregulators for example are – like biotoxins – on the borderline between “synthetic” and “natural” are neither clear distinct chemical nor biological agents. They are also naturally occurring agents, produced by living organisms but lacking genetic information and regulate diverse cellular processes and have adverse health effects on humans in a short period of time.

It is impossible to enumerate all “mid-spectrum agents” that have influenced warfare or terroristic efforts or even can be used for such purposes. However it remains to be emphasised for the biotoxins, only around twenty have been discussed in public as weapon capable of causing death or disease on a large scale at a certain point by different credible international conventions or bodies. This offers an opportunity to discuss challenges and requirements with respect to public health preparedness. Additionally these twenty biotoxins can serve as the basis for the development of appropriate methods of management and countermeasures including decontamination and Personal Protective Equipment strategies.

7.32 Assessing and minimising dual use risks of research in the life sciences

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Research in the biosciences has contributed immensely to the improvement of health and living conditions of humans. Research results – material products, technologies, data, knowledge – can, however, generally also be used to harm humans and the environment. This dual use character of research has different degrees. Research that "based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health" is termed dual use research of concern (US Government 2015).

Dealing with dual use risks of research has legal as well as non-legal aspects. Legally, the transfer of a considerable number of dual use items (including in intangible form) is regulated by export control rules. (EU 2009) In addition, scientists, research institutions, funders and journal editors have an ethical obligation to deal responsibly with research risks. This requires an assessment of the risks during planning, conduct and publication of research and, if necessary, the implementation of risk reduction measures. Guidelines on how to take this responsibility have been developed at institutional level (RKI 2013) and federal level (Leopoldina 2014).

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7.33 Practice-driven approach to harmonisation of reproductive and thyroid hormones measurements in the evaluation of pesticides and biocides

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In collaboration with EFSA, the BfR has conducted a screen of open published literature, performed an online survey and gathered experts with practical background to review current practices of conduct of hormonal assays in toxicological field.

Background
Measurement of hormonal levels is widely used in endocrinological practice and it is anticipated that concentrations of circulating hormones will be more frequently determined and subsequently reported as part of the toxicological evaluation of endocrine disruptive properties of active substances in plant protection products and biocides. There are guidance available in medical field, for example practical guidelines to support laboratories in design and interpretation of the thyroid hormonal tests (Demers and Spencer 2003), but for toxicological purposes specific recommendations are needed to harmonise hormonal measurements in regulatory practice. A number of factors (e.g. stress, circadian rhythm, oestrous cycle) may interfere with physiological concentrations of hormones and thus may lead to false negative results.

Methodology
To gather information on practices that were developed over years in order to reduce the impact of external factors, we have screened literature, published in 2007-2016, in particular the method sections of research papers. Besides, we have directly addressed contract research organisations, industry and academia by means of an online survey tool. Collected answers generated an overview of the applied methods and formed the basis for a discussion by experts from contract research organisations, industry, academia and regulatory agencies which took place in October, 2017, at the BfR in Berlin.

Results
Consequently, lists of recommendations for measuring thyroid and sex hormones were compiled describing aspects of experimental design, sample collection, hormone detection methods, assay validation and applicability of internal historical control data. These recommendations were submitted to European Food Safety Authority (EFSA) for potential inclusion in the Guidance Document for the implementation of the hazard-based criteria to identify endocrine disruptors (ED) in the context of Regulations (EC) No 1107/2009 and (EU) No 528/2012. A paper summarising the discussions at the expert hearing will be submitted to a toxicological journal in 2018.

Conclusion
There is a body of expertise and knowledge accumulated in laboratories routinely conducting measurement of thyroid (T3, T4, TSH) and reproductive hormones (testosterone, estradiol, luteinizing hormone, follicle-stimulating hormone, progesterone). Different methods (quantification, blood sampling etc.) may be applied, but it is essential to justify their use and to provide evidences of their validation. Decision on study design should be made with consideration of hormonal physiology, measures of stress reduction, randomisation of sampling time. Additionally, most of the experts concluded that measurement of a battery of hormones is preferential over measuring a single hormone in isolation. In particular case of reproductive

hormones, selection of hormones should be based on previous toxicological information on the substance. If incorporation of hormonal evaluation in the regulatory pivotal studies is not feasible, then specific mechanistic study may be conducted. In spite of the fact that changes in hormone levels may contribute to identification of endocrine disrupting properties, they must not be used as “stand alone” information.

References

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