Posters & Presentations of Research Ideas

2018 Utrecht

Risk
Assessment
Research
Assembly

Version: 07/03/2018

Introduction

RARA participants presented and discussed research ideas in the **Ideas Showcase** session (posters) and/or by pitches (presentations) in four parallel **Break-out group sessions**. After the event, most participants agreed to publish their contribution that is made available in this document compiling **27 posters** and **38 presentations**.

Bookmarks (in the left navigation panel) are allowing quick browsing, keeping the assigned numbering to 48 registered researched ideas published alongside with more details in the e-Inventory.

Internalization of Foodborne Pathogens
Does it make difficult their control?

M. L. Cabo
CSIC Consejo Superior de Investigaciones Científicas

Knowledge

- The main human pathogenic bacteria adopt an intracellular lifestyle to infect hosts
- It has been evidenced that some foodborne bacterial pathogens can internalize within plant tissues

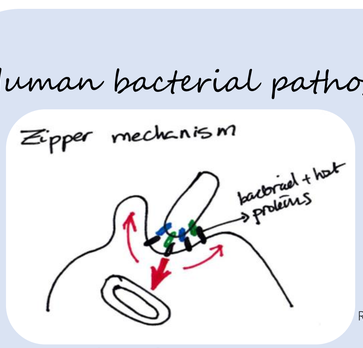
Hypothesis

- Our research idea is aimed to elucidate whether food bacterial pathogens internalize within food myosystems (seafood or meat)

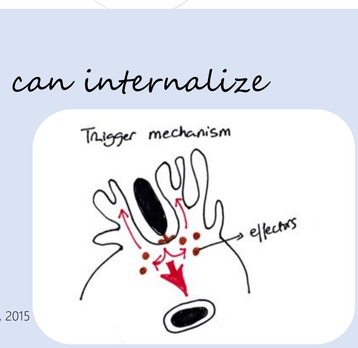
Importance

- Internalization would allow them to enter silently into the food chain and to better resist food-processing conditions

Human bacterial pathogens can internalize



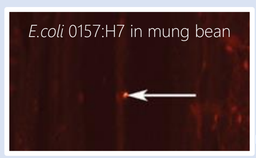
Internalization of *Listeria monocytogenes* via a "zipper" mechanism



Ribet & Cossart, 2015

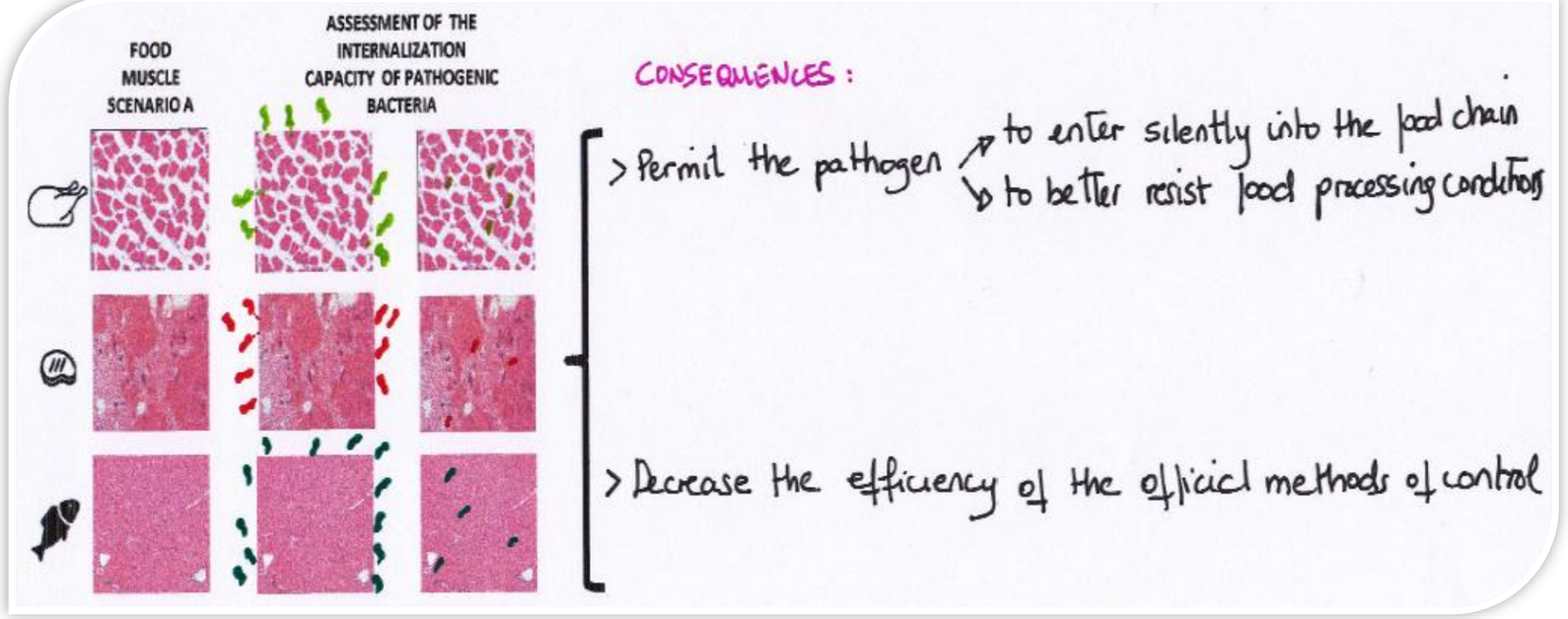
Internalization of *Salmonella typhimurium* via a "trigger" mechanism

Internalization in different plant tissues

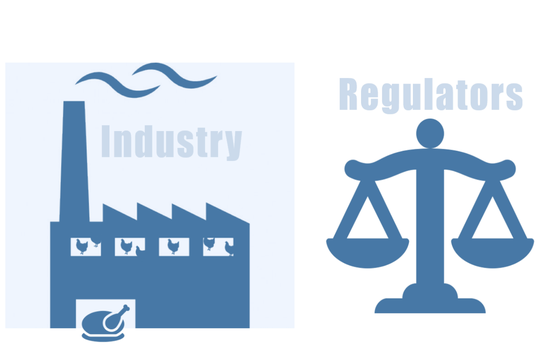


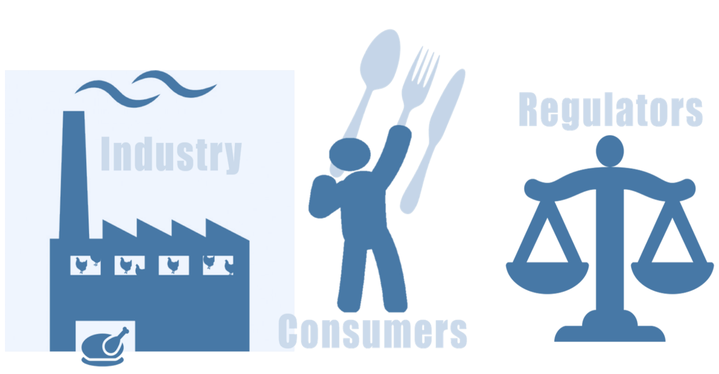
Deering et al. 2011

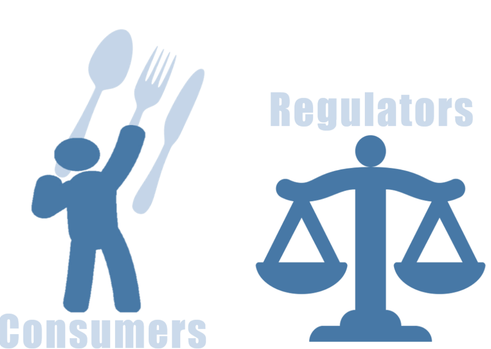
Shenoy et al. 2017



Foreseen impact and benefit





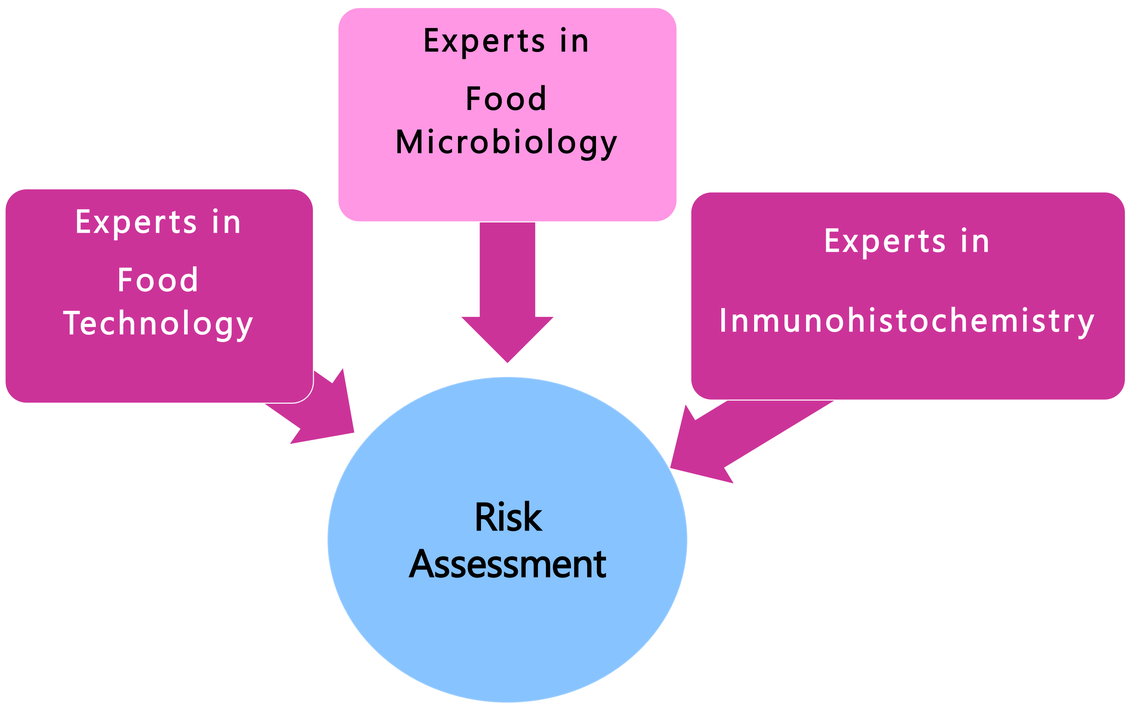


New risk factor to be considered in research

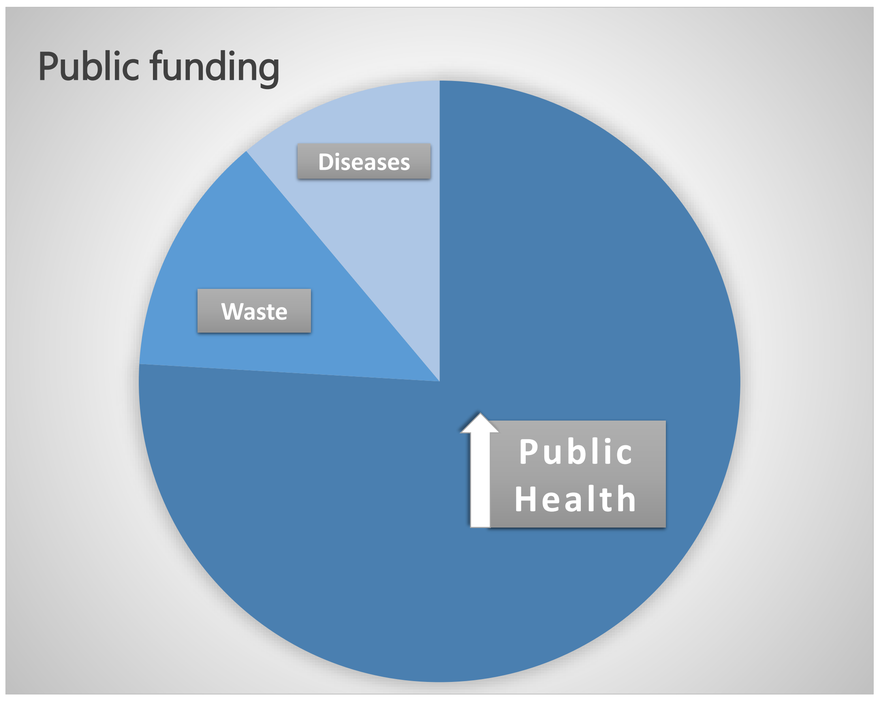
New strategies for control in food myosystems

New inputs for risk assessment

Project needs



Funding needs



Risk Assessment Research Assembly (RARA) communication

INTERNALIZATION OF FOODBORNE PATHOGENS. DOES IT MAKE DIFFICULT THEIR CONTROL?

GENERAL DESCRIPTION

Foodborne human pathogenic bacteria like *Listeria monocytogenes*, *Escherichia coli* and *Salmonella* adopt an intracellular lifestyle to infect hosts (Irenton, 2007; Ribet and Cossart, 2015). In fact, even microorganisms considered exclusively as extracellular pathogens (eg. *Vibrio parahaemolyticus*) during years have been recently found to have an intracellular lifestyle (Souza Santos and Orth, 2014).

Scientific literature have evidenced that such foodborne bacterial pathogens can actively internalize within plants tissues from both pre-harvest and post-harvest contamination (Hirneisen et al. 2012, Deering et al. 2012). Internalization of *Salmonella typhimurium* and Shiga toxin-producing *E. coli* has been also reported to occur in marinated meat products, particularly when vaccuum-tumbled (Pokharel et al., 2016).

Our research idea is aimed to find out whether foodborne bacterial pathogens internalize within food myosystems (seafood or meat). This would allow them to enter silently into the food chain and better resist food-processing conditions. Moreover, internalization could also affect the effectiveness of the official methods of analysis.

IMPACT AND BENEFICIARIES

That bacteria internalizes within food myosystems would have a significant scientific and technological impact since:

- It would reveal an unknown risk factor associated with presence of bacterial which would give rise to new lines of research for the scientific community.
- It would be needed to address new strategies of control of bacteria pathogens, particularly for minimally-processed and ready-to-eat food.
- It would give new inputs for risk assessment and, presumably, food legislation. Also, reference methods of analysis could require a re-evaluation aimed to find out whether bacterial counts could be underestimated in particular occasions.

This impact would have benefits for consumers, industry and regulators.

PROJECT NEEDS

To undertake the proposed idea, it would be needed experts in food microbiology, food technology and risk assessment.

REFERENCES

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Hirneisen, K, Sharma, M and Kniel, K.E. 2012. Human enteric pathogen internalization by root uptake into food crops. Foodborne Pathogens and Disease. 9(5): 396-403.
Irenton, K. 2007. Entry of the bacterial pathogen *Listeria monocytogenes* into mammalian cells. Cell. Microbiol. 9(6):1365-1375.
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Ribet, D. and Cossart, P. 2015. How bacterial pathogens colonize their host and invade deeper tissues. Microbes and Infection 17: 173-183.
Shenoy, A.G., Haley, F.O. and Deering, A.J. 2017. *Listeria monocytogenes* internalizes in romain lettuce growth in greenhouse conditions. Journal of Food Protect. 80 (4):573-581.
Souza Santos, M. and Orth, K. 2014. Intracellular *Vibrio parahaemolyticus* escapes the vacuole and establishes a replicative niche in the cytosol of epithelial cells. mBio.asm.org 5(5), e01506-14.

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Risk Assessment Research Assembly

feb '18

Internalization of foodborne pathogens. Does it make difficult their control?

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MICRO TEC

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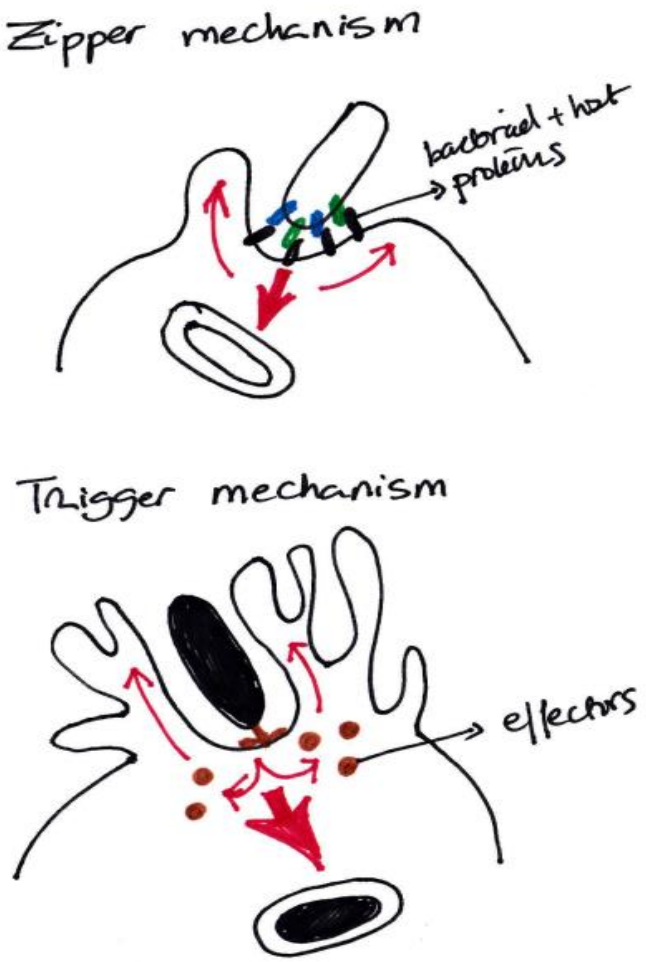
CSIC Consejo Superior de Investigaciones Científicas GALICIA

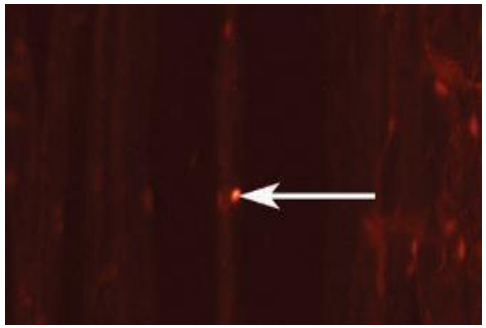
THE KNOWLEDGE

- Human bacterial pathogens internalize

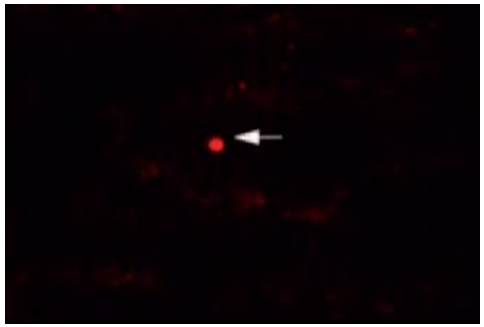


Ribet & Cossart, 2015

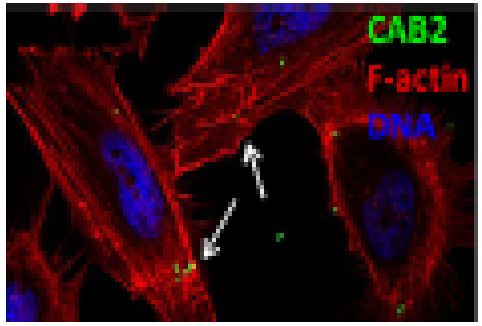
- Internalization in plants



***E.coli* 0157:H7 in seed contaminated mung bean tissue**
Deering et al. 2011



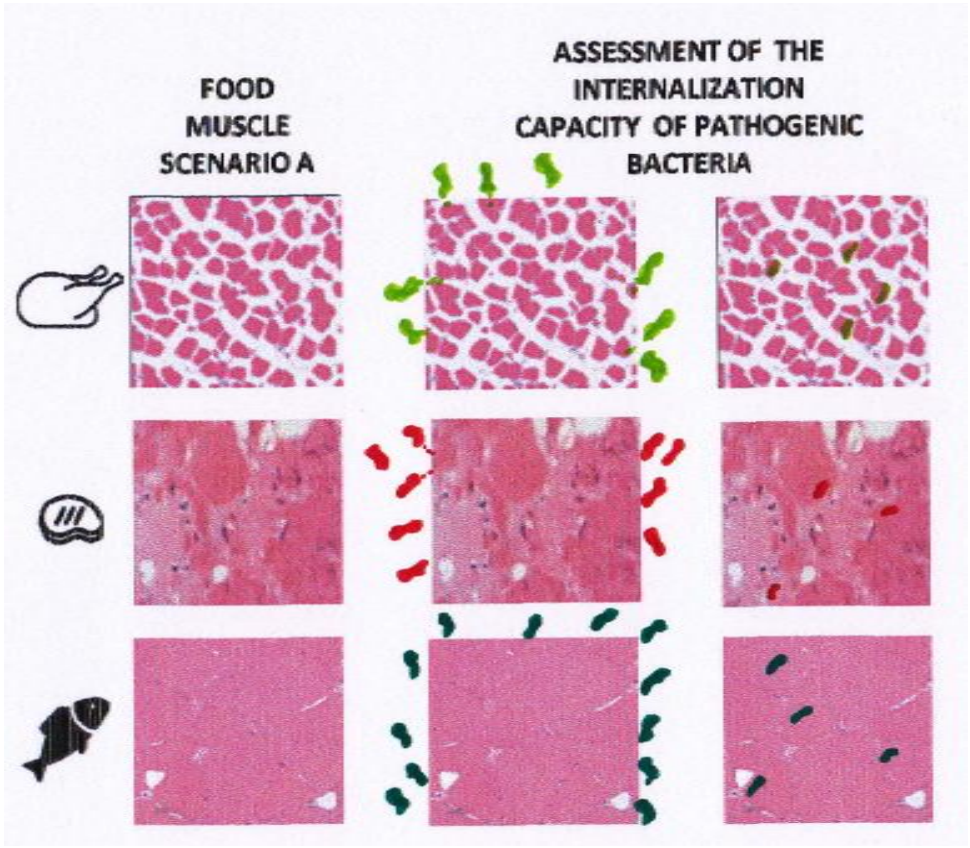
***L. monocytogenes Romain* lettuce**
Shenoy et al. 2017



***V. parahaemolyticus* HeLa cells**
Sousa Santos & Orth 2014

THE HYPOTHESIS

- Intracellular bacterial pathogens can internalize within muscle food



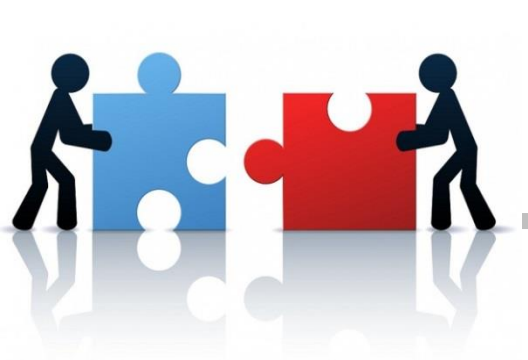
- Permit the pathogen to get silently into the food chain.
- Permit the pathogen to better resist food processing conditions.
- Decrease the efficiency of the official methods of control.

THE IMPACT

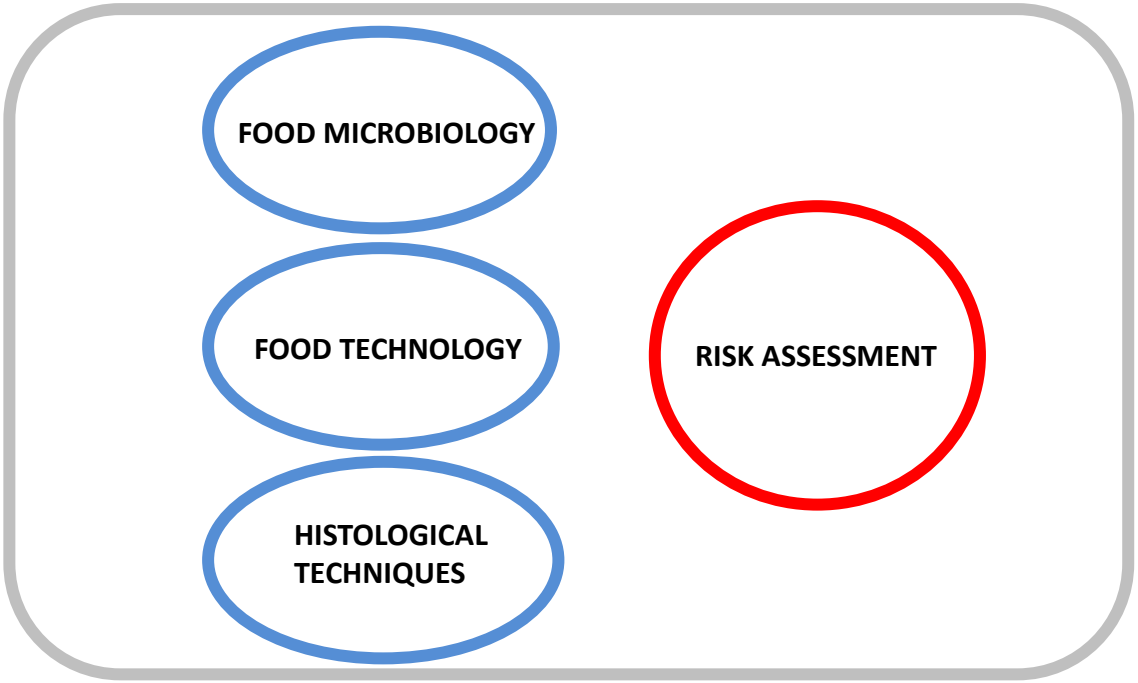
THE BENEFICIARIES

Consumers Industry Regulators

- ❑ New risk factor to be considered in researh
- ❑ New strategies for control in food myosystems
- ❑ New inputs for risk assessment



THE PROJECT


FOOD MICROBIOLOGY
FOOD TECHNOLOGY
HISTOLOGICAL TECHNIQUES
RISK ASSESSMENT
FUNDING

The use of next generation sequencing data in microbial risk assessment

Francis Butler

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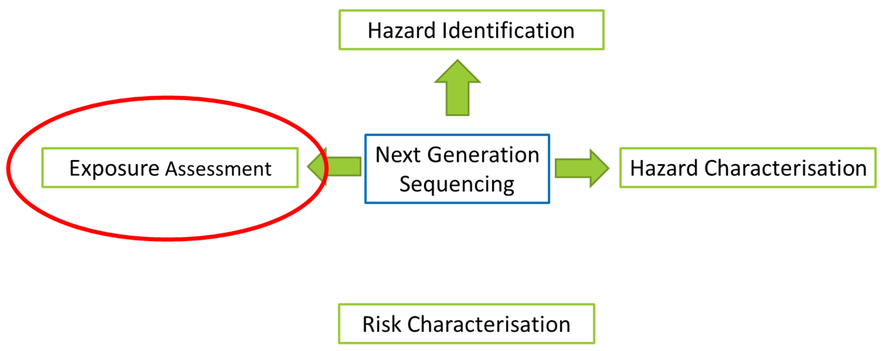
Using NGS within the paradigm of microbial risk assessment

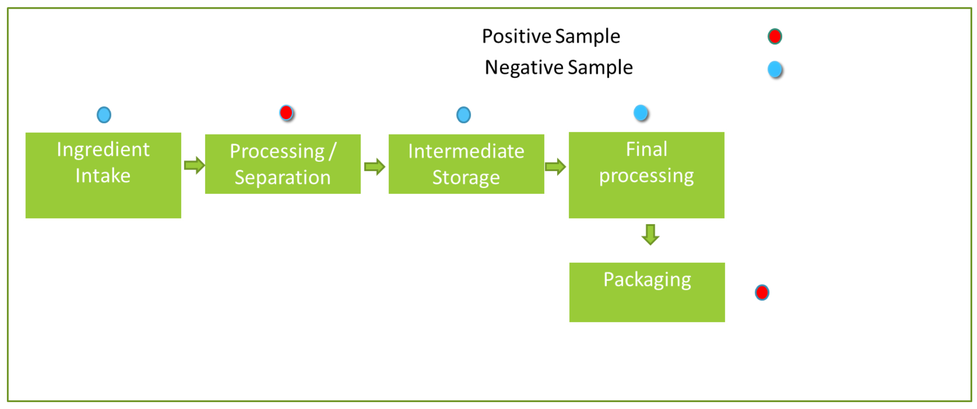


Next Generation Sequencing techniques provides valuable insights into the three main components of microbial risk assessment: Hazard Identification - through improved characterisation of the organism (heat tolerance, biofilm formation, etc.); Hazard characterisation (virulence characteristics, etc.); Exposure assessment – through precise 'fingerprinting' of the organism and tracking it through the food chain.

The central theme of this 'Call to Action' is to use Next Generation Sequencing as an identification tool to manage and control bacterial pathogens along the food chain, but particularly during the processing of foods in manufacturing companies

The Concept

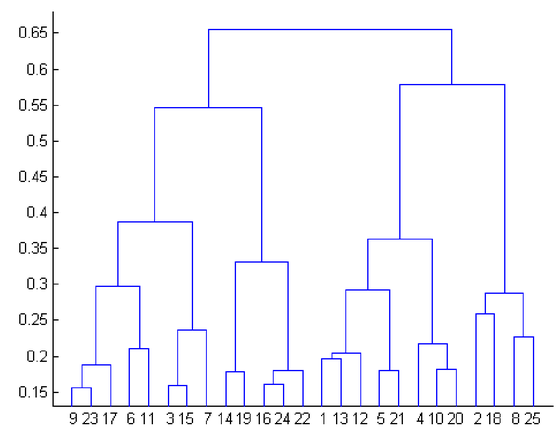
The approach is to undertake intensive monitoring programmes for pathogens of concern over extended periods of time in food manufacturing facilities. An example is monitoring for *Salmonella* in a pork processing facility. Sampling includes product and environmental samples. All positive isolates are sequenced to precisely molecularly 'fingerprint' and characterise the pathogens detected.



The UCD Centre for Food Safety has successfully undertaken a number of large scale surveillance programmes using Next Generation Sequencing in several large dairy processing facilities in Ireland

Data interpretation through Bioinformatics

Advanced data analysis / bioinformatics of the sequence data obtained from the surveillance studies gives a very good understanding of the spatial and temporal distribution of the pathogen in the production facility. Phylogenetic analysis allows comparison of the positive isolates recovered from the processing facility and identifies:



- Entry points of the pathogen into the process facility
- Routes of cross contamination within the process facility
- The occurrence of long term persistence of the organism in the facility
- Possible multiple sources of contamination

Application to Microbial Risk Assessment

NGS allows precisely molecular 'fingerprinting' and characterisation of pathogens through the food chain. This allows much better exposure assessment of the hazard to be undertaken and so dramatically improves the accuracy and utility of the risk assessment. The approach allows food manufacturers improved surveillance approaches to control potential pathogens in their products. Ultimately, this leads to better food safety for the European and global consumer.

Funding Needs

Substantial funding is urgently needed within the EU to address the following challenges:

- Initial industry demonstration type projects (Pan European)
- Pan European skills and data sharing
- Bioinformatics emerging as a bottleneck – Skills gap and shortages

The use of next generation sequencing data in microbial risk assessment

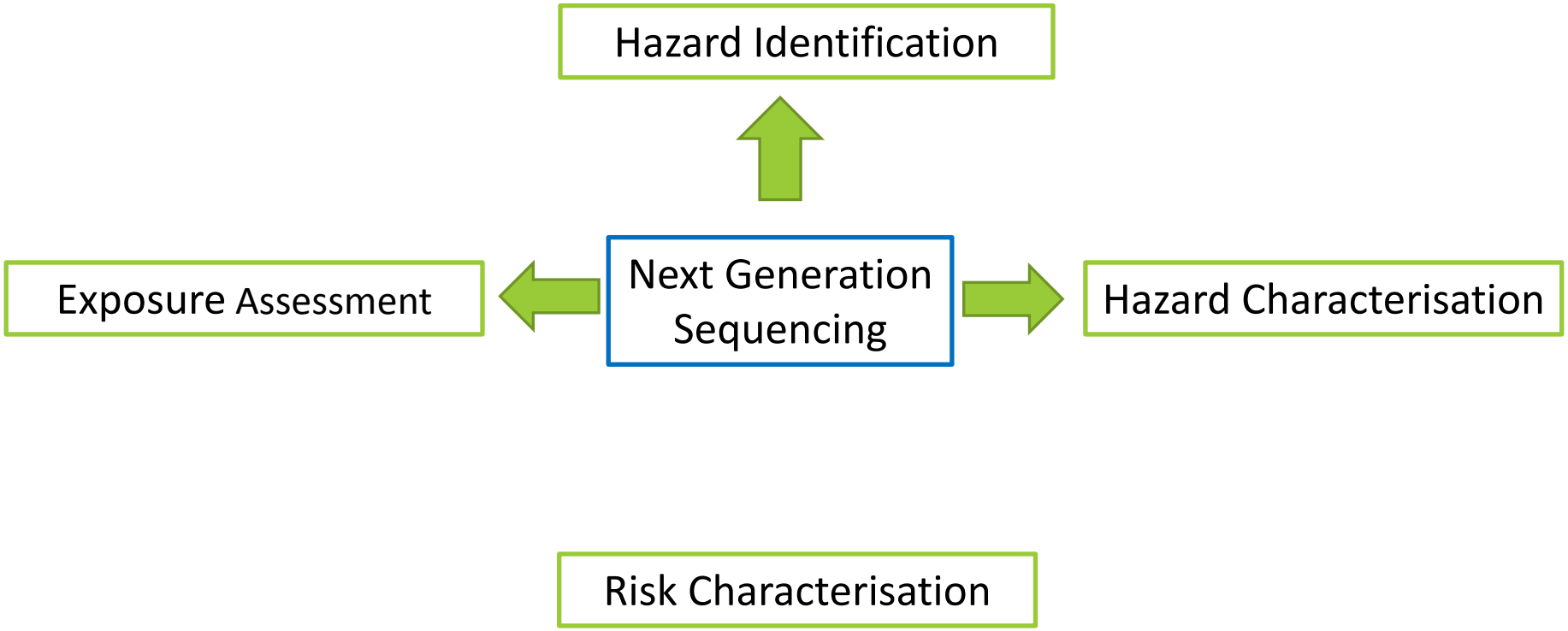
PROFESSOR FRANCIS BUTLER

UCD CENTRE FOR FOOD SAFETY

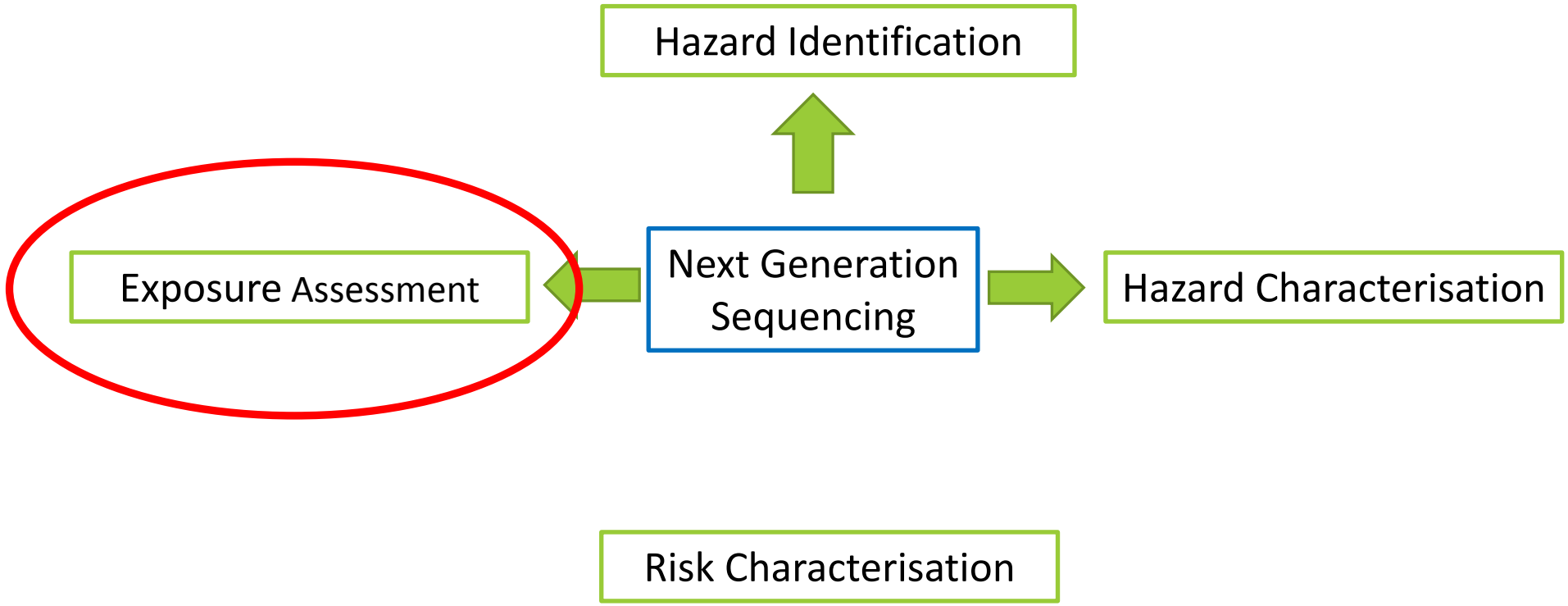
UNIVERSITY COLLEGE DUBLIN

IRELAND

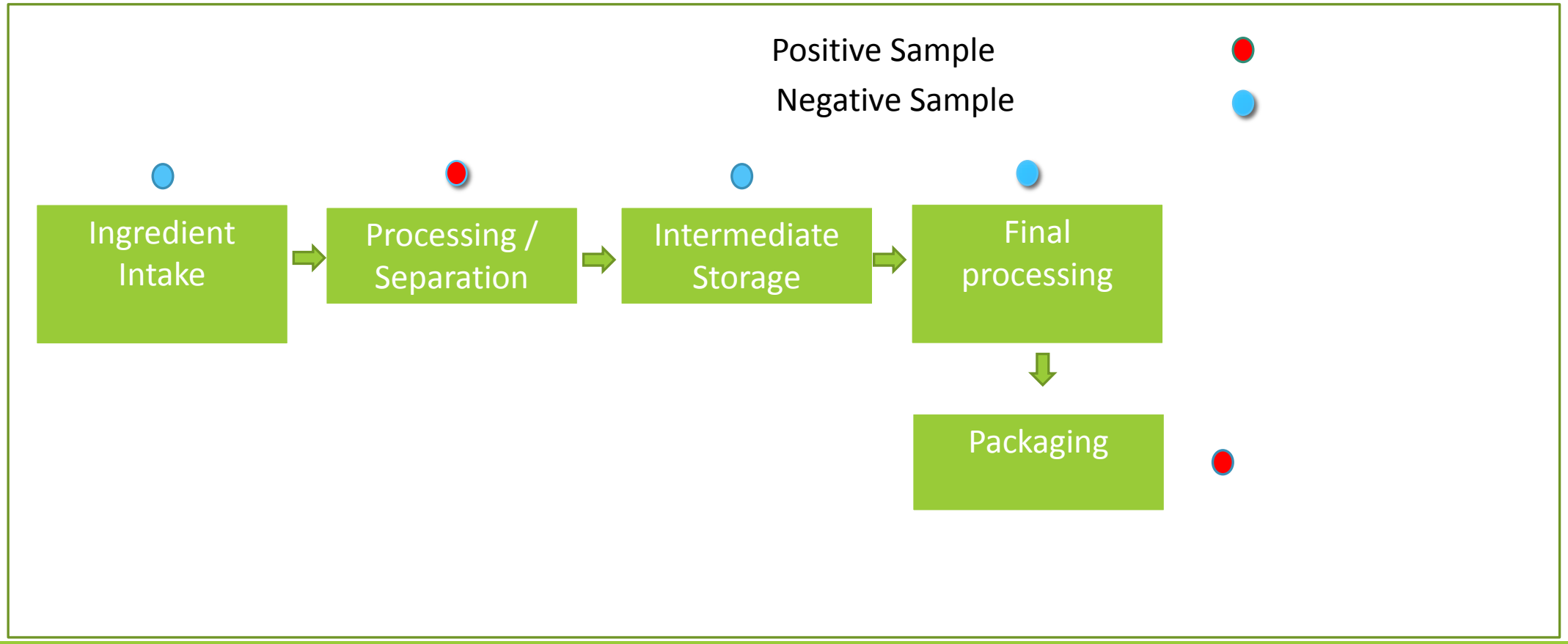
Using NGS within the paradigm of microbial risk assessment



Using NGS within the paradigm of microbial risk assessment



Food Production Facility Intensve Monitoring Programme



Production Facility Monitoring Programme Outputs

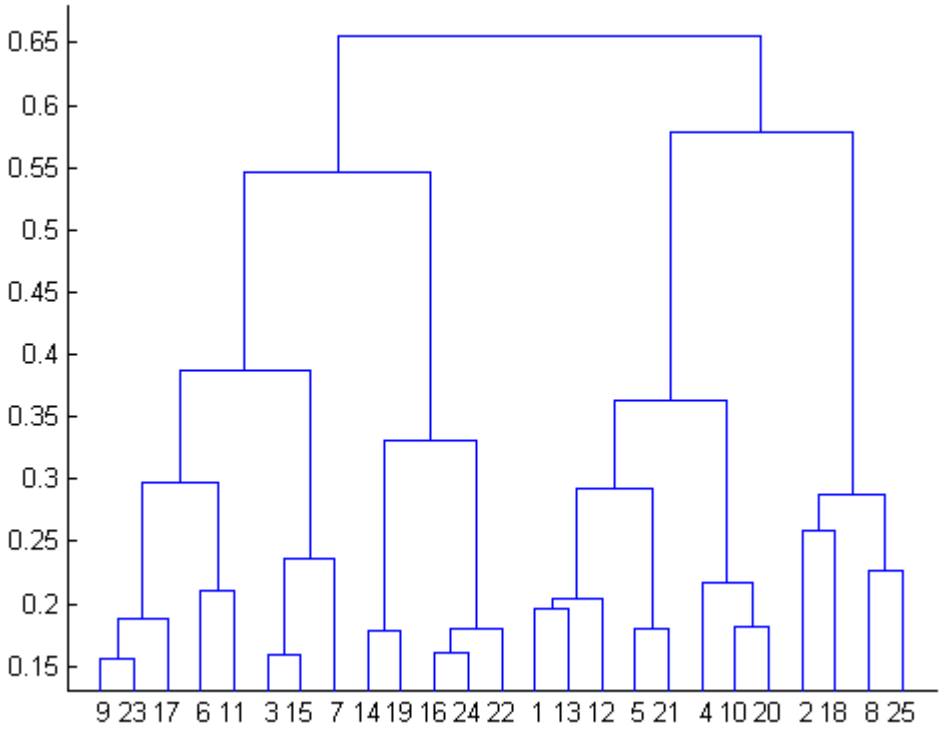
Ongoing/ targeted monitoring of the facility

Understanding of the spatial / temporal distribution of the pathogen

NGS ‘fingerprints’ positive isolates

Phylogenetic analysis allows comparison of isolates

- Similar isolates – possible cross contamination routes occurring
- possible long term persistence
- Large variation – possible multiple sources of contamination



NGS in Microbial Risk Assessment
Impact and Funding Needs

Impact

Improved food safety

Better risk assessments

Industry empowered to control food borne pathogens

Funding needs

Initial industry demonstration type projects (Pan European)

Pan European skills and data sharing

Bioinformatics emerging as a bottleneck – Skills gap and shortages

GERMAN FEDERAL INSTITUTE FOR RISK ASSESSMENT

Strengthen microbial Next-Generation Sequencing in Europe

15 YEARS Science in the Service of Humanity

BfR Bundesinstitut für Risikobewertung

Burkhard Malorny, Carlus Deneke, Karin Schlesier, Lea Herges, Karsten Nöckler, Andreas Hensel

German Federal Institute for Risk Assessment, Berlin, Germany

Outline of research idea

Whole genome sequencing (WGS) is increasingly moving into microbiological laboratories and is considered as a ultimate revolutionary new method generating large amounts of microbial genome sequence data. In combination with powerful bioinformatic tools those data enable scientists to achieve more effective global surveillance, public health and food safety by improved sharing and analysing genomic sequences.
The European Food Safety Authority (EFSA) and the European Centre for Disease Control and Prevention (ECDC) supports already various activities but having limited capacities to integrate WGS for microbial characterization of foodborne pathogens. However, despite the potential of the technology, it needs further more intensive capacity building, harmonization and transition across European research institutions for providing qualitative comparable data sets applicable in risk assessment studies and into routine use in modern public health and food safety labs.

The vision of the research idea is:

- to establish an integrated genomic risk assessment approach
- to build capacities for routine application of whole genome sequencing in public health and food laboratories across Europe
- to form a large collaborative research network for knowledge and data transfer of barrier-free accessible WGS data between institutions
- to bring together scientists in the field of epidemiology, informatics, bioinformatics, genomic biology, public health, veterinary medicine, and food hygiene to translate genome sequences in new tools applicable in outbreak investigations, surveillance, source attribution and genomic risk assessment studies.
- to harmonize and standardize next-generation sequencing technologies
- to implement WGS across all EU Member States as tool for risk assessment investigations

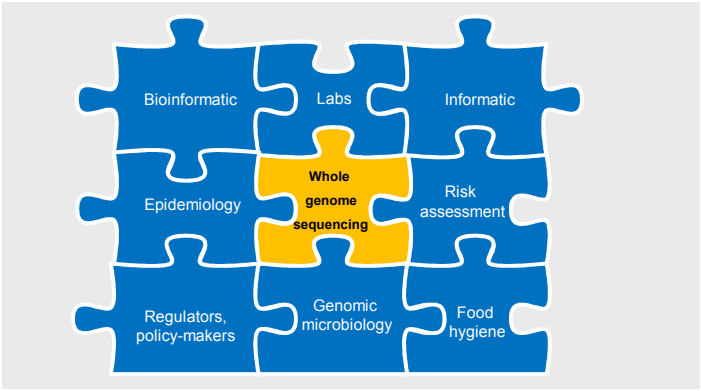


Figure 1. Expertise of network to be established

Foreseen impact

- to implement next-generation technologies in routine use as powerful method for characterization of pathogens in all EU Member States
- to strengthen data exchange and management
- to predict early public health risks and epidemic potential of emerging foodborne pathogens
- to monitor antimicrobial resistance and virulence of foodborne pathogens on a routine basis
- to harmonize source back investigations across countries
- to advance genomic risk assessment in food safety
- to give regulators improved tools for decision making (e.g. pathogenicity, antimicrobial resistance in regulatory products)

Keywords of research idea

Whole genome sequencing, capacity building, international database, risk assessment studies, source attribution, epidemiology, genome microbiology, outbreak investigations, standardization

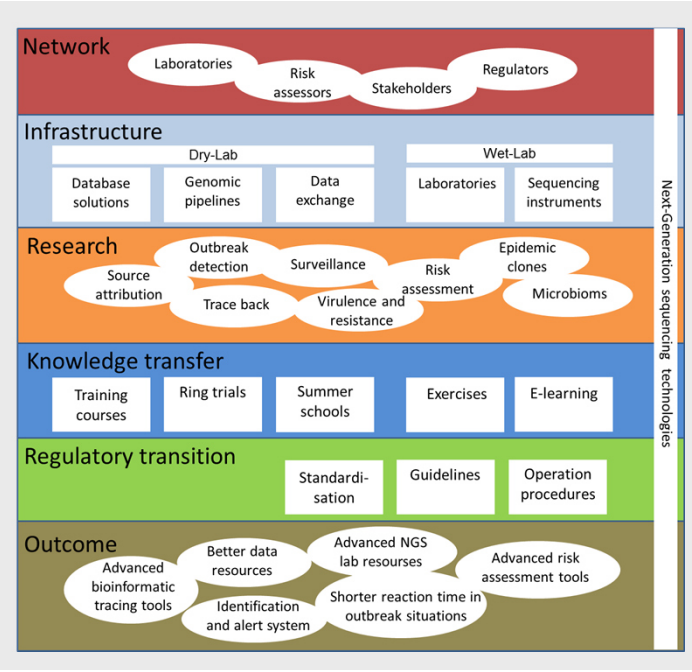


Figure 2. Main working elements: From input to output

Reasons for public funding

- to lower the burden of infectious diseases and antimicrobial resistance for European population
- to boost microbial food safety
- to promote the collaboration of institutions on local, national and international level
- to lower the barrier of entry for Member States to establish and to profit of the new technology
- to promote expertise in National Reference Laboratories functioning as a multiplier in their country, respectively
- to sustain capacities in those countries who have already established WGS
- to generate comparable genomic data applicable in risk assessment

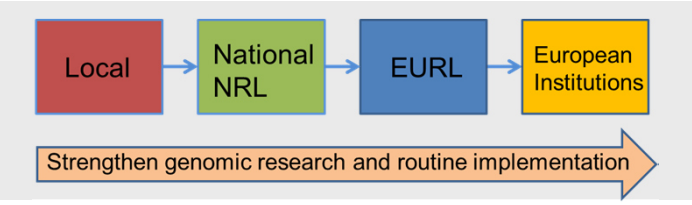


Figure 3. Different levels of partners to involve

Expertise and partner consortium needed

The network shall be composed of partners from institutions with intra- and interdisciplinary experience in the microbiological, public health, veterinary, food, epidemiological, regulatory, and genomic field (Figure 1) having an intention to use WGS data in risk assessment and regulatory applications

Institutions: research, official labs, regulators, policy-makers, stakeholders

Contributing countries: all European countries

Microorganisms to be considered: Foodborne pathogens (bacterial, viral, parasital) with impact on food-producing animals and human population

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Strengthen microbial Next-Generation Sequencing in Europe

Burkhard Malorny

Background

- A **paradigm change in surveillance** of foodborne pathogens takes place triggered by Microbial Whole Genome Sequencing
  “One Health approach”

NCBI

GenomeTrakr

GMI
Global Microbial Identifier

ENGAGE

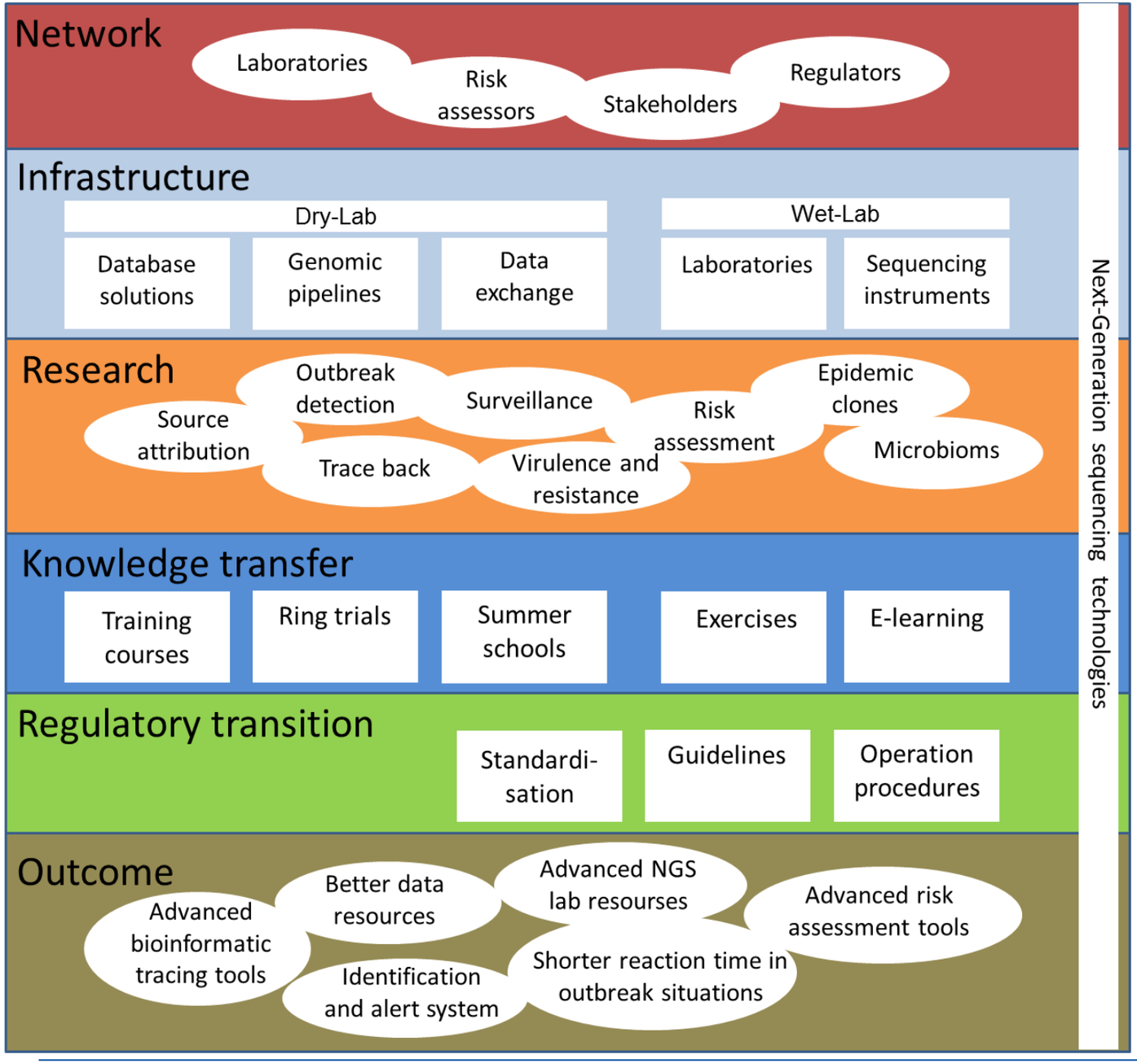
INNUENDO

Compare

The challenge

- Knowledge, capacities, data analysis and management, transition into practise and regulations

The research idea



- integrated genomic risk assessment approach
- Multidisciplinary collaborative network
- Capacity building in WGS across Europe
- Free accessible data policy
- Implementation of WGS data in regulations

Beneficiaries

- European consumers ⟹ Safer food, less cases
- Managers and regulators ⟹ Specified decisions and legal certainty
- Industry ⟹ Less recalls

Public funding because…

- boosting the implementation of WGS in all European countries in public health and food safety
- promoting the collaboration of institutions on local, national and international level
- implementing genomic applicable in risk assessment

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Thank you for your attention

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feb '18 Risk Assessment Research Assembly

TRACKING

Transdisciplinary Risk Assessment Combining KInetics aNd Genotyping

The TRACKING Consortium

Netherlands
Wageningen University
NIZO Food Research
Unilever

Switzerland
Nestec Ltd, Nestlé R&D

United Kingdom
PepsiCo international
Unilever

Spain
University of Cordoba
IRTA

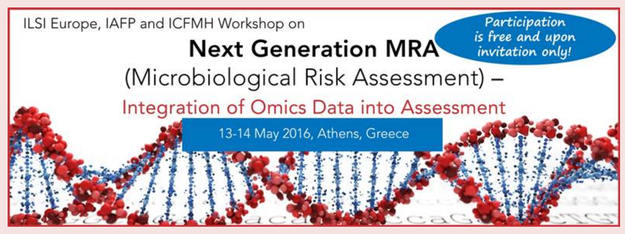
France
Université Bretagne Loire
INRA
Fromageries Bel
Groupe Danone

Italy
University of Torino

Greece
Agricultural University of Athens, Greece
Hellenic Agricultural Organization "DIMITRA"

USA
North Carolina State University

Established at



ILSI – IAFP – ICFMH
Next Generation MRA– Integration of Omics Data into Risk Assessment

Breakout Group 1: Epidemiology
Breakout Group 2: Metagenomics
Breakout Group 3: Exposure Assessment
Breakout Group 4: Hazard Characterisation

Limitations of current MRA approaches

1. Use of data obtained *in vitro*
2. Underestimated prevalence and concentration of the foodborne pathogens which owe to the imperfect nature of the diagnostic media
3. Use of empirical mathematical equations without mechanistic insights/biological meaning
4. High uncertainty in the characterization of risk which originates from other sources of high uncertainty, e.g., dose-response models, microbial behavior and virulence (variability/environmental influence), and microbial interactions (ecology)

Objective

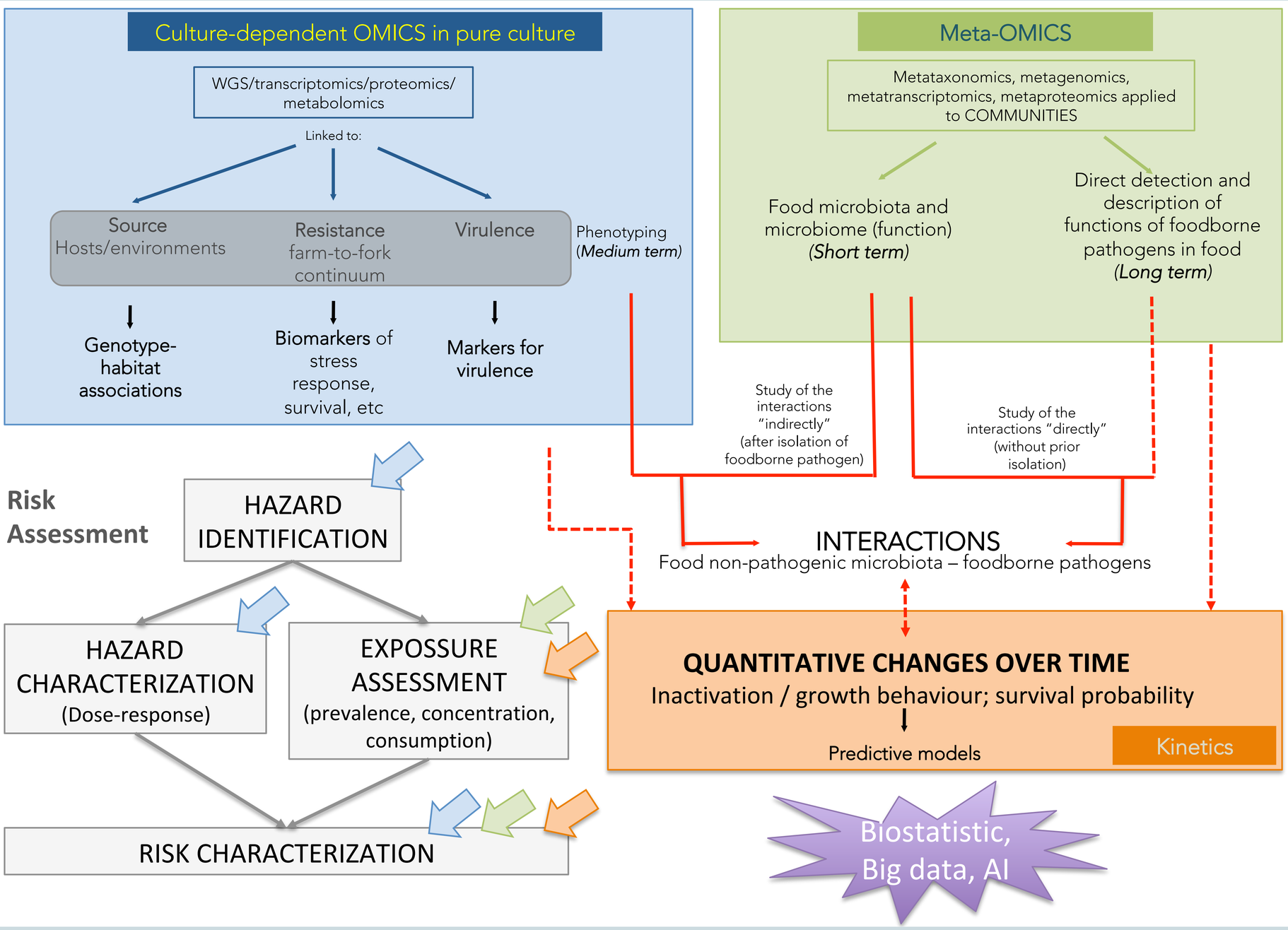
Development of Next Generation Microbiological Risk Assessment: translating 'omics' data to biologically relevant information for MRA

[development of a toolbox for risk assessment (decisions trees, validated approaches to predict microbial behaviour and assess risks) enriched by integrating omics data]

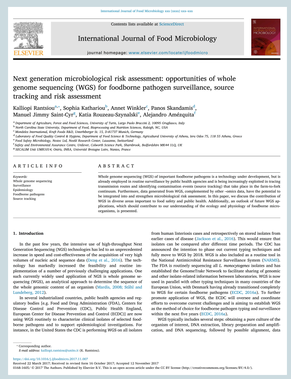
Key performance indicators (KPIs)

- More precise information than those brought by classical microbiological tools, to food safety decision makers
- New insights in outbreak-source-attribution analysis for aiding in public health decision
- Risk characterisation steered by mechanistic insight
- Reduce uncertainty
- Reliable answers to the posed health questions of a policy maker in an accessible manner

How to do it



Preparatory work



Next generation microbiological risk assessment: opportunities of whole genome sequencing (WGS) for foodborne pathogen surveillance, source tracking and risk assessment

Kalliopi Rantsiou[1,*], Sophia Kathariou[2], Annet Winkler[3], Panos Skandamis[4], Manuel Jimmy Saint-Cyr[5], Katia Rouzeau-Szynalski[5], Alejandro Amézquita[5]

Next generation microbiological risk assessment meta-omics: The next need for integration

Luca Cocolin[1,*], Marios Mataragas[2], Francois Bourdichon[3], Agapi Doulgeraki[4], Marie-France Pilet[5], Balamurugan Jagadeesan[6], Kalliopi Rantsiou[1], Trevor Phister[6]

Next generation microbiological risk assessment: Potential of omics data for exposure assessment

Heidy M.W. den Besten[1], Alejandro Amézquita[2,*], Sara Bover-Cid[3], Stéphane Dagnas[4], Mariem Ellouze[5], Sandrine Guillou[6], George Nychas[7], Cian O'Mahony[8], Fernando Pérez-Rodríguez[9], Jeanne-Marie Membre[10,*]

Next generation Microbiological Risk Assessment

- Potential of Omics data for Hazard Characterisation -

Nabila Haddad, Nick Johnson, Sophia Kathariou, Aline Métris[1], Trevor Phister, Annemarie Pielaat[2], Chrysoula Tassou, Marjon H.J. Wells-Bennik, Marcel H. Zwietering[*]

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TRACKING

Transdisciplinary Risk Assessment Combining KInetics aNd Genotyping

The TRACKING Consortium

Next generation MRA

development of a toolbox with integrated omics data

Where are we now:

- Underestimated prevalence of pathogens (imperfect diagnostic tools)
- Empirical equations without biological meaning
- Uncertainty in RC due to uncertainty in dose response models, microbial behaviour, interactions/stress (ecology)

TRACKING brings:

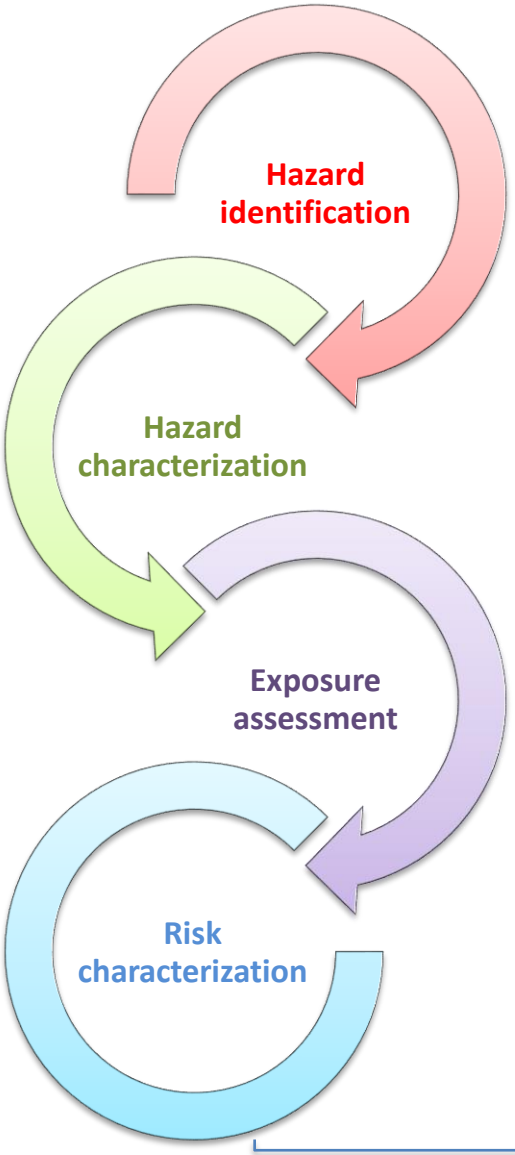
- Improved HI for more precise information for decision makers
- Outbreak-source-attribution (HI) and biomarkers for behaviour to fine tune HC and EA
- RC steered by mechanistic insight to give reliable answers to policy makers in an accessible way

Key performance indicators (KPIs)

- More precise information than those brought by classical microbiological tools, to food safety decision makers
- New insights in outbreak-source-attribution analysis for aiding in public health decision
- Risk characterisation steered by mechanistic insight
- Reduced uncertainty
- More reliable answers to the posed health questions of a policy maker in an accessible manner

- **Omics**: WGS/Transcriptomics/proteomics/metabolomics
- **Meta-Omics**: Metaxanomics, metagenomics, metatranscriptomics, metaproteomics applied to communities

MICROBIAL RISK ASSESSMENT PROCESS



- ❑ Tool for foodborne pathogen detection characterization
- ❑ Source identification
- ❑ Dose response model
- ❑ Predictive models
- ❑ Exposure routes
- ❑ Biological variability

OMICS

Genotype habitat association

Biomarkers of stress response

Markers for virulence

Framework for integration in MRA

META-OMICS

Food microbiota and microbiome

Microbial community interactions

ACCURATE RISK ESTIMATES

The TRACKING Consortium

Academia

Agricultural University of Athens, Greece
North Carolina State University, USA
Université Bretagne Loire, France
University of Cordoba, Spain
University of Torino, Italy
Wageningen University, Netherlands

Food producing companies

Fromageries Bel, France
Groupe Danone, France
Nestec Ltd, Nestlé R&D, Switzerland
PepsiCo international, United Kingdom.
Unilever, UK/Netherlands

Research Institutions

Hellenic Agricultural Organization –DEMETER, Greece
INRA, France
IRTA, Spain
NIZO Food Research, Ede, Netherlands

The outcome (… so far …)

International Journal of Food Microbiology xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Food Microbiology

journal homepage: www.elsevier.com/locate/ijfoodmicro

Editorial: Integration of omics into MRA

Luca Cocolin[a,*], Jeanne-Marie Membré[b], Marcel Zwietering[c]

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Manuscript Number: FOOD-D-17-00281

Title: Next generation Microbiological Risk Assessment - Potential of Omics data for Hazard Characterisation -

Article Type: SI: Omics in MRA

Keywords: dose-response, virulence, pathogenicity, functional genomics, quantitative transcriptomics and proteomics, risk analysis, food safety, public health

Corresponding Author: Professor Marcel H Zwietering, Ph. D.

Corresponding Author's Institution: Wageningen University

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Order of Authors: Nabila Haddad; Nick Johnson ; Sophia Kathariou; Aline Métris; Trevor Phister; Annemarie Pielaat; Chrysoula Tassou; Marjon H.J. Wells-Bennik; Marcel H Zwietering, Ph. D.

A new method for identification of antimicrobial resistance genes based on whole plasmid sequencing.

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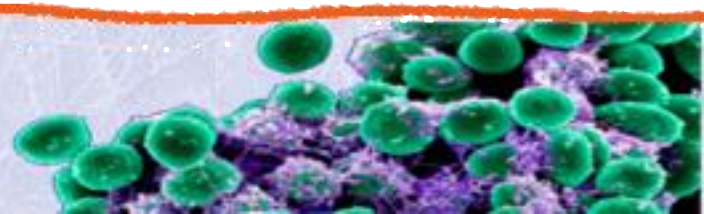
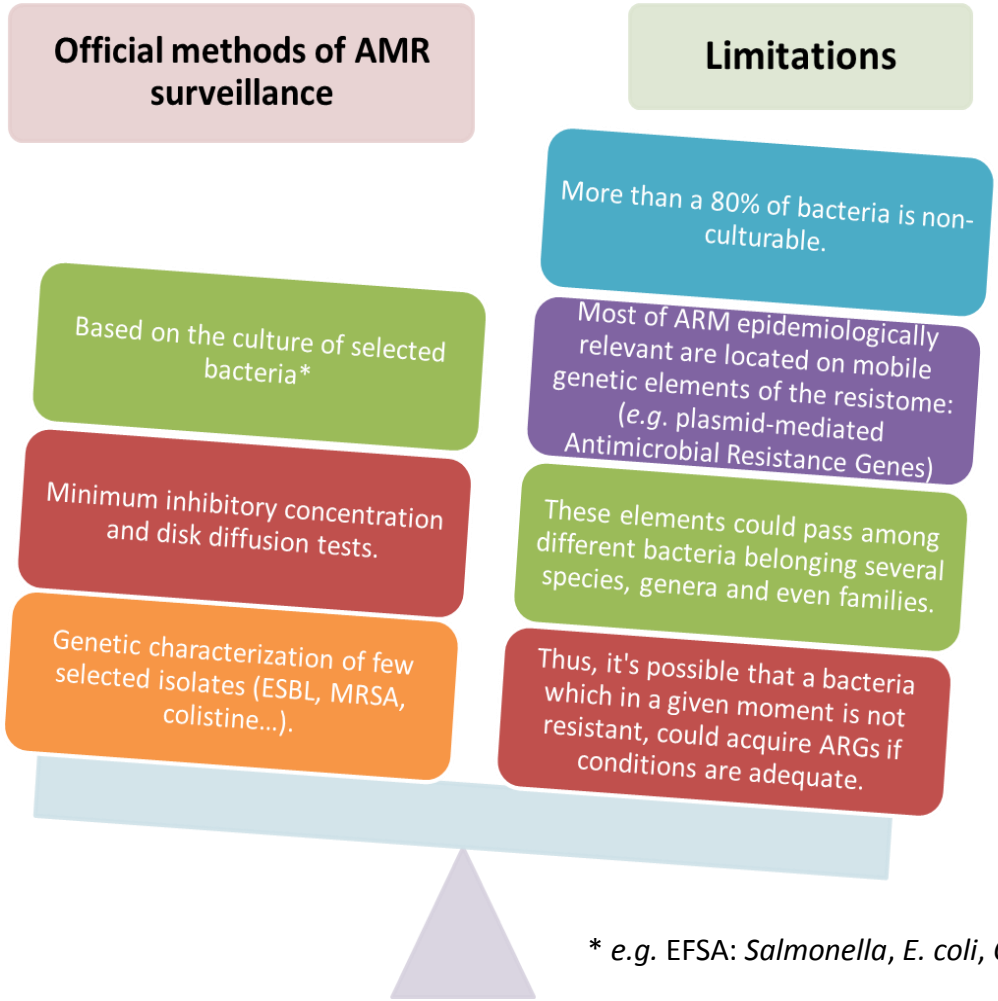
[*] esperon@inia.es



BACKGROUND

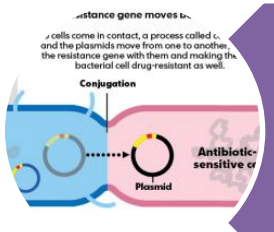
Antimicrobial resistance is an emerging and global problem.



* *e.g.* EFSA: *Salmonella*, *E. coli*, *Campylobacter.*

THUS, 1- THE RISK OF AMR COULD BE HIGHER THAN IS CURRENTLY DETECTED
2- SURVEILLANCE SYSTEMS OF AMR COULD NOT BE REPRESENTATIVE OF THE CAPABILITY OF ANTIMICROBIAL RESISTANCE OF A GIVEN BACTERIAL COMMUNITY

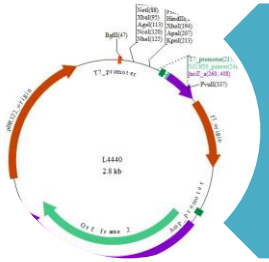
ALTERNATIVE METHOD: Evaluation of ARM based on the characterization of THE ENTIRE PLASMID DNA SEQUENCES IN THE WHOLE MICROBIAL COMMUNITY.



Knowing the potential capability of AMR of the total microbiome.

MOBILE ELEMENTS

ADVANTAGES/ ADDED VALUE



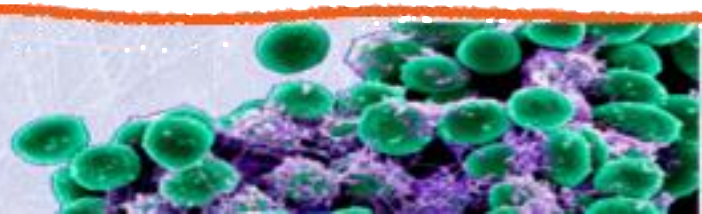
Establish relationships within the plasmids (resistance genes with each other, with other pathogenicity factors, with other genes ...)

pDNA extraction → Nanopore sequencing (MinIon) → Data analysis

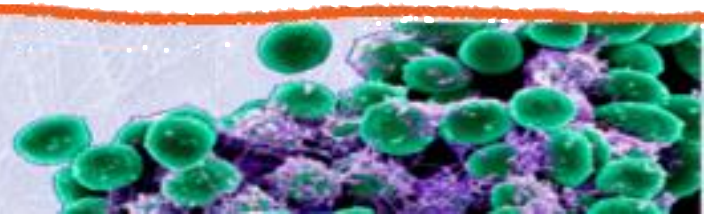
WHAT WE NEED?

- **Funds**

- **Partners**:
  - **To acomplish the proposed objectives we need experts in bioinformatics and microbiologists.**
  - **We also wellcome all supporting ideas related to plasmid identification and microbiome!!**



THANK YOU FOR YOUR ATTENTION!!!!



National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

Measurement of prevalence and concentration of ESBL-producing *E. coli* in meat and non-meat food

Authors: Eric G. Evers, Annemarie Pielaat, Joost H. Smid, Engeline van Duijkeren, Francy B. Vennemann, Lucas M. Wijnands, Jurgen E. Chardon
Contact: eric.evers@rivm.nl

Centre for Zoonoses and Environmental Microbiology, National Institute for Public Health and the Environment

Introduction

- Bacteria that produce extended-spectrum β-lactamases (ESBLs) are resistant to β-lactam antibiotics.
- Humans who are carrier of ESBL-producing *E. coli* are considered at risk for antibiotic therapy failure following e.g. urinary tract *E. coli* infection.
- In The Netherlands about 5% of the human population is carrier of ESBL-producing *E. coli*.
- Meat consumption is considered an important transmission route for ESBL-producing *E. coli*.

Previous work

Table 1. Contribution of food animals to the exposure of humans to ESBL-producing *E. coli* (EEC) through meat at the moment of consumption in The Netherlands.

Category	Exposure per contaminated portion (No. EEC/portion)	Fraction of contaminated portions	Total* number of consumed portions	Total* exposure (No. EEC)
Beef	1.88E+1	1.46E-2	3.29E+9	**9.05E+8 [77.5%]**
Chicken	1.75E+0	6.85E-2	1.75E+9	**2.09E+8 [17.9%]**
Pork	2.44E+0	3.05E-3	7.12E+9	**5.29E+7 [4.5%]**
Veal	3.56E+0	1.35E-2	2.81E+7	**1.35E+6 [0.1%]**
Mutton/lamb	N.a.	0.00E+0	5.22E+7	**0.00E+0 [0%]**
Mean (^{m}) or sum (^{s})	6.15E+0^{m}	1.55E-2^{m}	1.22E+10^{s}	**1.17E+9^{s}**

**'total' refers to the consumption by the Dutch population in a year.*

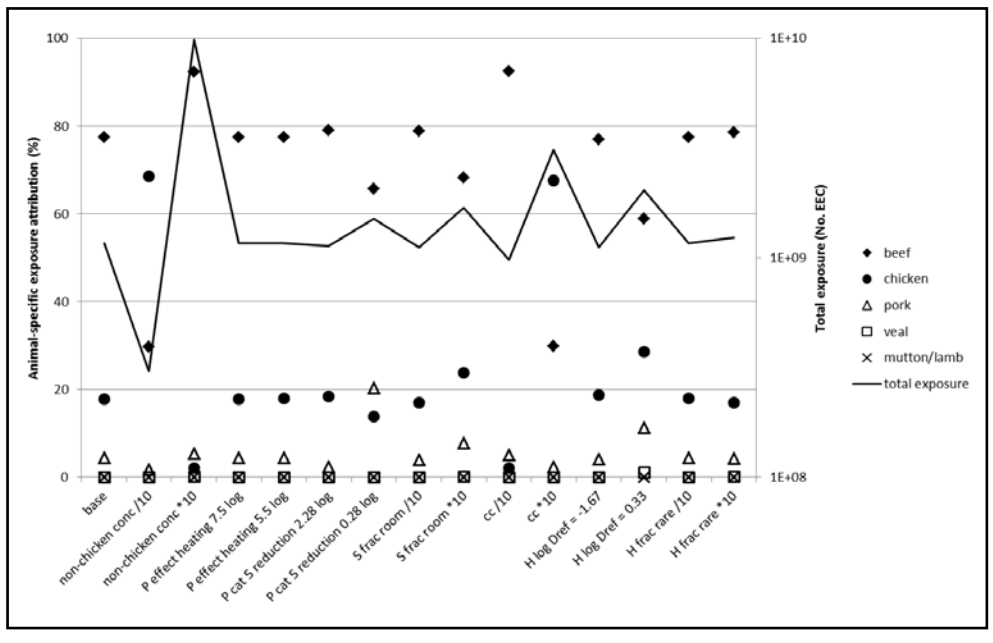


Fig 1. Sensitivity analysis results. Effect of 10-fold changes in parameter base values on total exposure (No. EEC) and food animal-specific attribution of exposure. P = preretail, S = storage, H = consumer heating, conc = concentration, cat = category, frac = fraction, cc = cross-contamination.

Research idea

- Research revealed very significant data gaps on prevalences and concentrations of ESBL-producing *E. coli* for food products.
- For food products other than meat, ESBL *E. coli* prevalence data are very scarce.
- For ESBL E. coli **concentrations**, only data for chicken meat data are available.
- **High numbers of food samples are to be analyzed to fill this data gap**. Especially since low-prevalence products which are eaten raw and often (e.g. vegetables, fruit) can be an important contribution to human ESBL *E. coli* exposure.
- Is there a relation between ESBL *E. coli* concentration and prevalence?
- Is there a difference between EU countries? If so, what is the cause?

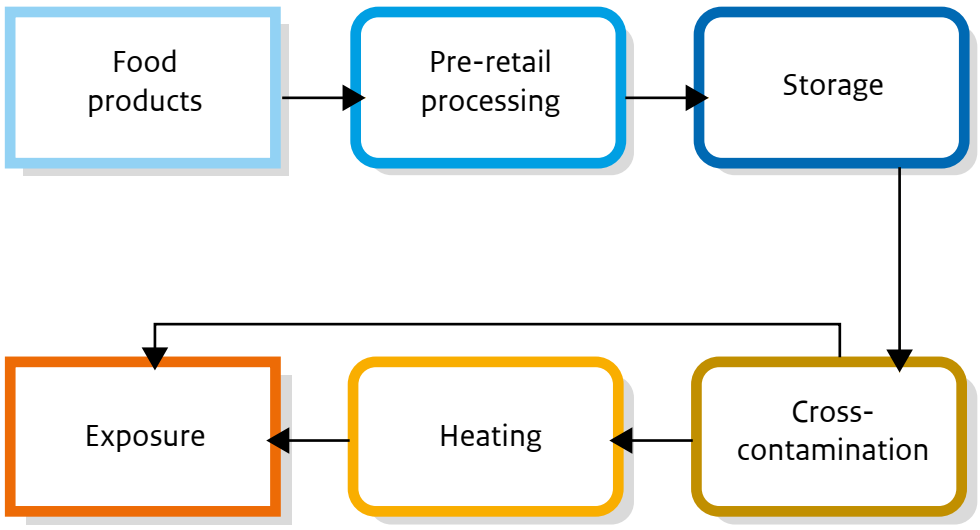


Fig. 2. Overview of sQMRA model used for exposure calculations

Foreseen impact / benefit

- A comparative exposure assessment can be used as an indication of the attribution of human ESBL *E. coli* carriage.
- This provides governments with a list of most important food products or food categories.
- For these food products, interventions by the government are most likely to lead to a reduction of ESBL *E. coli* exposure and carriage and therewith to a reduction of public health risk.
- These interventions can cover the whole food chain, from a reduction in ESBL *E. coli* load in primary production by hygiene measures, to changing consumer behavior by an information campaign or a warning on the food product in retail.

Realization

- This research needs to be sustained by public funding as public health and not primary production and food industry benefit from the results.
- This project requires large laboratory capacity preferably from institutes in multiple EU countries.
- Inclusion of foodborne pathogens in this research would be very efficient.

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National Institute for Public Health
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Ministry of Health, Welfare and Sport

Measurement of prevalence and concentration of ESBL-producing *E. coli* in meat and non-meat food

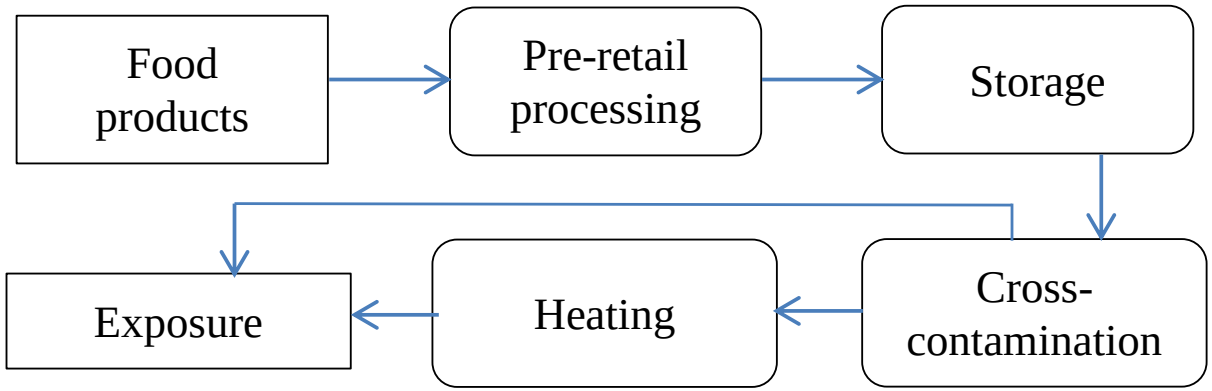
Eric G. Evers, Annemarie Pielaat, Joost H. Smid, Engeline van Duijkeren, Francy B. Vennemann, Lucas M. Wijnands, Jurgen E. Chardon

Carriage of antimicrobial resistant (AMR) bacteria is a public health risk

- In The Netherlands about 5% of the human population is carrier of ESBL-producing *E. coli,* an AMR resistant bacterium
- Human carriers are at risk for antibiotic therapy failure, leading to extended and aggravated disease
- Meat consumption is suspected to be an important transmission route for ESBL-producing E. *coli.*

Quantitative Microbial Risk Assessment (QMRA) can assess which food products are important for AMR

- By calculating the human exposure, in this case for ESBL E. *coli*
- Using farm-to-fork or retail-to-fork calculations
- **Interventions are to be aimed at the high exposure food products**



We did this for meat …

Category	Human exposure to ESBL-producing E. coli
Beef	78 %
Chicken	18 %
Pork	5 %
Veal	0.1 %
Mutton/lamb	0 %

… but in general the calculations are hampered by large data gaps

- ESBL E. coli prevalences are only available for meat products
  - Not for non-meat products
- ESBL E. coli concentrations are only available for chicken
  - Not for other products (be it meat or non-meat)

We need high numbers of food samples to be analyzed to fill this data gap …

- Especially since low prevalence products which are eaten raw and in large quantities can give a high human ESBL *E. coli* exposure
  - Vegetables and fruit
- This requires large laboratory capacity from multiple institutes
- Public funding as only public health will benefit

… then we can advise policy makers on food products to focus on

- Country-specific differences can be very insightful for effective interventions

Viruses in fish
A clear view of the dangers associated with production and consumption

Maria Teresa Barreto Crespo & Mónica Nunes
iBET - Instituto de Biologia Experimental e Tecnológica, Oeiras, Portugal

Risk Assessment Research Assembly (RARA)
Utrecht, 7 February 2018

Proposal

Assess virus distribution in wild and farmed fish with special attention to those that can impose significant negative impact to fish production, but also that threaten human health

Why is it important?

- **European Union (EU) coastline: 66 000 km long, bordering the Atlantic Ocean, Mediterranean Sea, Black Sea, and Baltic Sea**
- **Fishing industry: world's 4th largest, with a gross value between 500-1000 billion euros/year, providing jobs for over 5.4 million people**
- **Average EU seafood consumption: 25.8 kg/per capita, being the Southern part of Europe, France, Spain and Italy, the largest seafood consumers**
- **At least 10 different virus families have been associated to fish**
- **The majority of foodborne viruses outbreaks are caused by Norovirus and Hepatitis A virus (specially in bivalves, berries, and leafy greens)**
- **In EU the virologic control of foods is still poorly done, known results are from studies carried out at research institutes and universities**

Impact/Benefit

Improvements

- **Increase knowledge on fish virome**
- **Generate data for a thorough food safety risk assessment**
- **Contribute to science-based decisions on proper food safety control measures**

Beneficiaries

- **EU consumers – contribute to a safer plate / Fisheries / Aquaculture producers / Food safety control authorities**

Direct impact

- **Knowledge of the virome of the selected fish species and evaluation of their potential food safety hazards to humans and fishes in the "One Health" perspective**
- **UN Sustainable Development Goals: the 2030 Agenda for sustainable development – Goal 14: Sustainable use of marine resources, fisheries, aquaculture, and tourism**

Public funding

- **Basic research for up-to-date scientific knowledge and data on fish virome**
- **Responsibility towards the EU consumers safety and trust**
- **Objective and science-based advice on future food safety legislation**

Expertise and technical knowledge needed

- **NGS equipment and experience**
- **High knowledge in constructing virus libraries necessary for the NGS analyses**
- **Virologists**
- **Other case studies from different geographical areas and biotopes**

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Risk Assessment Research Assembly (RARA)

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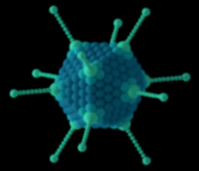
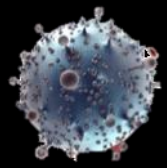




Viruses in fish

A clear view of the dangers associated with production and consumption

Teresa Crespo and **Mónica Nunes**

tcrespo@ibet.pt mnunes@ibet.pt

iBET
Instituto de Biologia Experimental e Tecnológica | www.ibet.pt

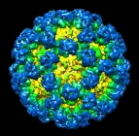
Background

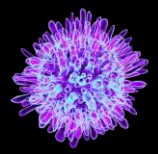
Seafood economical importance

- European Union (EU) coastline: 66 000 km long, bordering the Atlantic Ocean, Mediterranean Sea, Black Sea, and Baltic Sea
- Southern part of EU: largest seafood consumers
- Fishing: traditional, cultural, and high impact economic activity with an enormous economic value / 5,4 million jobs / gross value added of ~€500 billion/year
- EU fish consumption (2017): 25,8 kg per capita

Viruses in food

- There are at least 10 families of viruses transmitted by food, resulting in infections that range from mild diarrheal illness to severe encephalitis
- The majority of foodborne outbreaks are caused by Norovirus and Hepatitis A virus (specially in bivalves, berries, and leafy greens)





Proposal

This proposal aims to characterize the virome of 4 selected fish species (as a starting point) from aquaculture and fisheries, namely:

- Gilthead seabream (*Sparus aurata*)
- European seabass (*Dicentrarchus labrax*)
- European pilchard (*Sardina pilchardus*)
- Horse mackerel (*Trachurus trachurus*)

The virome assessment in fish meat and organs will allow surveying the presence of:

- Known pathogenic viruses to humans
- Known pathogenic viruses to fish
- New viruses potentially pathogenic, or not, to humans and fishes

Objectives

- Assess the genomes of potential pathogenic and non-pathogenic viruses in different fish species (wild and farmed), by targeted and untargeted approaches
  - For known viruses: targeted approach 
  - For unknown viruses: untargeted approach 

- Evaluate the potential food safety hazards by an in-depth characterization of the molecular diversity of viral populations, by a wide range of clustering and phylogenetic inference analyses, complementing the metagenomics analysis

- Access to the viral genomic content, bringing unique insights into the main viral families present in fish, and indirectly in the aquatic environment.

Improvements

- Increase knowledge on fish virome
- Generate data for a thorough food safety risk assessment
- Contribute to science-based decisions on proper food safety control measures

Direct impact

- Knowledge of the virome of the selected fish species and evaluation of their potential food safety hazards to humans and fishes in the “One Health” perspective
- UN Sustainable Development Goals: the 2030 Agenda for sustainable development – Goal 14: Sustainable use of marine resources, fisheries, aquaculture, and tourism

Beneficiaries

- EU consumers – contribute to a safer plate / Fisheries / Aquaculture producers / Food safety control authorities

Expertise and partners

Portuguese team:

- High knowledge in molecular biology
- Experience in animal cell culture (risk evaluation studies for detection and infection)
- Expertise in phylogenetic analysis/studies on viruses

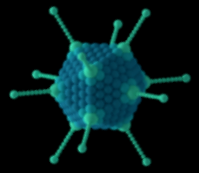
Expertise and technical knowledge needed:

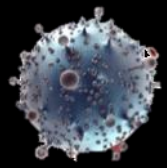
- NGS equipment and experience
- High knowledge in constructing virus libraries necessary for the NGS analyses
- Virologists
- Other case studies from different geographical areas and biotopes

Funding from public sources

- Basic research for up-to-date scientific knowledge and data on fish virome
- Responsibility towards the EU consumers safety and trust
- Objective and science-based advice on future food safety legislation

Risk Assessment Research Assembly (RARA)
Utrecht, 7 February 2018





Viruses in fish

A clear view of the dangers associated with production and consumption

Teresa Crespo and **Mónica Nunes**
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Consumer perception of food contamination and food-borne disease produced by Campylobacter jejuni.

Julieta Moreira Abeijon
Msc Food Technology and Quality Assurance.
University of Reading

CAMPYLOBACTER FACTS

- Responsible each year for more than 280,000 cases of poisoning in UK.
- It is estimated that causes more than 100 deaths a year.
- **72%** of the UK is not familiar with the bacteria.

HOW THE CONTAMINATION CAN BE REDUCED?

- ✓ BETTER INFORMED CONSUMERS
- ✓ IMPROVEMENT OF THE FOOD SAFETY BEHAVIOR

RESEARCH IDEA

1. To develop an **electronic survey** to measure the level of knowledge in consumers about the bacteria.
2. To develop a **guide** about good food safety behavior.

IMPACT AND BENEFICIARIES

- ✓ More informed consumers and more responsible manufacturers.
- ✓ Less cases of food borne disease and less cost in public health.

EXPERTISE AND FOUNDS NEEDED

- Electronic survey: development and launching.
- Food safety and Public surveys expertise.
- Guide development, design and publication.

Consumer perception of food contamination and food-borne disease produced by Campylobacter jejuni.

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University of Reading

Campylobacter FACTS

- UK: Responsible each year for more than **280,000** cases of poisoning (FSA, 2014).
- It is estimated that causes more than **100** deaths a year (FSA, 2014).
- Europe: shows the same trend(International Journal of Food Microbiology (2010)).
- **72%** of the UK is not familiar with the bacteria (FSA, 2014).

HOW THE CONTAMINATION CAN BE REDUCED?

- **BETTER INFORMED CONSUMERS**
- **IMPROVEMENT OF THE FOOD SAFETY BEHAVIOR**

RESEARCH IDEA

- ✓ First part: To develop an **electronic survey** to measure the level of knowledge and perception in consumers about the bacteria, the illness that ensues and how food gets contaminated by this microorganism.

Purpose: to identify areas that need reinforcement of knowledge.

- ✓ Second part: Development of a **guide**, containing information about good food safety behavior when manipulating food to prevent the contamination by Campylobacter jejuni.

IMPACT AND BENEFICIARIES

- ✓ MORE INFORMED CONSUMERS
- ✓ MORE RESPONSIBLE MANUFACTURERS
- ✓ LESS CASES OF FOOD BORNED DISEASE BY CAMPYLOBACTER JEJUNI
- ✓ LESS COST IN PUBLIC HEALTH

TO ACHIEVE A FULL IMPACT:

- Understand that the perception of the risk could vary in different cultures in the EU.
- Further studies in relation to the perception of biological hazards in the food industry are needed.

EXPERTISE AND FOUNDS NEEDED

- Electronic survey development and launching. → Easy Access and completion by the consumer.

- Food Safety expertise.
- Public surveys expertise. → Satisfactory level of understanding of the questions.

- Guide development, design and publication. → To develop a guide with the relevant key points, with access to the public.

"If people feel they can take steps to limit or to avoid a risk they are more likely to accept it".

(World Health Organization, 2014)

THANK YOU
QUESTIONS?

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- Diane G. Newell, et al. (2010) Food-borne Diseases. The Challenge of 20 years ago still persist while new ones continue to emerge. International Journal of Food Microbiology. 139 (2010) S3–S15. Published by Elsevier B.V. Available from: doi:10.1016/j.ijfoodmicro.2010.01.021 [Accessed 14th October]

- Food Standards Agency. (2014) Acting on Campylobacter Together. Available from: https://www.food.gov.uk/news-updates/campaigns/campylobacter/actnow [Accessed 2nd October 2017].

- World Health Organization (2014). Risk Perception conference pages. Available from: http://europa.eu.int/food/riskperception/index.htm [Accessed 29th December 2017].

Model for the survival of methicillin-resistant *Staphylococcus aureus* (MRSA) in aged cheese

Spinelli E.[1], Normanno G.[2]

1 Ph.D. student, Department of Science of Agriculture, Food and Environment (SAFE). University of Foggia, Italy.
2 Associate Professor of Food Inspection, Department of Science of Agriculture, Food and the Environment (SAFE). University of Foggia, Italy.

RESEARCH FOCUS GENERAL DESCRIPTION

BACKGROUND

As well known in literature food, especially meat and milk, may be contaminated by methicillin-resistant *Staphylococcus aureus* (MRSA). In addition, some MRSA strains are known to produce enterotoxins. Eating and handling contaminated food is a potential vehicle for transmission.

The cheese consumption *pro capite* in Europe, is very high. This may pose issues to human health, as raw milk cheese have frequently been contaminated with pathogens. However there is a few date dealing with the survival of pathogens and MRSA in fermented food.

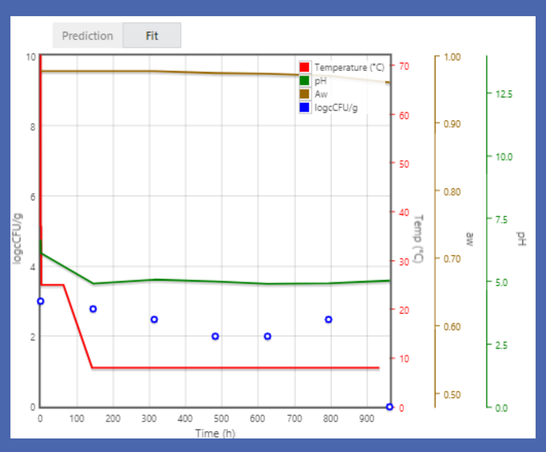
AIM

Evaluate the survival of human and animal enterotoxigenic MRSA strains during cheese-making and ripening processes.

FORESEEN BENEFIT

RESEARCH DESIGN AND METHODS

Predictive Microbiology



Challenge Test

PUBLIC FUNDING AND PARTNERS

Resources and Materials

- Predictive microbiology software
- Equipment and consumables
- Milk samples
- Human and animal enterotoxigenic MRSA strains

Collaborations

- Experimental cheese dairies (high reprouducibility of challenge test)

IMPACT ON PUBLICH HEALTH

To date, despite the high prevalence of MRSA in food, it is unclear whether MRSA can act as a foodborne-pathogen. The study of the survival of MRSA in aged cheese will allow us to know more about the potential growth and outgrowth of this widespread pathogen in fermented food.

This research proposal attempts to improve risk analysis by giving access to new sources of data.

Moreover, the outcomes of this work will provide more in-depth information for consumers regarding the health risks represented by the presence of MRSA in contaminated food.

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Prof. Giovanni Normanno
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Model for the survival of methicillin-resistant *Staphylococcus aureus* (MRSA) in aged cheese

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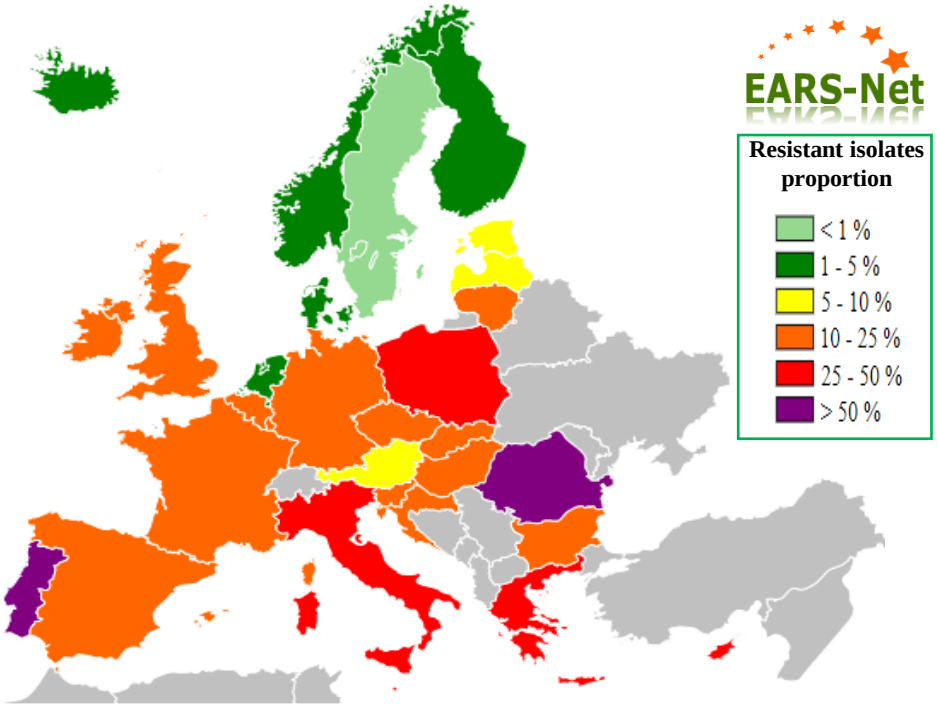
The widespread of methicillin-resistant *Staphylococcus aureus* (MRSA)



Data from invasive (blood and cerebrospinal fluid) MRSA isolates (2016)

MRSA is a well-known antimicrobial-resistant bacterium able to cause a wide range of human pathologies

Staphylococcal food poisoning due to enterotoxigenic MRSA

MRSA

Human and Animal Pathogen

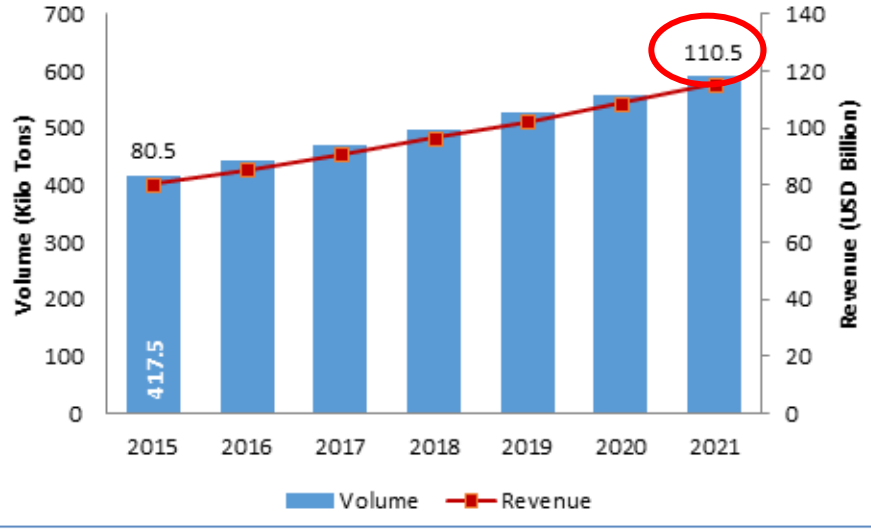
Raw Materials

Handling Eating

Cheese consumption

18 Kg *pro capite* (EU 2016)

Global Cheese Market, 2015 – 2021 (Kilo Tons) (USD Billion)



Source: Zion Research Analysis 2016

***Salmonella* spp.**

Listeria monocytogenes

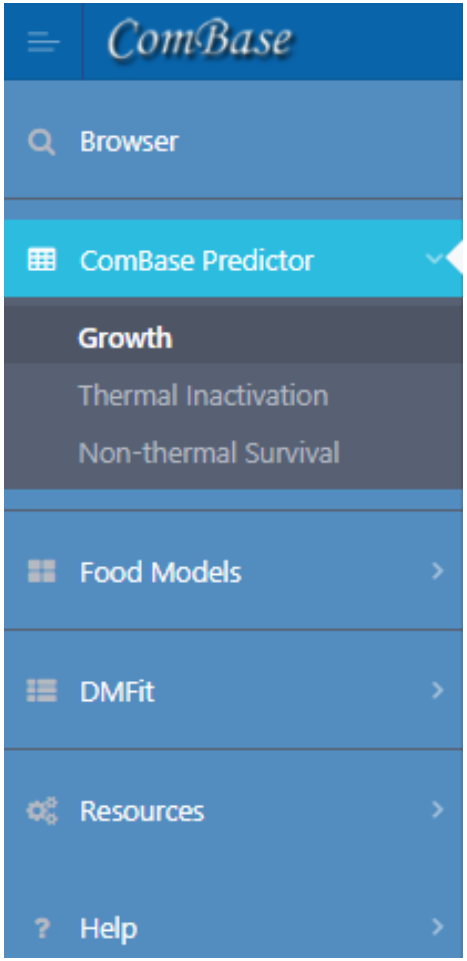
***Escherichia coli* O157:H7**

Staphylococcus aureus

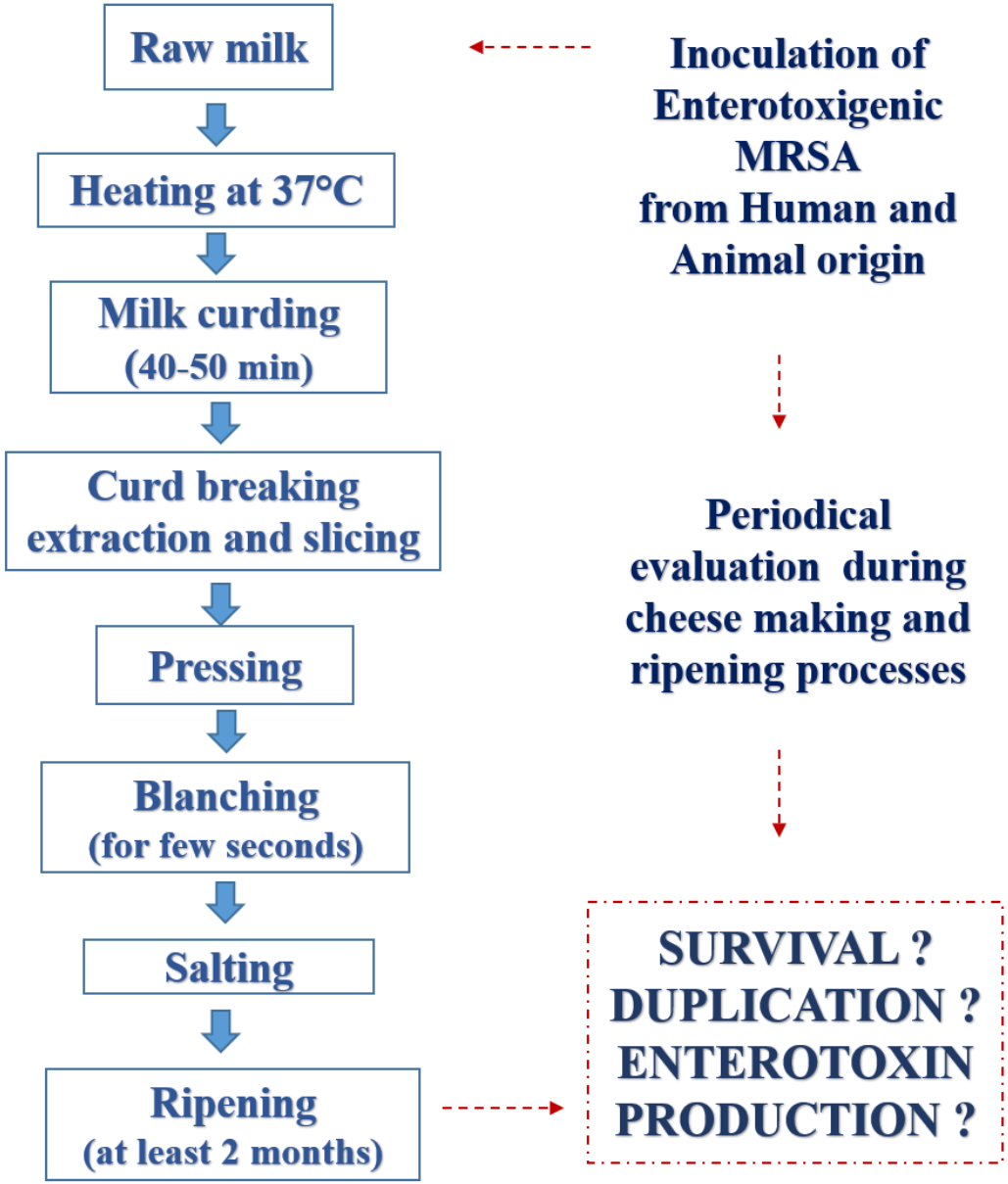
MRSA ?

https://www.clal.it/?section=tabs_consumi_procapite

Predictive Microbiology



Challenge test

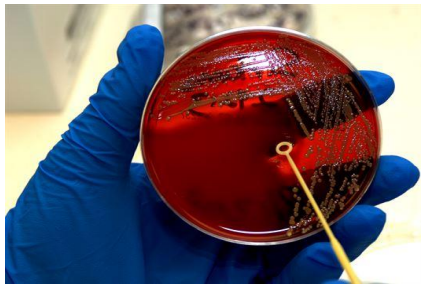


Dialogue between Research Centers, Food Industry and Consumers

Impact on Food Safety

Public Health Intervention

Unexpected Major Developments



THANK YOU

FOR

YOUR ATTENTION

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Animal Health Research Center

CISA

GOBIERNO DE ESPAÑA
MINISTERIO DE ECONOMÍA, INDUSTRIA Y COMPETITIVIDAD

INIA
Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria

BIOSAFETY REFERENCE CENTRE

RLASB
Red de Laboratorios de Alta Seguridad Biológica

Infraestructuras Científicas y Técnicas Singulares

Centro de Investigación en Sanidad Animal. INIA-CISA
Carretera Algete-El Casar de Talamanca, Km. 8,1, 28130 Valdeolmos, Madrid
www.inia.es; http://agripa.org/

Ana de la Torre
torre@inia.es
91 6202300 ext 185

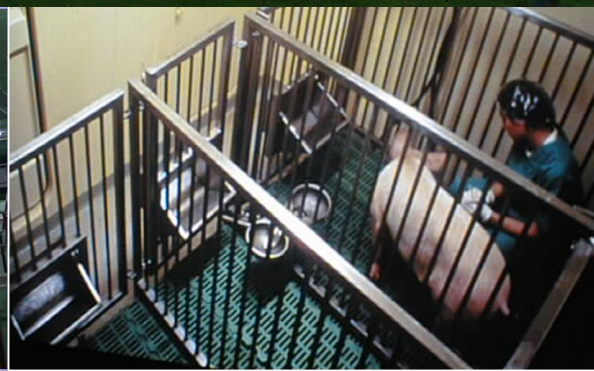
BIOSAFETY LEVEL 3 and 3+ FACILITY

26 Laboratories BSL-3

2 Laboratorios BSL-4 (OIE)

19 Animal facilities BSL-3

14 Common rooms BSL-3

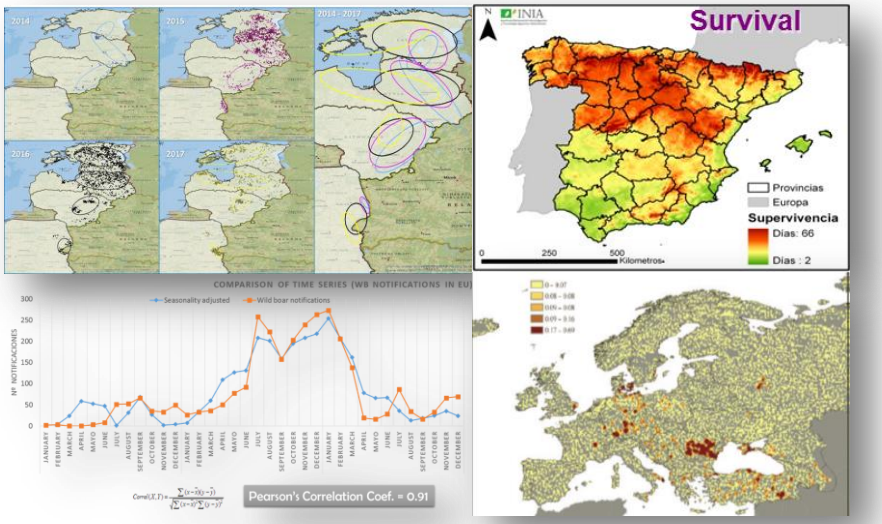


RESEARCH ON PREVENTION, DETECTION AND CONTROL

TRANSBOUNDARY AND EMERGING DISEASES OF OBLIGATORY REPORT

ZOONOTIC AND/OR ECONOMIC RELEVANT DISEASES FOR LIVESTOCK AND THE ENVIRONMENT

ANTIMICROBIAL RESISTANCE



LABEPI

Rift Valley Fever

West-Nile virus

Avian Influenza

Crimean-Congo Hemorrhagic fever

Aujezsky disease

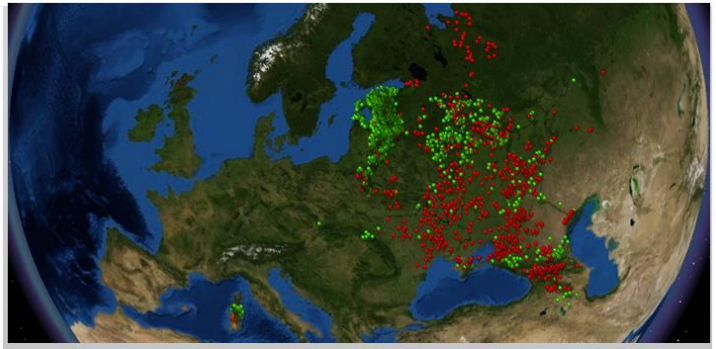
Bacterial zoonoses (Brucella, Salmonella, Campylobacter…)

Antimicrobial resistance genes

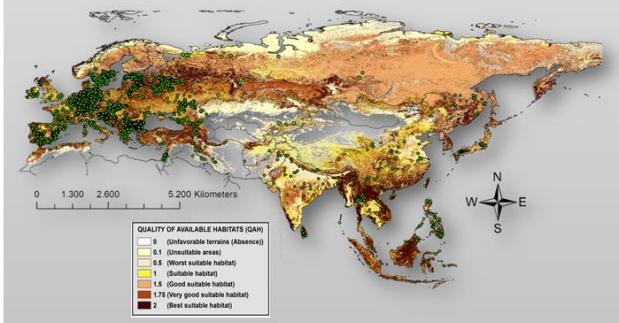
Laboratory

- Animal models for studies on pathogenesis and transmission mechanisms.
- Research on development of diagnostic test and surveillance tools.
- Phylogenetic analyses of zoonotic pathogens, antimicrobial resistances & molecular epidemiological inference.

Epidemiology



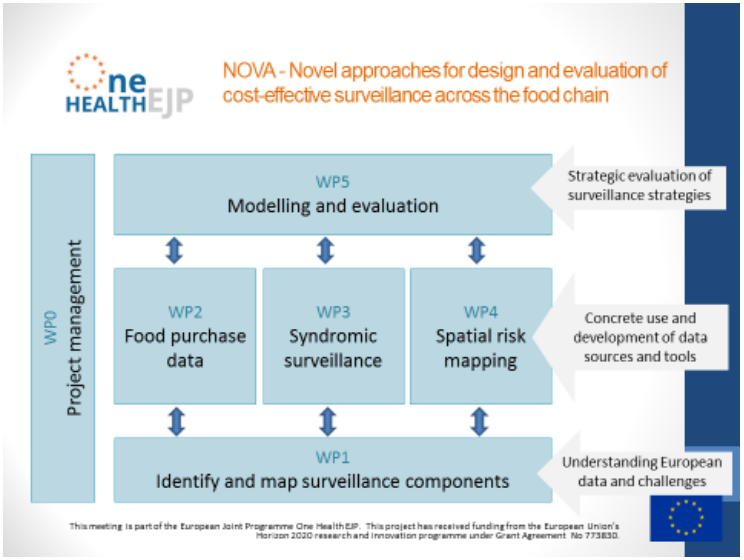
Epidemiological diagnosis
Risk assessment on disease spreading
Improvement of surveillance plans

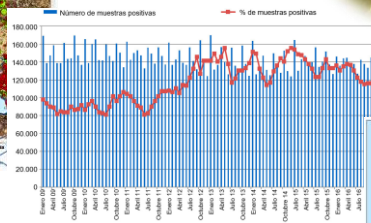


Development and validation of cartographic tolos on wild species distribution based on habitat quality

Highlights on risk assessment:

ZOONOTIC DISEASES NOVA project





- Across the food chain
- Mix of Med and Vet institutes
- Partners across Europe (10-20)
- Focus on sharing knowledge and methods
- Plan to integrate new methods in our everyday work and improve our ability to support decision makers

ANTIBIOTIC RESIDUES & RESISTANCES

POSTER A11 about antibiotic residues map at the Research Ideas Showcase

RESEARCH IDEA: Built an enabling more sophisticated and updated modelling including all antibiotics. It would be associated to an user-friendly web-interface

EU Inter-regional approach to Marine Shellfish Toxin regulation.

A proposed study to inform risk based management of offshore scallop fisheries

Silke, J. [1], Duffy, C. [1], Clarke, D [1], & Nolan, B. [2]

1: Marine Institute, Ireland.
2: Sea Fisheries Protection Authority, Ireland

Research Background

There are four main groups of naturally occurring toxins which occur in European molluscan shellfish. These are 1. Diarrhetic shellfish poisoning (DSP), 2. Paralytic Shellfish Poisoning (PSP), 3. Amnesic Shellfish Poisoning (ASP) and 4. Azaspiracid Shellfish Poisoning (AZP). These groups of toxins are produced naturally by a small number of phytoplankton species and can build up in the stomach tissues of filter feeding bivalve molluscs such as mussels, oysters, clams, scallops and other bivalve species. They are regulated under various EU legislations and directives [1] & [2]. These require that bivalve shellfish placed on the market should be tested for the presence of these marine toxins and should not exceed threshold levels as laid down in the appropriate legislation.

In most cases the usual monitoring of shellfish is carried out on shellfish produced in the bays and estuaries of each member state. The national competent authority regulate the production in these locations by placing temporary bans on harvesting whenever the threshold levels are breached. Effective enforcement of these closure orders is possible due to the inshore nature of most bivalve production. Local arrangements are in place to ensure that shellfish landed from these areas have been subject to monitoring and have passed the official controls on biotoxins as set out in the relevant legislation. An exception to the normal practice is however in species of molluscan shellfish that are fished outside of 12 mile limits such as the king scallop (*Pecten maximus*). Scallops are an important commercially exploited species in northern European waters from Norway to Spain. It attains a large body size, is a high value species and is also the subject of extensive and intensive aquaculture in northern Europe. The Irish offshore fishery for king scallops occurs mainly off the south east Irish coast, the south Irish Sea and in the western approaches to England and Wales (Fig 1). Fleets from the UK, France Spain and Ireland exploit stocks outside of national 12nm territorial limits in these areas (Fig 2).

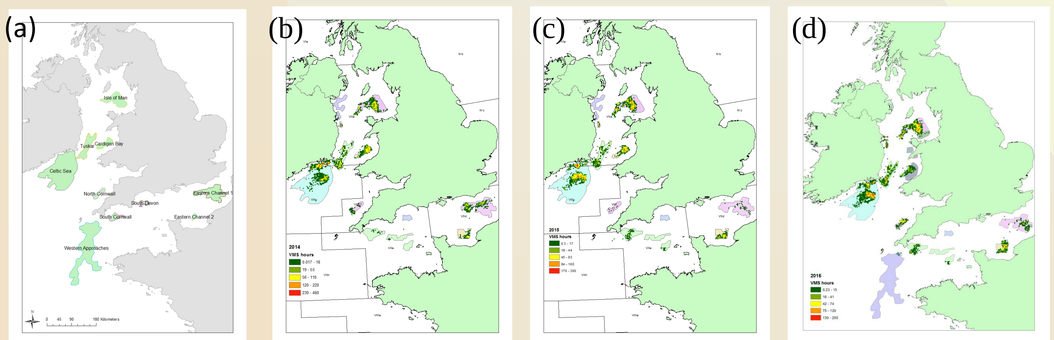


Figure 1: (a) Distribution of scallop beds as collated from Irish vessel activity 2000-2011 (Irish vessels operating outside of UK 12nm). (b) The activity (VMS hrs) for 2014. (c) The activity (VMS hrs) for 2015 (d) The activity (VMS hrs) for 2016

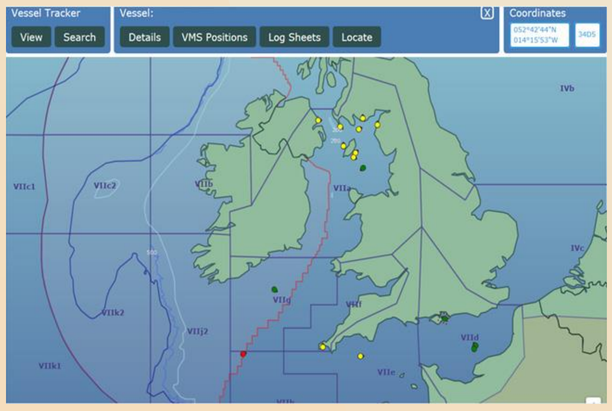


Figure 2: Chart showing various fishing boats from different member states reporting scallop fishing via VMS on a single day in November 2017. Irish (Green) UK (Yellow) and Spanish (Red) boats are shown fishing in the area.

The official controls for king scallops are complicated due to the uneven distribution of toxins throughout the whole scallop; scientific evidence can show that the majority of the toxins are retained in the digestive tissues. Scallops are particularly affected by ASP toxins with high concentrations found in the parts of the scallop that are typically removed prior to consuming (Gills, Mantle and digestive tissues). These regularly contain in excess of 99% of the total ASP loading with approximately 90% occurring in the hepatopancreas alone. Therefore when the risk is considered, carefully processed scallops can be placed on the market following removal of these inedible parts. This processing allows the continuation of marketing of shucked meat / gonad products but severely limits the sale of entire live scallop in the shell (Fig 3).

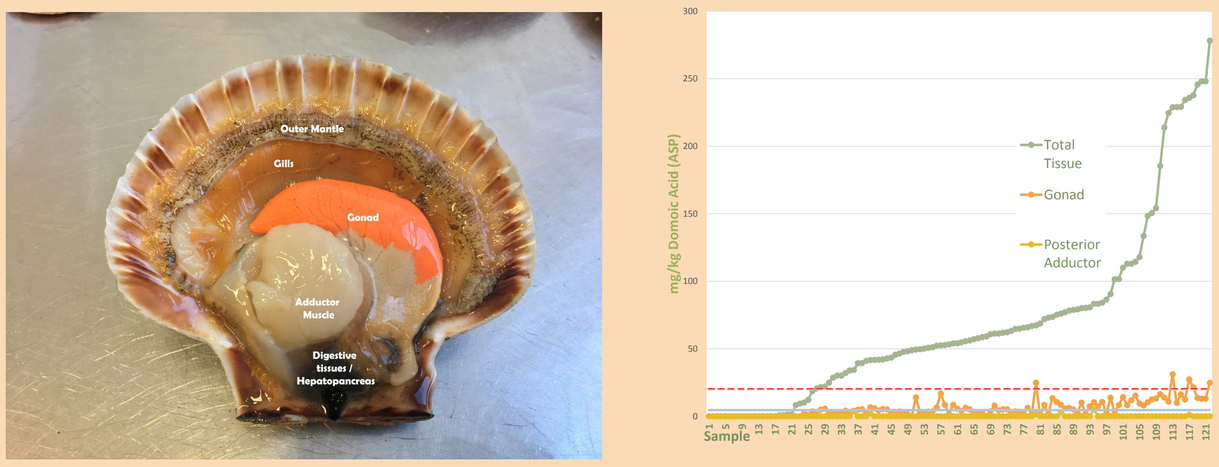


Figure 3: (a) Major internal organs of the King Scallop (*Pecten maximus*) (b) Graph showing the ASP concentration in total soft tissues, compared to Gonad and Adductor Muscle tissues (Samples n=122. Irish testing programme 2016).

There is high temporal and spatial variability in the level of Amnesic Shellfish Poison (ASP) in scallops. The nature of the distribution of the toxins, complex EU regulations and shared fisheries resources has resulted in differing methods of control in member states, which can potentially lead to conflicting advice. Member states are testing offshore scallops landed by their fleets from shared waters (fig. 4) and there is considerable duplication on testing. A project is therefore proposed to improve risk based advice on the management of ASP and other toxins in scallops within offshore fishing areas and assign appropriate sized fishing grids to optimise sampling and minimise sampling variability. The project would also develop a EU-wide shared platform to provide inter-MS biotoxin advisory information using an efficient inter-regional shared approach in order to introduce an efficient means to reduce risk from this fishery.

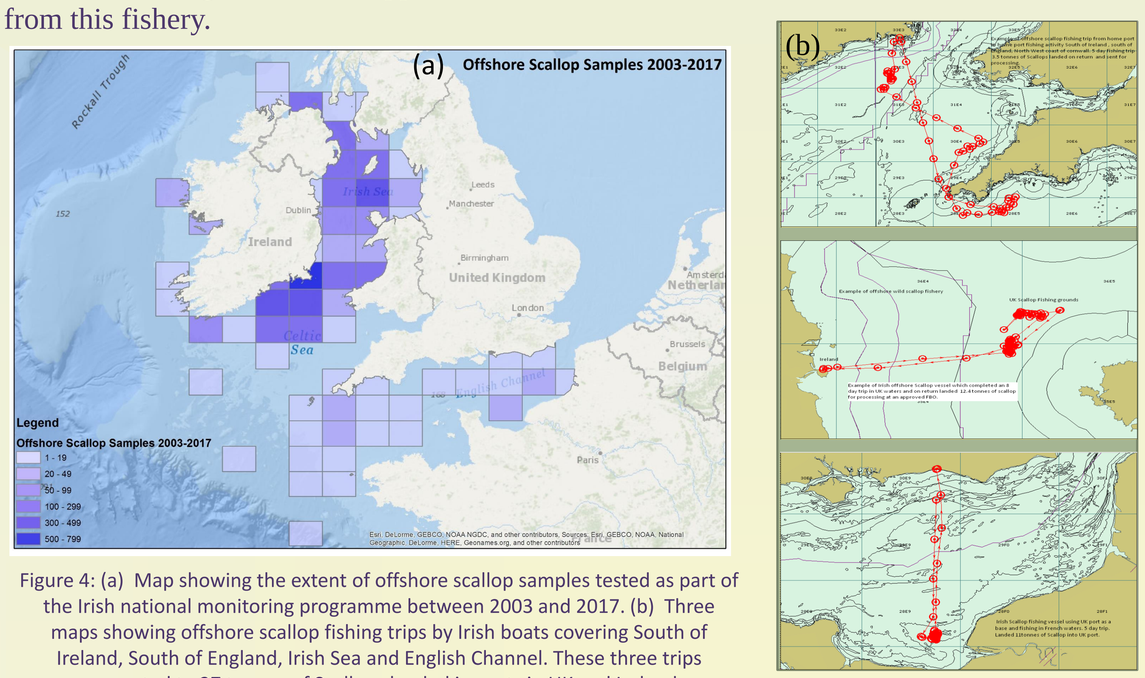


Figure 4: (a) Map showing the extent of offshore scallop samples tested as part of the Irish national monitoring programme between 2003 and 2017. (b) Three maps showing offshore scallop fishing trips by Irish boats covering South of Ireland, South of England, Irish Sea and English Channel. These three trips amounted to 27 tonnes of Scallops landed in ports in UK and Ireland

Impacts and Benefits

Scallops pose a particular difficulty due to the location of offshore fisheries, differing interpretation of the EU legislation and complex partitioning of toxins. In addition, ICES rectangles used as offshore biotoxin management areas can lead to differing results depending on where the sample was taken within the rectangle. Other live bivalves that are fished or farmed in inshore areas are controlled via defined production areas and normally tested by a single national authority to assign status. Scallops may, however, be tested by several member states after landing from offshore waters leading to potential conflicting advice because of field variability.

This proposal will improve the risk based management of Scallops by quantifying this variability, and based on this propose a jointly managed advisory system as part of improved risk management plans between member state's competent authorities. Current estimated annual production landed in Ireland is 2400 tonnes of scallops fished outside classified production areas, 600 samples of these have provided sufficient annual coverage to advise on the biotoxin status and no reports of illness have been received in relation to Irish harvested scallops to date. It would be desirable however to combine information from all member states testing from fishing areas to build up a better picture of the toxin profiles in these areas.

This proposal is made to provide much needed information to reduce potential risk of toxic shellfish being placed on the market. Legislation focusses on the placing of whole scallops on the market, while some markets for processed meats rely on interpretation of the legislation that are not implemented the same in all member states. The research is proposed to inform the assessment of risk for these shellfish and is for the common benefit of assisting regulatory authorities and should therefore be funded publicly.

Funding, Expertise Partners

In order to carry out this proposed study an appropriate funding opportunity needs to be identified and would be best carried out among a multinational interdisciplinary group with expertise in risk assessment, shellfish toxicity and fisheries management. Implementation of an interregional advice platform would require the development of a database by a subgroup with IT skills, and a management cell would need to be established among participatory member states and given the required authority to deal with the uploading of information onto this system. A consortium approach to drafting such a proposal would be established to conform with requirements of an identified funding call.

References

[1] Regulation (EC) No 853/2004 of the European Parliament and of the Council of 29 April 2004 laying down specific hygiene rules for food of animal origin. OJ L 139, 30.4.2004, p. 55–205

[2] Commission Decision 2002/226/EC of 15 March 2002 establishing special health checks for the harvesting and processing of certain bivalve molluscs with a level of amnesic shellfish poison (ASP) exceeding the limit laid down by Council Directive 91/492/EEC.OJ L 75, 16.3.2002, p. 65–66

Acknowledgements

Thanks to Oliver Tully (Marine Institute) for scallop bed information and maps presented in Figure 1

EU Inter-regional approach to Marine Shellfish Toxin regulation.

A proposed study to inform risk based management of offshore scallop fisheries

Joe Silke

Marine Institute Ireland

Shellfish Biotoxins

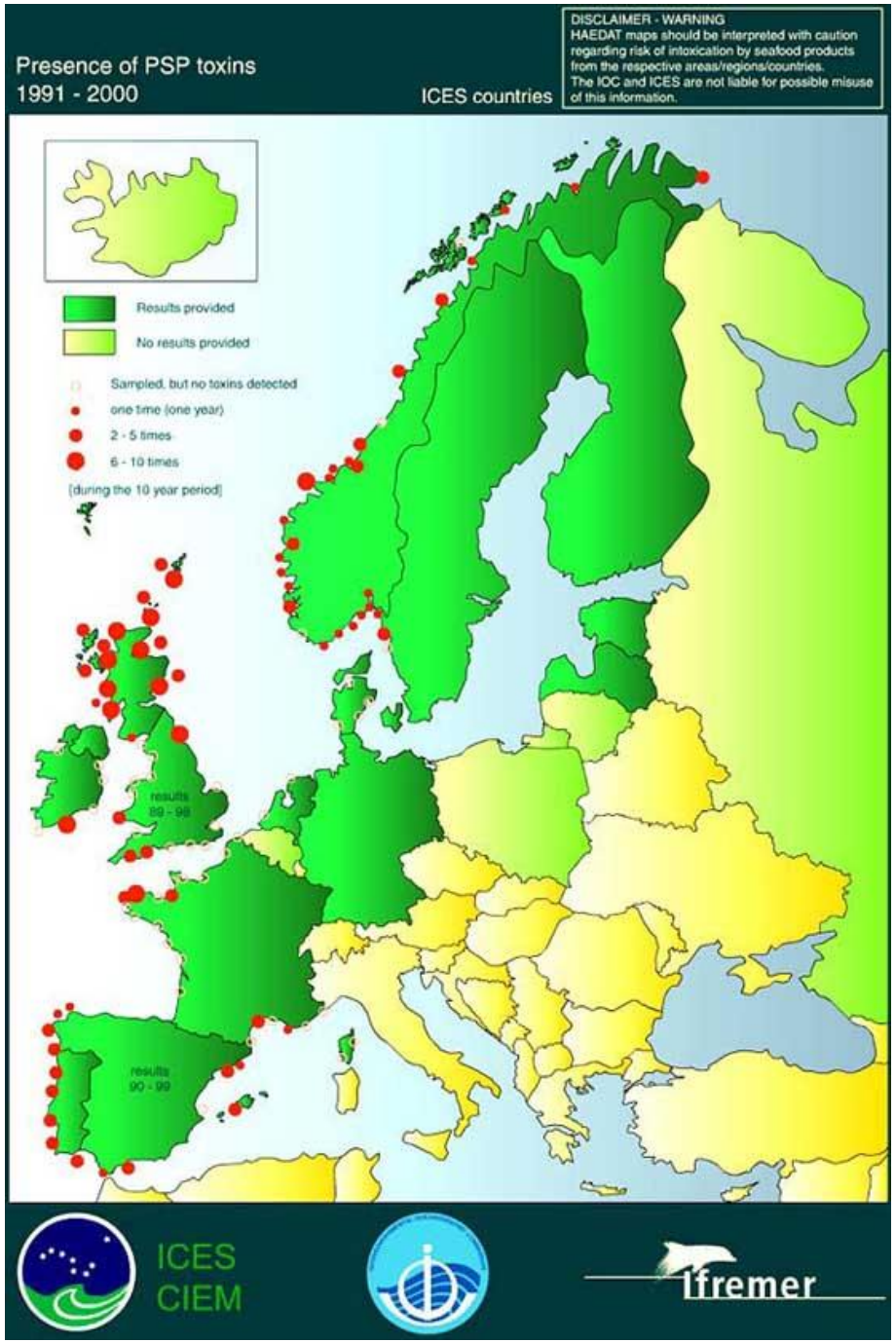
1.Diarrhetic shellfish poisoning (DSP),
2. Paralytic Shellfish Poisoning (PSP),
3. Amnesic Shellfish Poisoning (ASP) and
4. Azaspiracid Shellfish Poisoning (AZP).

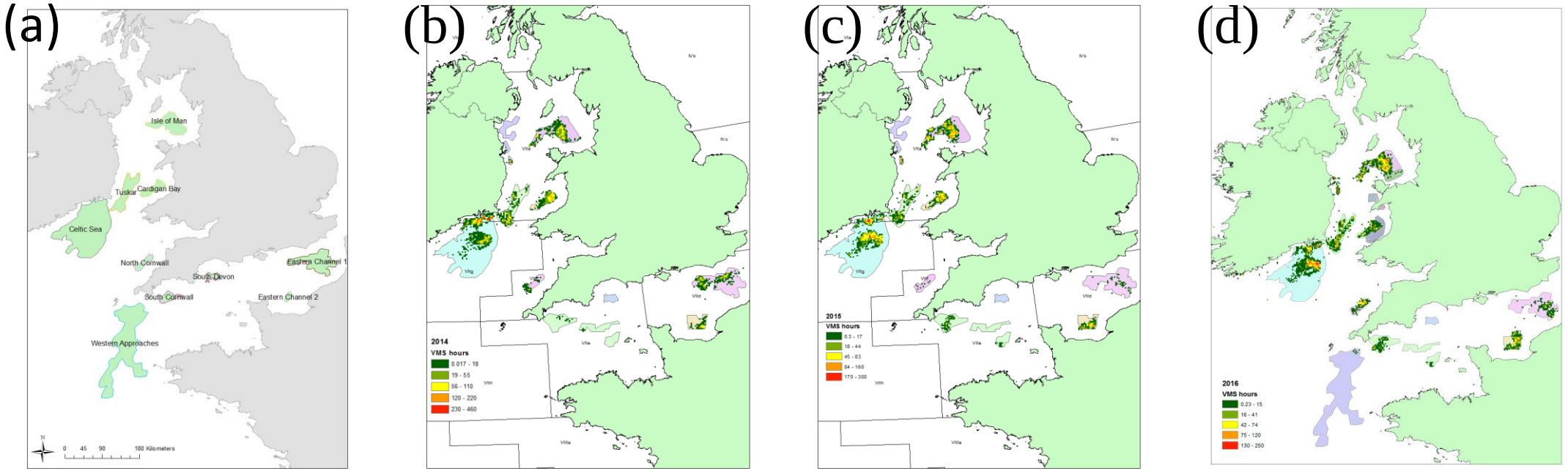
These groups of toxins are produced naturally by a small number of phytoplankton species and can build up in the stomach tissues of filter feeding bivalve molluscs such as mussels, oysters, clams, scallops and other bivalve species.

Shellfish Biotoxins Controls

In most cases the usual monitoring of shellfish is carried out on shellfish produced in the bays and estuaries of each member state.

The national competent authority regulate the production in these locations by placing temporary bans on harvesting whenever the threshold levels are breached.





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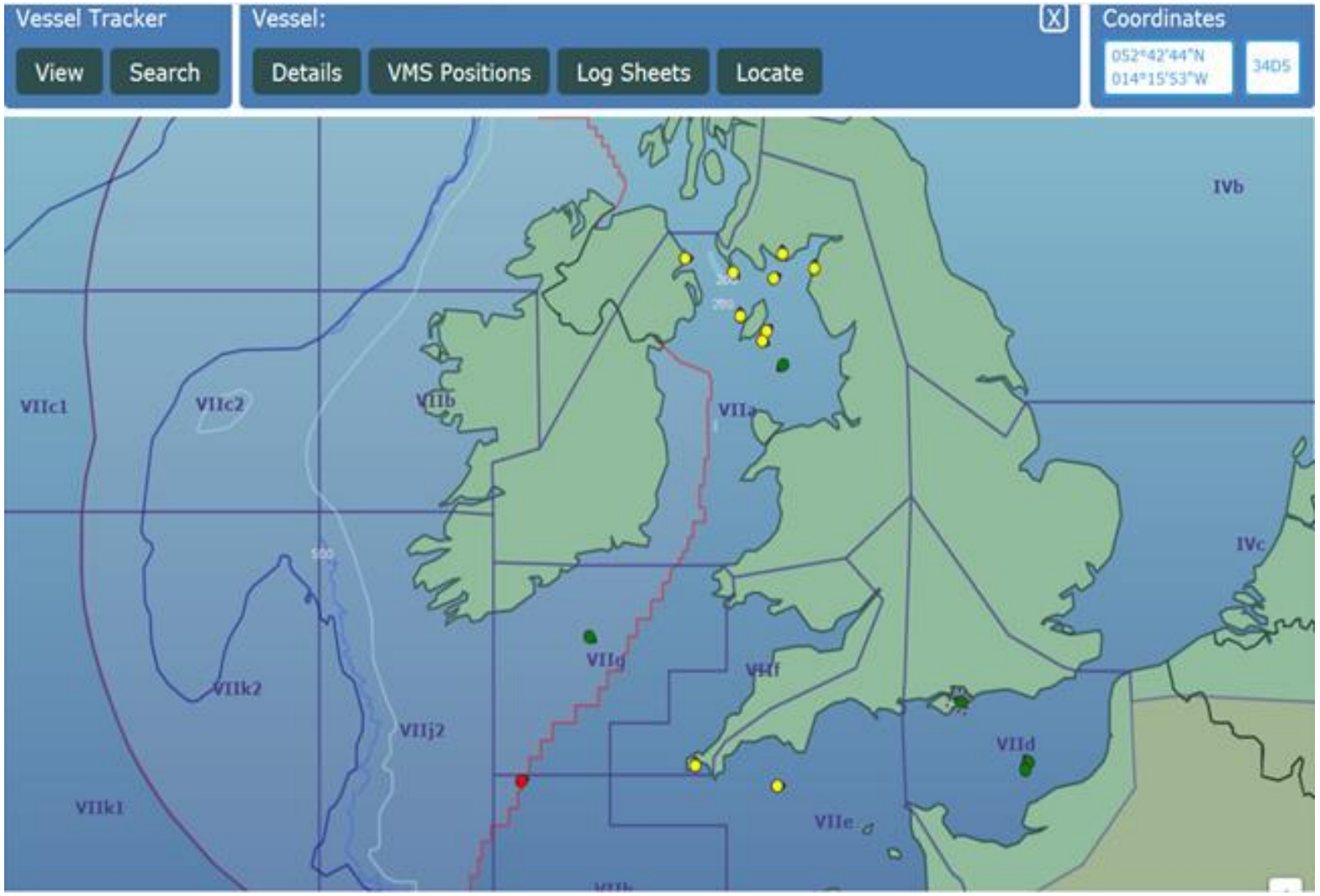
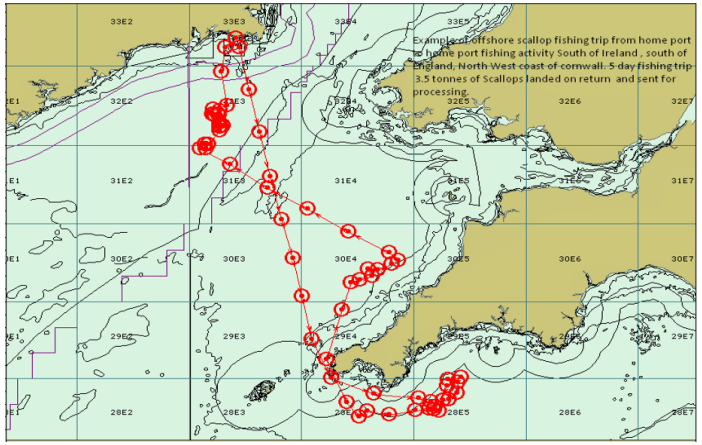
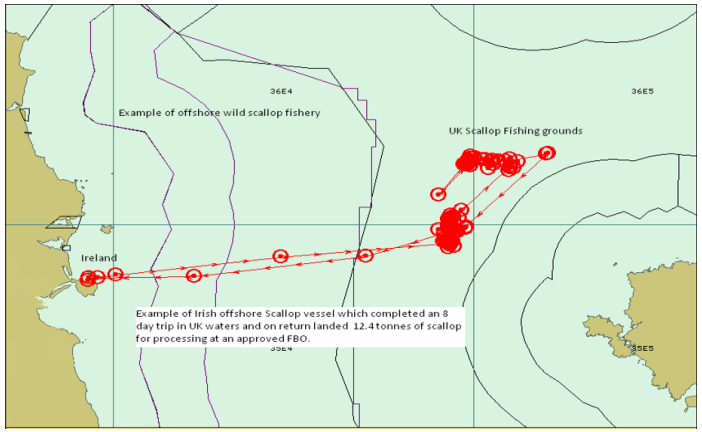
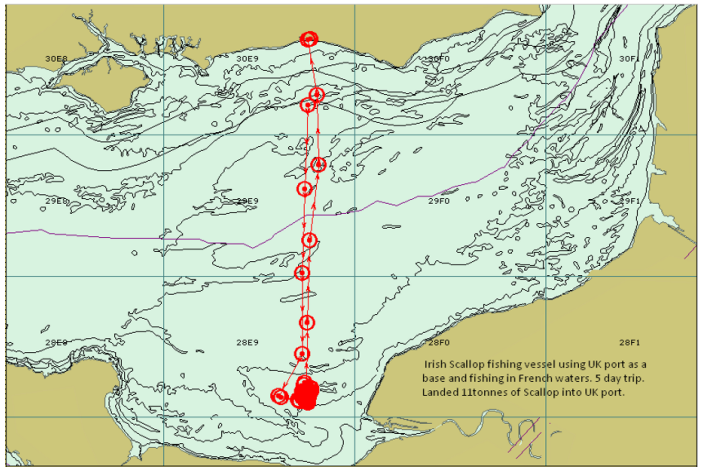


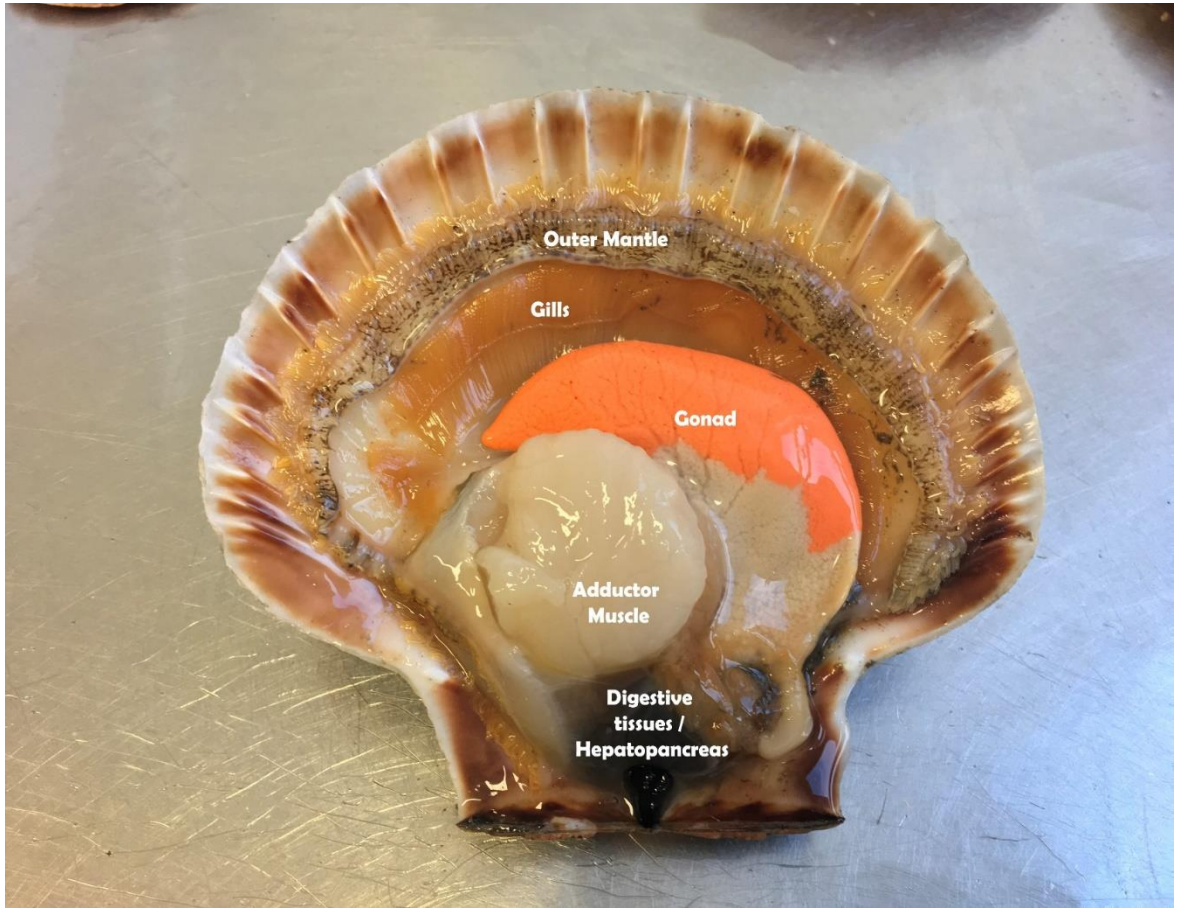
Figure 2: Chart showing various fishing boats from different member states reporting scallop fishing via VMS on a single day in November 2017. Irish (Green) UK (Yellow) and Spanish (Red) boats are shown fishing in the area.

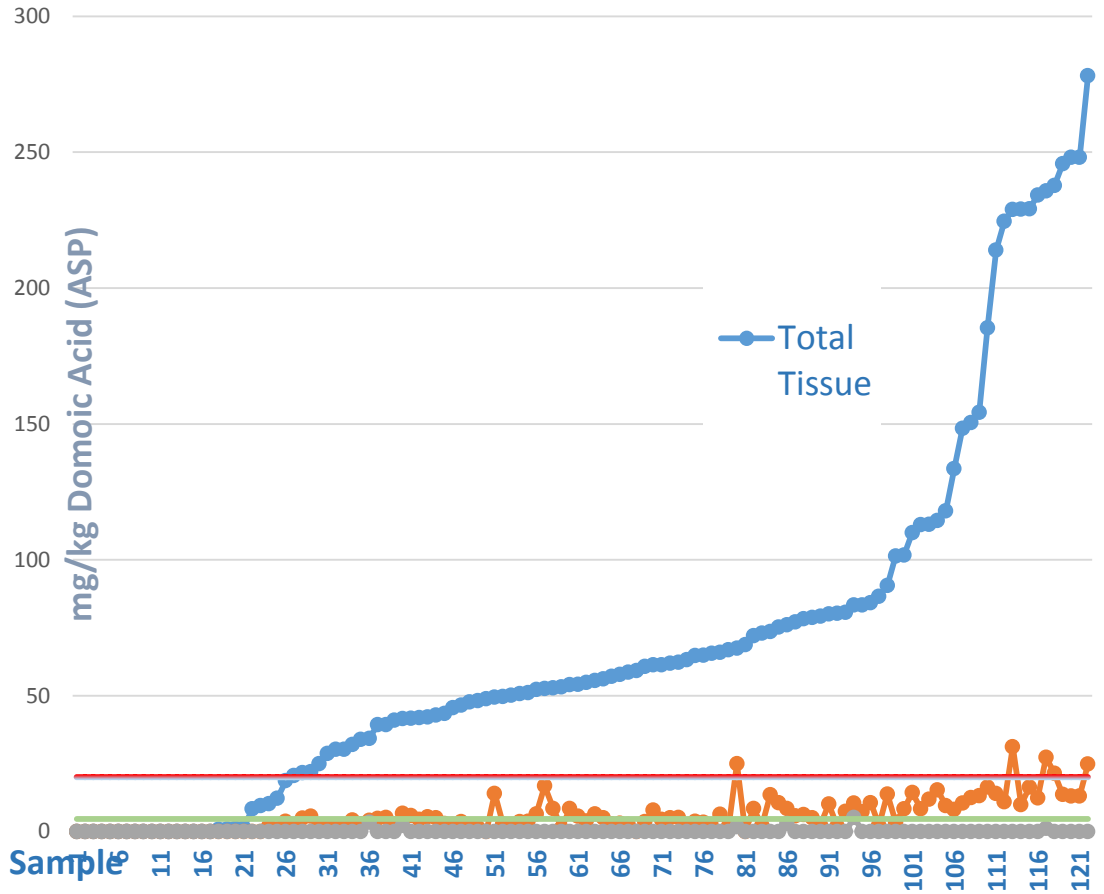






Three maps showing off-shore scallop fishing trips by Irish boats covering South of Ireland, South of England, Irish Sea and English Channel. These three trips amounted to 27 tonnes of Scallops landed in ports in UK and Ireland





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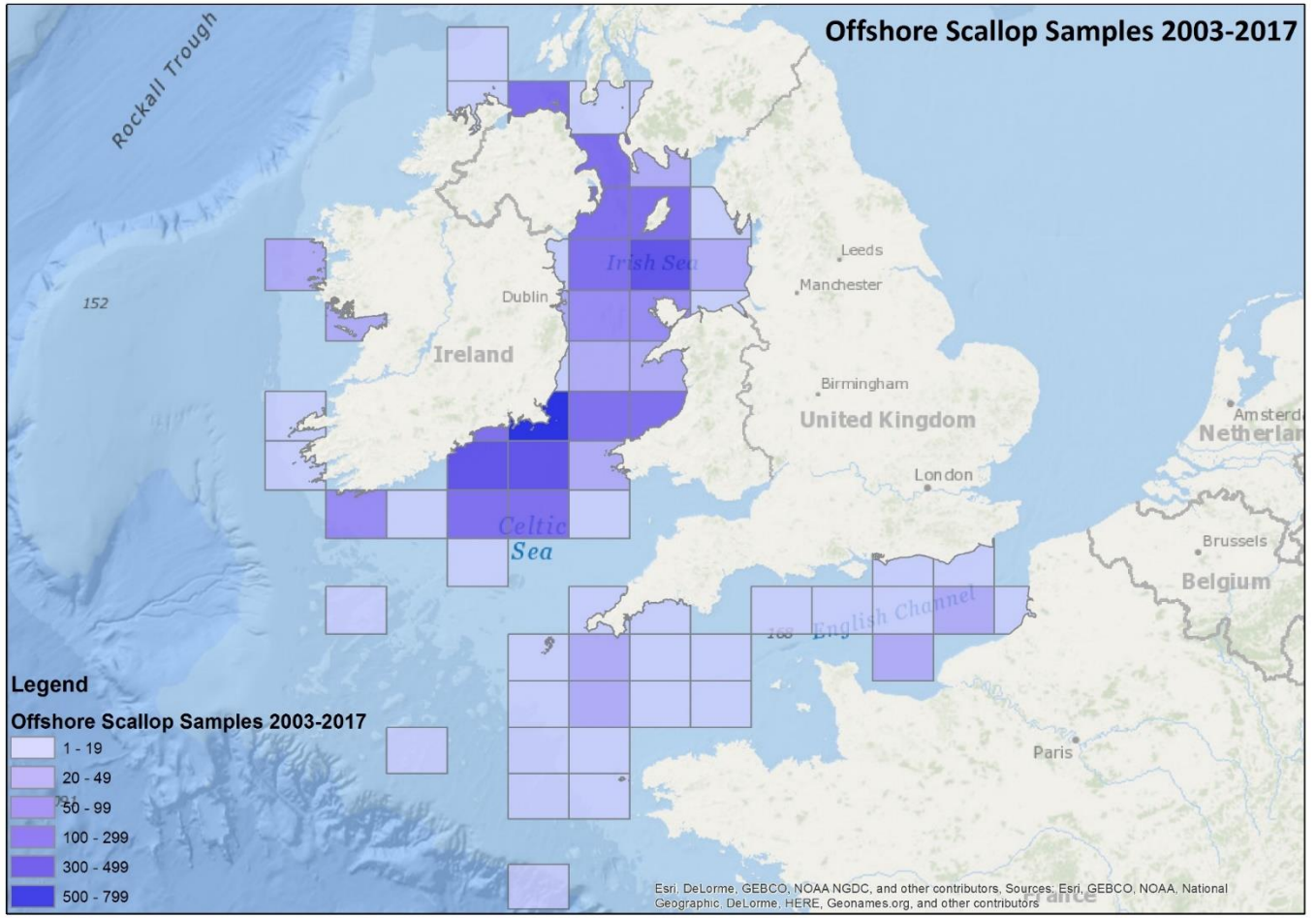


Figure 4: (a) Map showing the extent of offshore scallop samples tested as part of the Irish national monitoring programme between 2003 and 2017.

Scallop Biotoxin Research Study in EU Waters

- Scallops pose a particular difficulty due to the location of offshore fisheries.
- Fishery fleets harvest and landing in different juristictions, with ongoing movement after landing between member states
- Differing interpretation of the EU legislation.
- Complex partitioning of toxins.
- Variability within ICES rectangles used as offshore biotoxin management areas.

Proposal:

- Quantifying this variability to inform risk assessment of sampling requirement.
- Evaluation of suitability of ICES rectangles as management areas.
- Assessment of existing processing methods across EU member states.
- A network of competent authorities to combine monitoring data from offshore areas
- A jointly managed advisory system as part of improved risk management plans

Benaki Phytopathological Institute

the **Laboratory of Toxicological Control of Pesticides**
Department of Pesticides Control and Phytopharmacy

Dr K. Machera, Dr A. Termentzi, P. Konstantinidou

UNIVERSITY OF THE AEGEAN

School of Engineering
Department of Information & Communication Systems Engineering

Dr M. Maragoudakis

Research Idea:

Creation of a HRMS-based platform for risk assessment of food supplements containing botanicals

(Area: Risks/benefits of botanicals/herbals in food supplements)

Risk Assessment Research Assembly (RARA)
Utrecht, 7 February 2018

efsa
European Food Safety Authority

Benaki Phytopathological Institute

It is considered that the **"whole product"** is responsible for the therapeutic or toxicological action.

From
Botanical Extracts

Proof of Biological Activity
Risk Assessment
Quality assurance

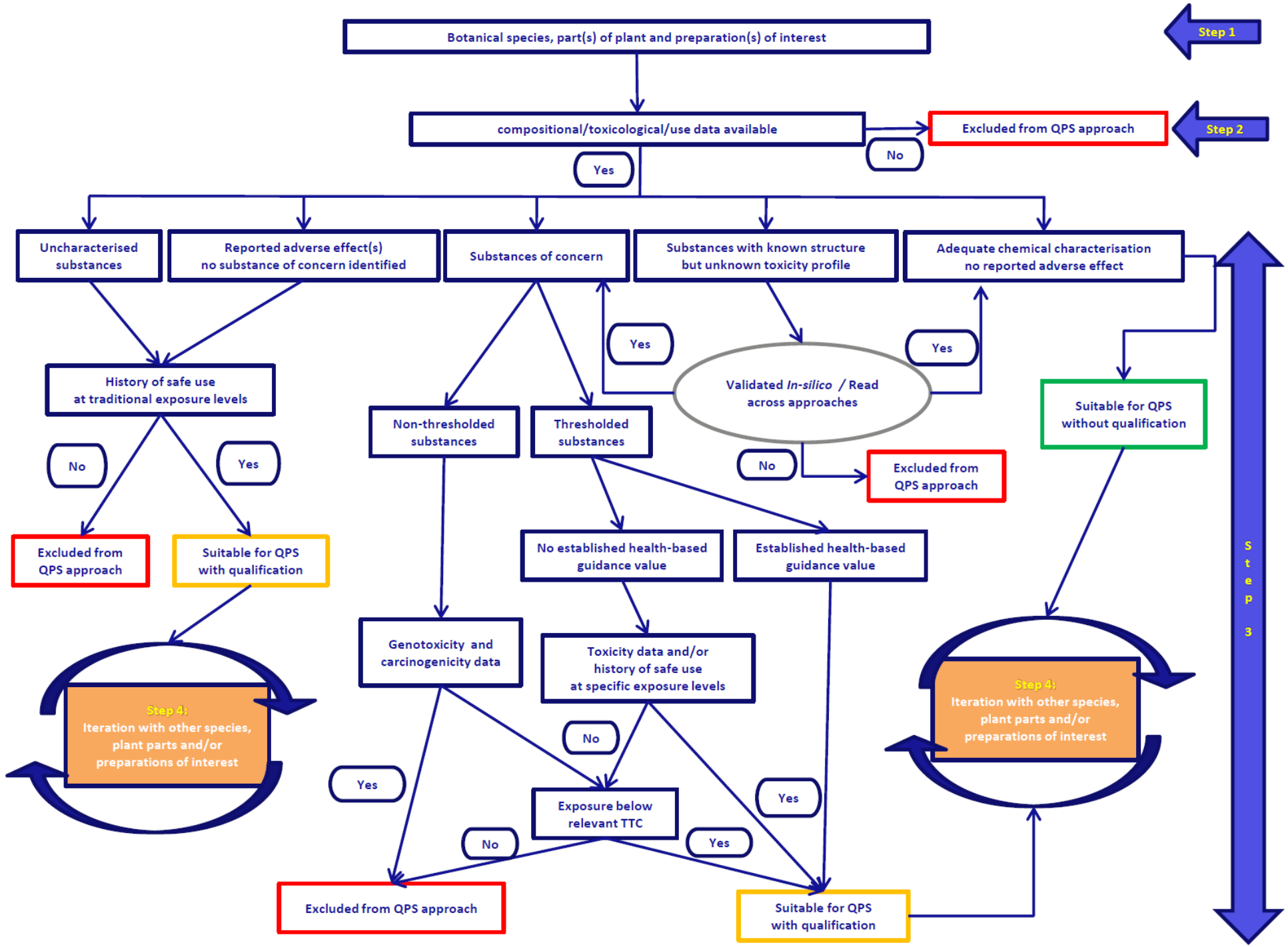
To
Food Supplements

- There is a large number of potential components that may affect the toxicity of other components.
- Plant products contain various antioxidant or pro-oxidant compounds that may affect the *in vivo* effects of other components in the same product

<u>However, toxicological characteristics of single substances cannot be neglected even if they are in a complex mixture.</u>

Very difficult to assess due to the following:

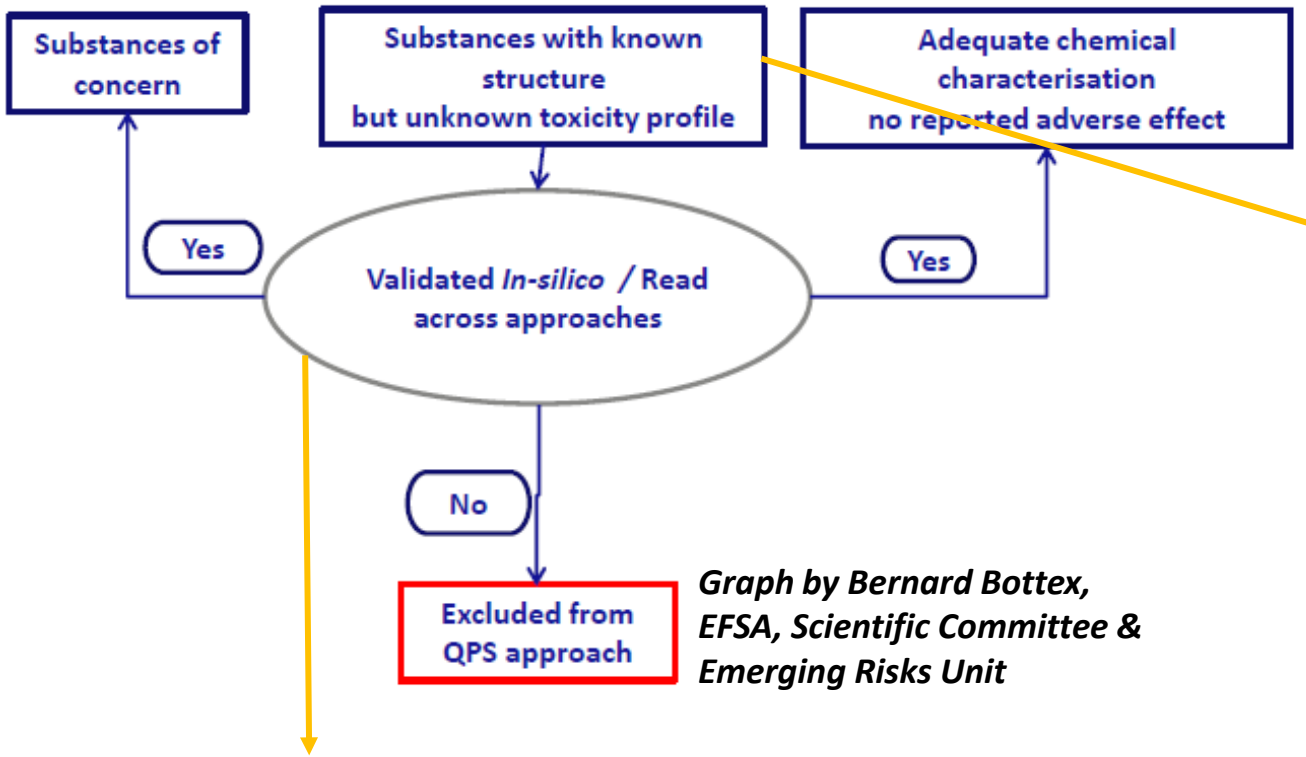
- Natural extracts are **extremely complicated mixtures** of secondary metabolites.
- This complexity is also enhanced by the **differentiation (mainly quantitative) of major and minor constituents** according to the botanical origin, time of harvest and way of extraction
- It is very difficult to have the **exact phytochemical profile** and characterization of all constituents in each extract



What do we Do *TODAY* for the *RISK ASSESSMENT* of *BOTANICALS*?

Decision tree by Bernard Bottex, EFSA, Scientific Committee & Emerging Risks Unit, in: Safety Assessment of Botanicals and Botanical Preparations, Overview of EFSA's activities, 2015

STEP 3



Graph by Bernard Bottex, EFSA, Scientific Committee & Emerging Risks Unit

Natural products extracts:

- Extremely **complicated** mixtures
- May include compounds of high risk in **low quantities**
- Content largely alternates by **season** and by geographical **origin**
- Quality control includes **specific molecul**es ignoring a large number of compounds that could be toxic

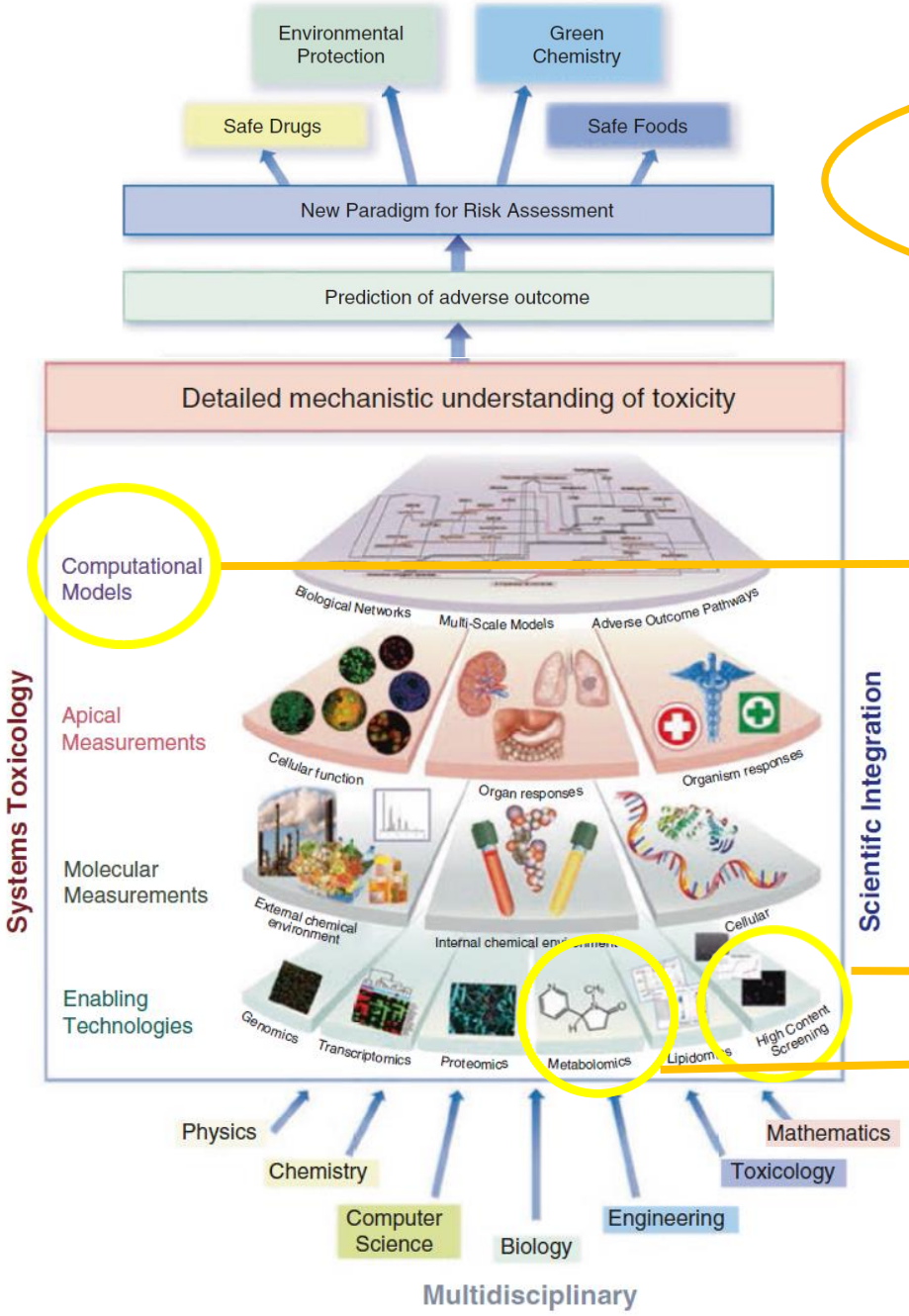
In silico approaches:

- They give predictions for **known structures**
- Most of the current platforms use **Bayesian networks**
- Integrated *in silico* platforms do predictions and proteochemometric modelling (PCM) for compounds pharmacology, potency, and affinity and adverse drug effects

Safety studies of herbal products are limited.

- Worldwide databases need to be established with full product monographs to ensure correct product identification;
- The full composition of products should be determined and compounds known to cause adverse effects flagged

The question of whether or not an herbal medicinal product is safe may be answered by using a multifocal approach.

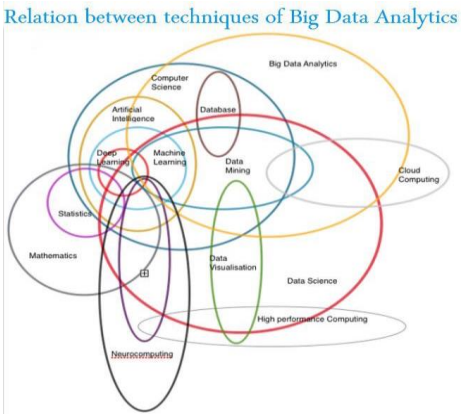


Development of a ready-to-use platform on which end users will be able to upload LC-MS/MS spectra and get feedback for the presence of compounds of concern (compounds bearing toxicophores) even at very low concentrations.

Novel Computational Models

Artificial Intelligence

Machine Learning



Dereplication Strategies Metabolomics

HRMS/MS spectrometry

Dereplication algorithms

Artwork by Samantha J. Elmhurst (www.livingart.org.uk)

Benaki
Phytopathological
Institute

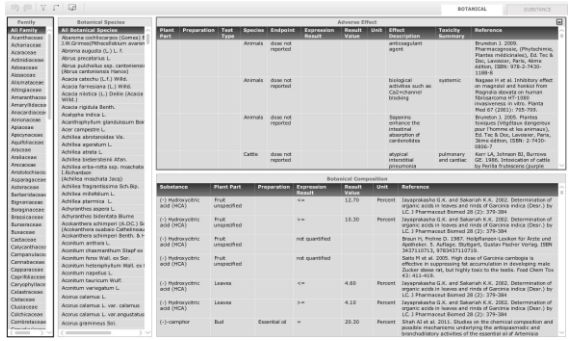
Workflow

A. Selection of approx. 100 toxic known real compounds (commercially available)

Selection of pure “flag” compounds from Tox databases that are well categorized as toxic and are highly likely to be met in natural extracts

efsa European Food Safety Authority

Compedium of Botanicals



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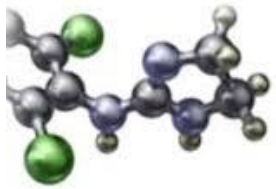
Toxic Exposome Database

C&L Inventory

ECHA
EUROPEAN CHEMICALS AGENCY
BOARD OF APPEAL



ChemIDplus
A TOXNET DATABASE

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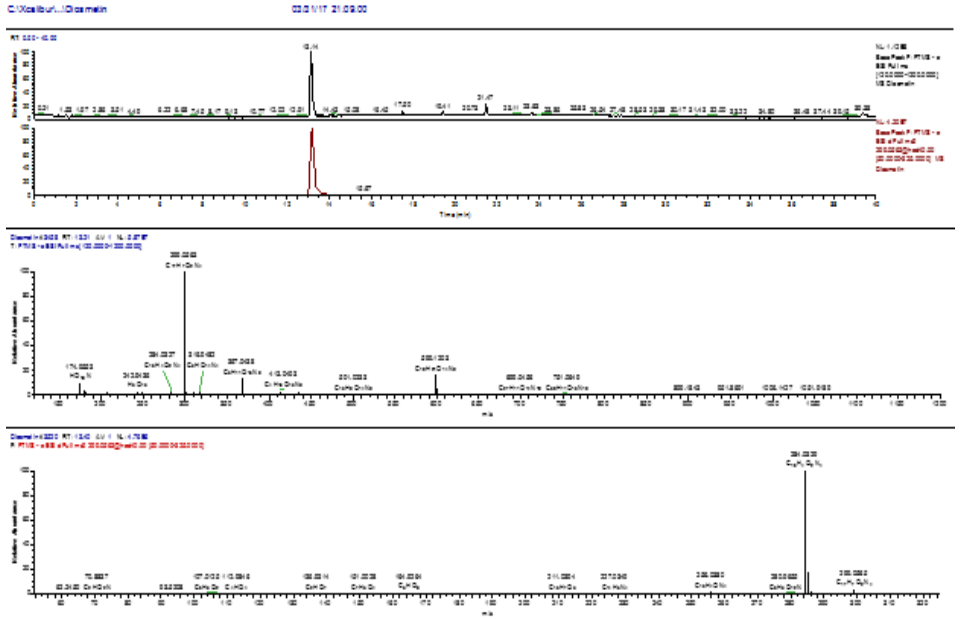
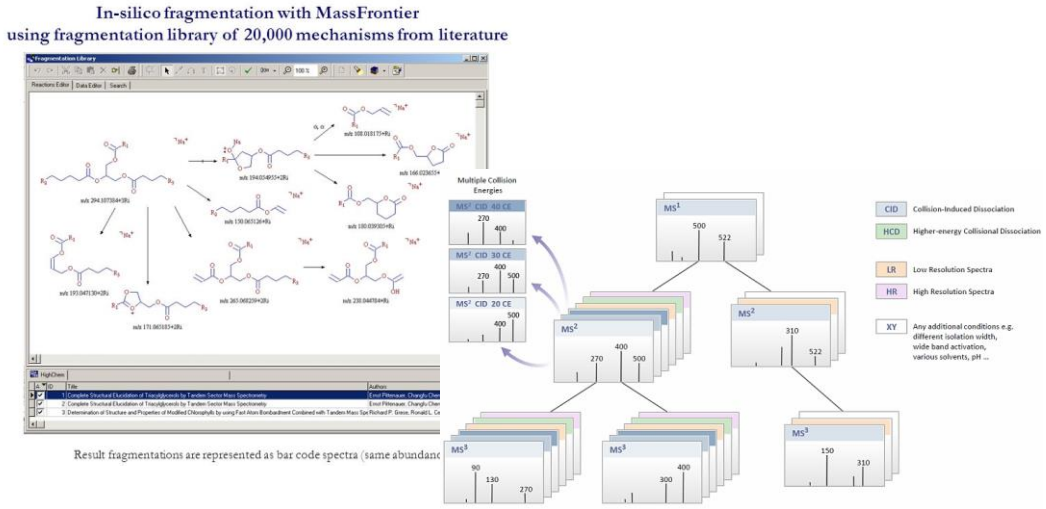
Phytopathological
Institute

Workflow

B. Recording of the UHPLC HRMS spectra and their MS/MS fragmentation patterns (real data)



C. Selection of molecules (from the Tox databases), most related to natural products and *in silico* fragmentation of those (MassFrontier, m/z Cloud).
→ Creation of Spectral Trees based on the real MS/MS



BRICKS for the Artificial Intelligence software building

Possibility of introduction of additional data from other databases

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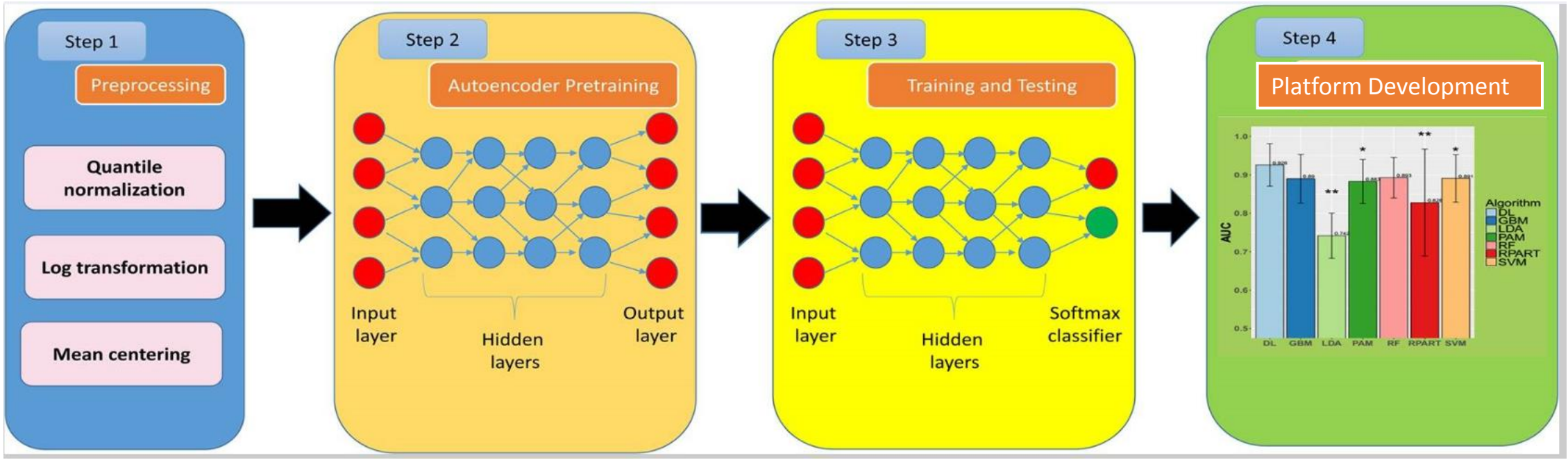
Workflow

D. Development of the software using machine learning/deep learning etc. that contains spectrometric features of real and in silico compound data.



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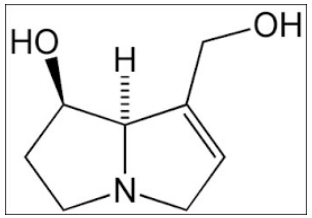
Workflow

E. Validation of the model by mixing known toxic compounds in commercial botanicals/food supplements

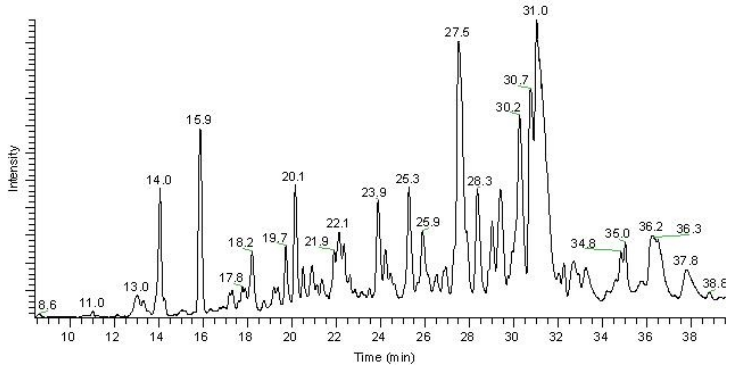
e.g.....

+



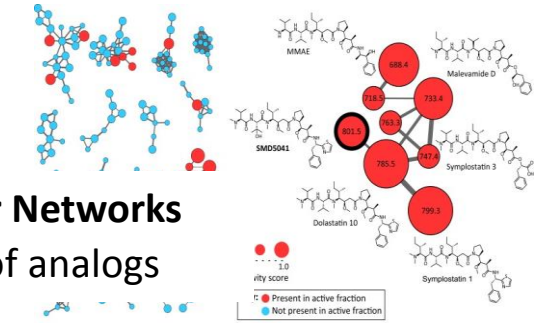
Pyrolizidine alkaloids

LCHRMS/MS data →



Raw data

Incorporation of **Molecular Networks** (GNPS) for identification of analogs



Toxicological alert

Impact

Expected Scientific Achievements:

- Exploration of **potential toxicity** of even **minor constituents** in **complex mixtures** with high confidence
- Development of an **open platform** for the **alert** of compounds bearing toxicophores in complex mixtures, continuously enriched
- The platform could also serve **QC purposes** for the raw materials and the final products
- Creation of a **LC-HRMS/MS compound database** of a great number of commercially and non-commercially available standards of **natural origin and high risk**.

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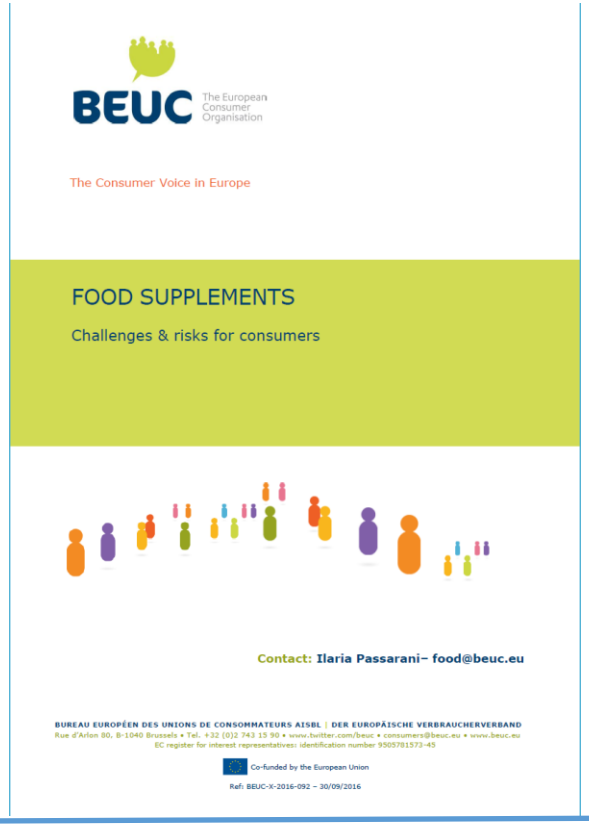
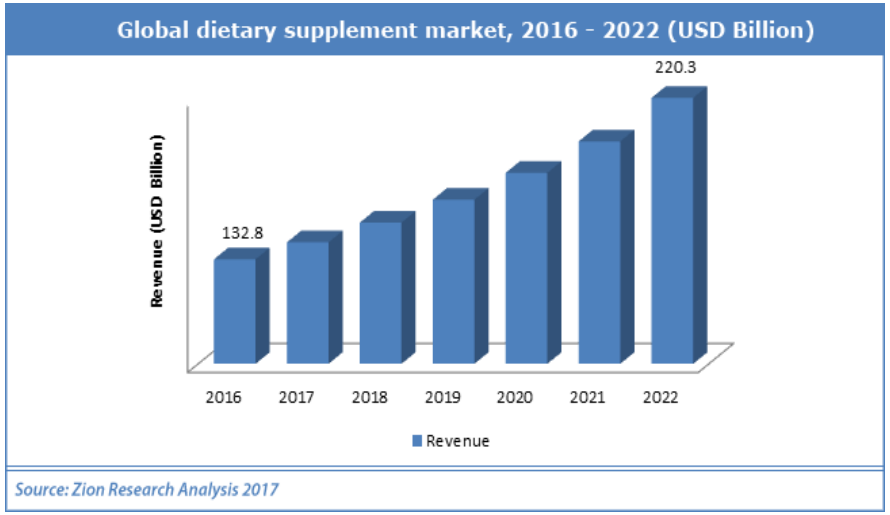
Impact



October 2016:
European Consumer Organization, BEUC
Issue article concerning Challenges & Risks for Consumers of Food Supplements
writing among the others for botanicals that:
“important risk factors should not be underestimated”
since plants and herbs may include toxicant and/or carcinogenic compounds.



The global market for food supplements continually grows
Expected to reach 220.3 B USD in 2022.

Health/Safety Consumers

Industry/ Economy

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What is needed?

Funding for:

- Purchase of **authentic standards** (pure natural products can be quite expensive, especially when exist in low concentrations in the mixtures)

- Networking for collaboration & recording **original LC-HRMS & MS/MS spectra**

Adaptation of a common protocol for recording all HRMS & MS/MS data → specific instruments need to be recruited, in our case **Orbitrap platforms**

- Development of bioinformating tools and **computers for big data analysis** can be quite expensive

- **Experts:** toxicologists, natural product chemists, analysts, bio-informaticians, computer engineers are needed for the implementation

Possibly the main support should be by public funding as this project is of the great interest of public safety – National Authorities will be the ultimate beneficiaries

Integrative approaches for developing safety assessment methodologies of botanicals

Dr. Liliana Vargas-Murga (BIOTHANI), Prof. Ivonne Rietjens (WUR-TOX)
lsvargas@biothani.com

RESEARCH IDEA

Safety assessment and risk-benefit assessment of botanical and botanical preparations using new aproaches and methodologies, based on Aguaymanto fruit and its preparations (AFP).
The research idea specific objectives are:
i. to analyse the chemical composition of AFP applying a wide range of complementary analytical methods, as a basis for the risk assessment, ii. to assess the risk of AFP using the MOA, the MOE and the TTC concepts by means of *in silico*, and *in vitro* including PBK modelling to facilitate read across, iii. to evaluate AFP on the basis of the matrix effect concept utilising PBK and PBD models, iv. to evaluate the risk-benefit of AFP, using Disability Adjusted Live Year model, v. to use array based characterisation of the cellular pattern of kinase activities (the kinome) and related signalling pathways in the risk-benefit assessment of AFP.
These strategies are focused on toxicity pathways, taking into account a case-by-case approach, and in line with the promotion of alternative methods to reduce animal testing.

IMPACT/BENEFIT

New knowledge and methodologies at European level in order to harmonise evidence- and risk-based approaches of botanicals and its preparations.
Help boost innovation in both public and private sectors and significantly improve the robutness and efficiency of risk assessment.
Support European and international initiatives (EU, WHO, EPA, etc.).
Accelerate the transition to a sustainable European bioeconomy.

PARTNERS /EXPERTISE

Research center with similar and complementary Knowledge and expertise in safety and risk-benefit assessment.
Industries with interest in developing methodologies for the safety assessment.
Industries with interest in developing novel product with safe and potential health benefits.

NEED OF PUBLIC FUNDING

Botanical risk assessment is one of the food safety risk assessment areas of priority identified by Member States and EFSA.
Botanical safety and risk-benefit assessment is presently underdeveloped.
EU will ensure the safe use of botanical and its preparations.

European Food Safety Authority

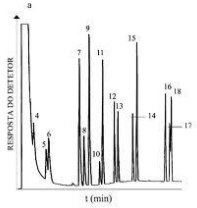
feb '18 Risk Assessment Research Assembly

INTEGRATIVE APPROACHES FOR DEVELOPING SAFETY ASSESSMENT METHODOLOGIES OF BOTANICALS

Dr. Liliana Vargas-Murga (BIOTHANI)
Prof. Ivonne Rietjens (WUR-TOX)

RESEARCH IDEA

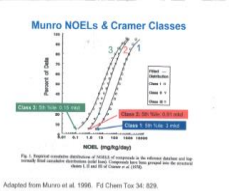
1.CHEMICAL ANALYSIS



Chromatogram

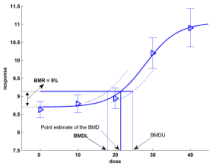
UPLC, HPLC-DAD, LC-MS

2. RISK ASSESSMENT



TTC concept

In silico & in vitro studies, MOE, MOA, TTC concepts

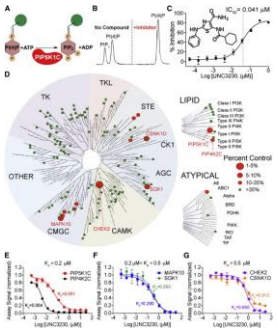


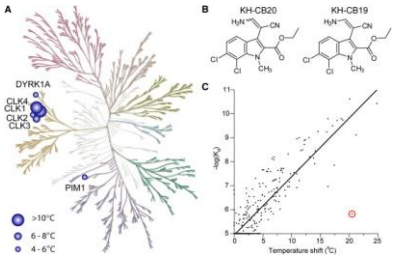
MOE = BMDL/EDI

Aguaymanto fruits and its preparations

5. KINOME ANALYSIS AS A NOVEL TOOL IN RISK BENEFIT ASSESSMENT

PamChip® microarrays PamGene's arrays



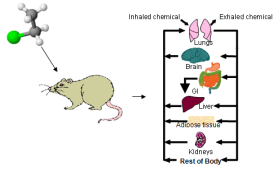


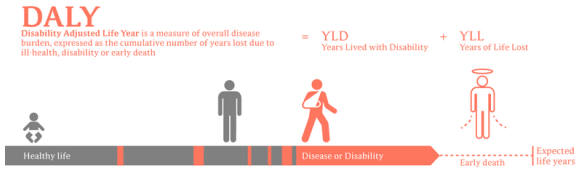
4. RISK-BENEFIT EVALUATION

DALY model

3. EVALUATION OF THE MATRIX EFFECT

PBK & PBD models





DALY = YLD + YLL

IMPACT/BENEFIT OF THE RESEARCH IDEA

- IMPACT:
  - Harmonised methodologies
  - Support to European and international initiatives
  - Development of a sustainable European bioeconomy
- BENEFICIARIES
  - Consumers (safe products)
  - Industry (novel products)

PARTNERS/EXPERTISE

- PARTNERS:
  - Research centers
  - Industries
- EXPERTISE
  - Complementary to the safety and risk-benefit assessment

NEED OF PUBLIC FUNDING

- Food safety risk assessment areas of priority
- Ensure consumer safety at European level
- Botanical risk assessment science is presently underdeveloped

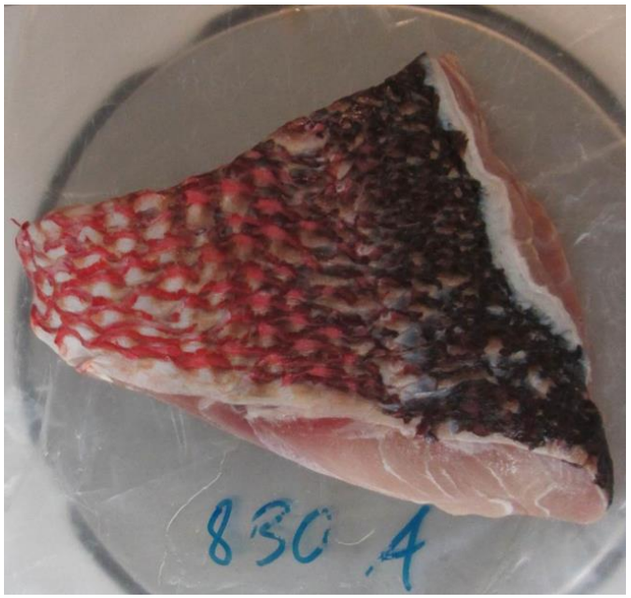
CONTACT DETAILS

THANK YOU AND ANY QUESTIONS!!

Dr. Liliana Vargas-Murga (BIOTHANI)

Prof. Ivonne Rietjens (WUR-TOX)

GERMAN FEDERAL INSTITUTE FOR RISK ASSESSMENT



15 YEARS
Science in the Service of Humanity

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Bundesinstitut für Risikobewertung

Project Idea

Detection of Ciguatoxins in Fish

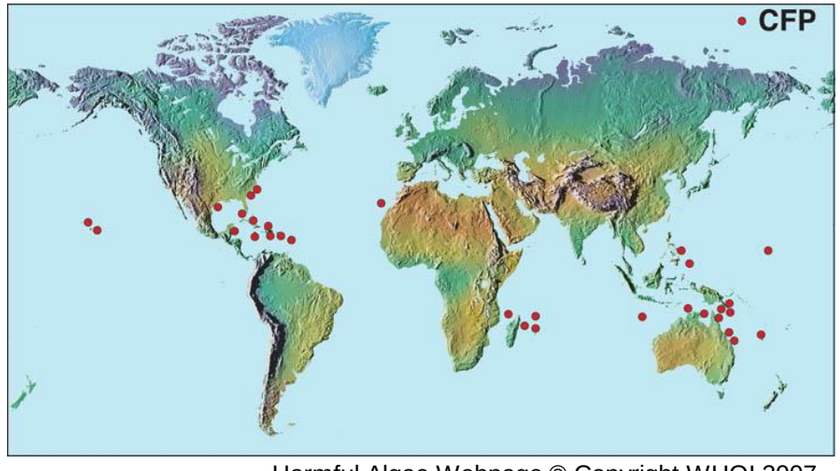
Integrated approach for Sreening and Confirmation Methods

Angelika Preiß-Weigert

Ciguatera Fish Poisoning (CFP) caused by Ciguatoxins (CTXs)

CFP - Common food borne disease

10.000 - 50.000 cases worldwide per year



Harmful Algae Webpage © Copyright WHOI 2007
http://www.whoi.edu/redtide/page.do?pid=16702&tid=542&cid=47588&c=3

Serious symptoms

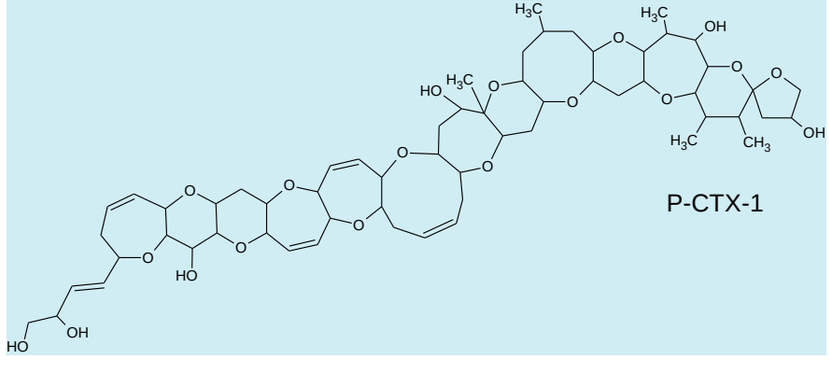
- ✓ gastrointestinal
- ✓ neurological (highly specific)
- ✓ cardiovascular symptoms up to fatality

Occurrence of CFP

- ✓ in tropical regions since a long time
- ✓ In fish importing countries since 10 years due to global trade

Methods for Detection of CTXs

- ✓ Few laboratories in concerned areas apply different methods (USA, Japan, New Zealand, EURL Marine Biotoxins Vigo/ES)
- ✓ No Harmonized or validated methods available



International Activities

FAO 2014 climate change causes increase of dinoflagellates producing CTX precursors

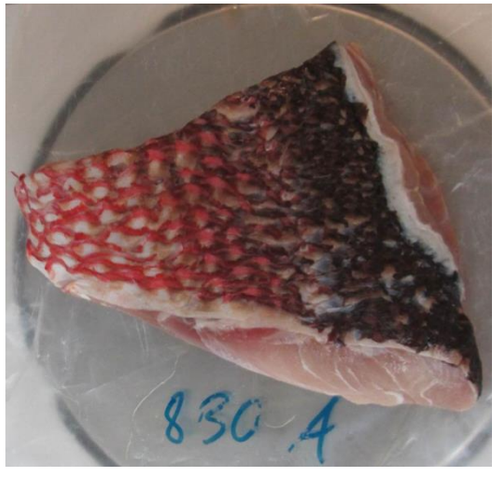
EFSA 2015 **EuroCigua**: 4 years project co-funded by EFSA/AECOSAN to determine incidence in Europe and epidemiological incident cases, assess pressence of CTXs in food and environment in Europe

RISK CHARACTERIZATION OF CIGUATERA FOOD POISONING IN EUROPE
GP/EFSA/AFSCO/2015/03

EuroCigua

CCCF 2017 addressed the need of validated methods for the detection of CTXs endorsed CTXs to be included in the „Priority List .. for evaluation by JECFA“

Aim of Project Idea



Protection of Consumer‘s Health against CFP by

Strengthening analysis of CTX in fish

- Improving reference standard availability
- Validation of a screening method Neuroblastoma (N2a) Assay
- Validation of a confirmatory method applying (HR)MS

Promotion of Animal Welfare aspects by

Replacement of Mouse Bioassay

Work Programme designed in 4 Modules

Module	Purpose	Activity	Transfer of Knowledge and Materials
I	CTX Screening	N2a Assay Implementation	**Expert Meetings**
II	Reference Standards	Availability Isolation from fish samples	
III	CTX Screening	N2a Assay Collaborative Validation	
IV	CTX Confirmation	Mass Spectrometry LC-MS/MS LC-(HR)MS Implementation Collaborative Validation	

Project Proponents

Ana Gago
European Reference Laboratory for Marine Biotoxins
University of Vigo/Spain, Department of Analytical and Food Chemistry
Leader of SA4 in EuroCigua

Marina Nicolas
French agency for food, environmental and occupational health safety, Laboratory for Food safety - site of Maisons-Alfort, France
NRL for Marine Biotoxins

Carmela Dell'Aversano
University of Naples Federico II, Italy, Department of Pharma
Acknowledged expert for mass spectrometric measurements of marine biotoxins

Ann Abraham
U.S. Food and Drug Administration, Chemical Hazards Science Branch, Center for Food Safety and Applied Nutrition, Office of Food Safety, Dauphin Island, USA
Division of Seafood Science & Technology

GERMAN FEDERAL INSTITUTE FOR RISK ASSESSMENT

15 YEARS
Science in the Service of Humanity

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Thank you for your attention

Angelika Preiß-Weigert

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FOOD PACKAGING CONTAMINANTS IN BABY AND INFANT FOOD: ANALYSIS OF PACKAGING MATERIALS AND FOOD

R. Sendón, P. Paseiro, A. Rodríguez Bernaldo de Quirós

Department of Analytical Chemistry, Nutrition and Food Science, Faculty of Pharmacy, University of Santiago de Compostela (Spain)
E-mails: raquel.sendon@usc.es, perfecto.paseiro@usc.es, ana.rodriguez.bernaldo@usc.es

State of the art

FOOD PACKAGING

RISK EVALUATIONS

https://www.foodmanufacture.co.uk/Article/2013/08/29/Tracking-Premier-Foods-businesses-almost-impossible-finance-firm

Food Contact Materials (FCM)

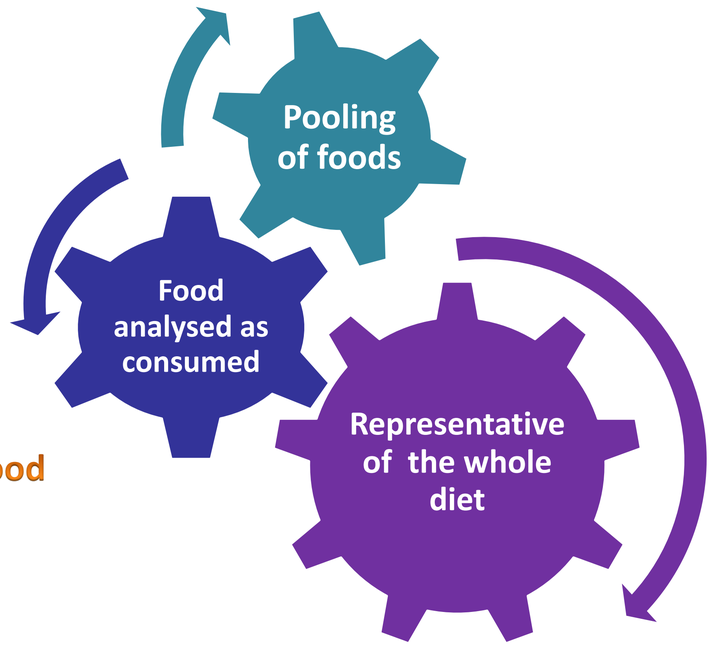
Exposure

Estimation of Dietary Exposure

$$Ei = \sum_{k=1}^{n} \frac{C_{i,k} \times L_k}{BW_1}$$

- Concentration of chemicals in food
- Consumption data

TOTAL DIET STUDY (TDS) APPROACH



Ongoing research

EXPOSURE TO CHEMICALS FROM FOOD PACKAGING. STUDY AND EVALUATION OF NEW-EMERGING CONTAMINANTS

PROPOSED METHODOLOGY BASED ON A TDS

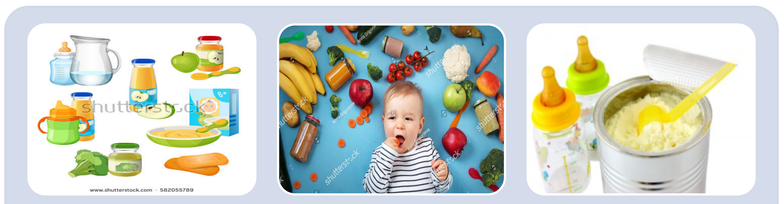
- Packaging materials: Screening method to identify potential migrants
- Sampling: Pooling foods
- Analysis of samples
- Exposure estimation

https://pixabay.com/es/collage-fideos-pasta-alimentos-1580853/

http://www.avensonline.org/blog/packed-food-health-issues.html

Project funded by “Ministerio de Economía y Competitividad, Agencia Estatal de Investigación and by "Fondo Europeo de Desarrollo Regional (FEDER), Ref. No. AGL2015-69609-P “MIGRAEXPO”. (MINECO/FEDER,UE).

Chemical Contaminants in Infant and Baby Food: Improving the Safety of Packaging Materials



https://www.freepik.es/index.php?goto=2&isCat=1&searchform=1&k=logo&order=2&only=1

http://enfamilia.aeped.es/vida-sana/preparando-biberon

Migration from FCM

Dietary Exposure

Considerations
- Lifestages
- Sensitive population
- ….

ISSUES TO BE ADDRESED

Emerging contaminants

Components from coatings, printing inks, NIAS, ….

Harmonised methodologies

Exposure to multiple chemicals

Beneficiaries
- **Risk Managers:** Public Health Agencies, Food Safety Organizations, …

Impact
- Limited data about chemicals from food packaging exposure in infants
- Emerging contaminants have not been evaluated

Partners
- Expertise on food packaging materials, on risk assessment and food chemical analysis

FOOD PACKAGING CONTAMINANTS IN BABY AND INFANT FOOD: ANALYSIS OF PACKAGING MATERIALS AND FOOD

Raquel Sendón, Perfecto Paseiro Losada and Ana Rodríguez Bernaldo de Quirós

Utrecht, 7 February 2018

FOOD PACKAGING

RISK EVALUATIONS

https://www.foodmanufacture.co.uk/Article/2013/08/29/Tracking-Premier-Foods-businesses-almost-impossible-finance-firm

Food contact materials (FCM)

Exposure

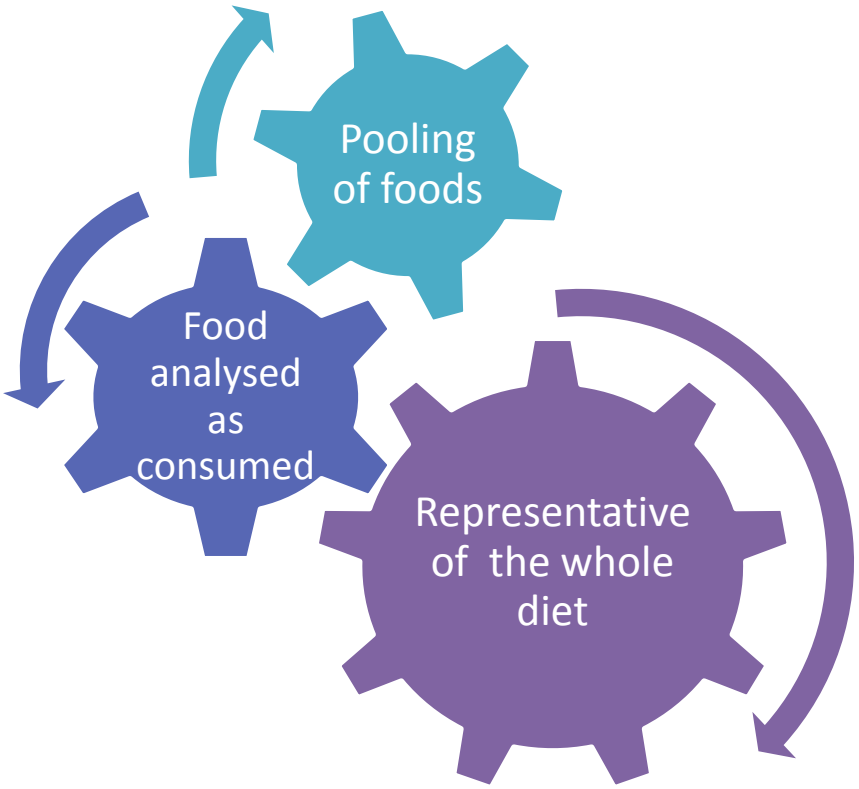
$$Ei = \sum_{k=1}^{n} \frac{C_{i,k} \; x \; L_k}{BW_1}$$

Estimation of dietary exposure

- Concentration of chemicals in food
- Consumption data

TOTAL DIET STUDY (TDS) APPROACH: ESTIMATING DIETARY EXPOSURE

ESSENTIAL STEPS OF A TDS



- **Valuable and reliable cost effective tool**
- **Complementary approach to food control and monitoring programs**

ONGOING RESEARCH

feb '18 Risk Assessment Research Assembly

Exposure to chemicals from food packaging. Study and evaluation of new-emerging contaminants

PROPOSED METHODOLOGY BASED ON A TDS

- Packaging materials: Screening method to identify potential migrants
- Sampling: Pooling foods
- Analysis of samples
- Exposure estimation

https://pixabay.com/es/collage-fideos-pasta-alimentos-1580851/

http://www.avensonline.org/blog/packed-food-health-issues.html

Project funded by "Ministerio de Economía y Competitividad, Agencia Estatal de Investigación and by "Fondo Europeo de Desarrollo Regional (FEDER), Ref.No. AGL2015-69609-P "MIGRAEXPO". (MINECO/FEDER,UE).

CHEMICAL CONTAMINANTS IN INFANT AND BABY FOOD: IMPROVING THE SAFETY OF PACKAGING MATERIALS

Migration from FCM

Dietary exposure

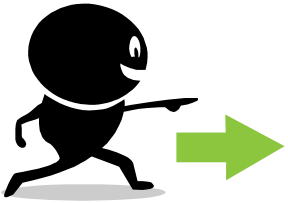
https://www.freepik.es/index.php?goto=2&isCat=1&searchform=1&k=logo&order=2&onlyf=1

Considerations

- Lifestages
- Sensitive population
- Highly exposed and susceptible groups

Utrecht, 7 February 2018

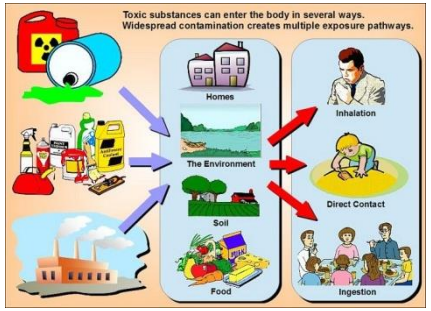
CHEMICAL CONTAMINANTS IN INFANT AND BABY FOOD: IMPROVING THE SAFETY OF PACKAGING MATERIALS



ISSUES TO BE ADDRESSED

- Harmonised methodologies
- Emerging contaminants
- Exposure to multiple chemicals

Non-intentionally added substances (NIAS)
Components from coatings, printing inks,
.....



http://experttoxicologist.com/newsite/toxicology-toxic-exposures.aspx?cln=1

CHEMICAL CONTAMINANTS IN INFANT AND BABY FOOD: IMPROVING THE SAFETY OF PACKAGING MATERIALS

Beneficiares

- **Risk Managers:** Public Health Agencies, Food Safety Organizations, …

Impact

- Limited data about chemicals from food packaging exposure in infants
- Emerging contaminants have not been evaluated

Partners

- Expertise on food packaging materials, on risk assessment and food chemical analysis

USC
UNIVERSIDADE DE SANTIAGO DE COMPOSTELA

Risk Assessment Research Assembly
feb '18

BIOTEST FOR TOXICITY EVALUATION OF MIXTURES OF CONTAMINANTS FROM EMERGING FOOD PACKAGING MATERIALS

Universidad Zaragoza

Marga Aznar, Cristina Nerín
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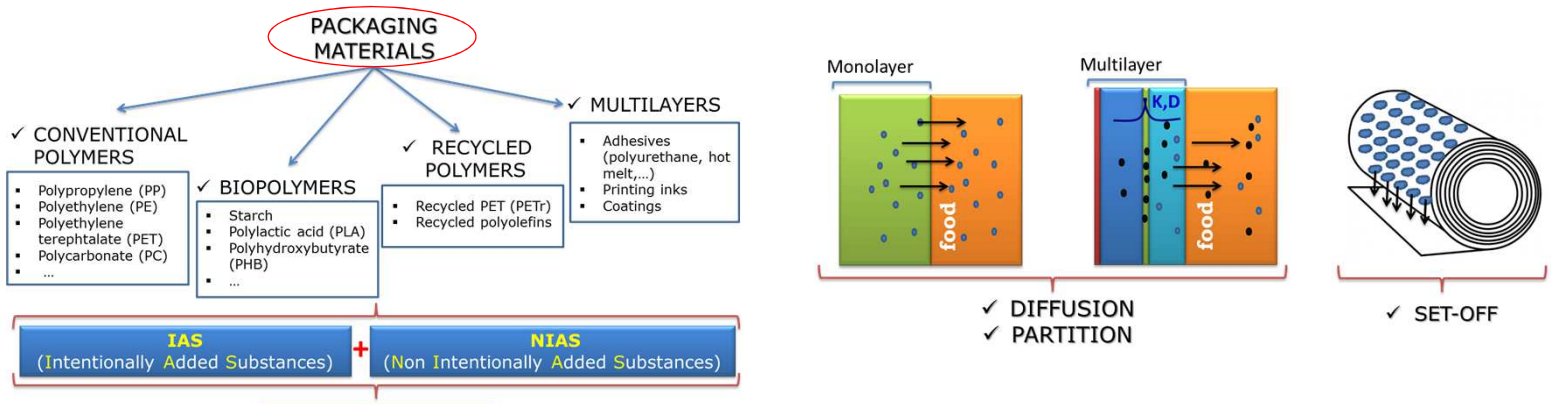
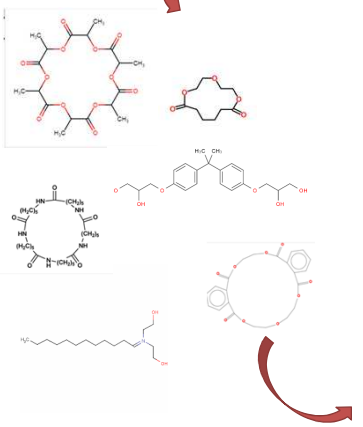
marga@unizar.es; cnerin@unizar.es

Instituto Universitario de Investigación de Ingeniería de Aragón Universidad Zaragoza



EMERGING CONTAMINANTS → **POTENTIAL RISK** → **MIGRATION TO FOOD**

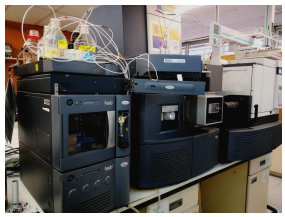
WHAT WE DO



1. Migration test

2. Identification
- ✓ GC-MS (EI)
- ✓ APGC-HRMS
- ✓ UPLC-HRMS

3. Quantification
- ✓ GC-MS
- ✓ UPLC-MS/MS



RISK ASSESMENT — One by one
- ✓ European Legislation
- ✓ National Legislation
- ✓ EFSA opinion
- ✓ CRAMER rules (TTC)

- ✓ Time consuming
- ✓ Unknown effects of mixtures
- ✓ Expensive

PROPOSAL

Evaluation of the **migrants mixture** toxicity instead of an individual evaluation of each component.

Collaboration

Toxicity research :
- ✓ Development of **biotests** able to be applied to mixtures of compounds

Analytical research:
- ✓ Identification of compounds
- ✓ Quantification of compounds

BENEFIT

Improve risk assesment in food packaging materials

BENEFICIARIES

- **Packaging companies**
- **Consumers**
- **Food companies**

Acknowledgements: Projects AGL2015-67362-P from MINECO (Spain) and FEDER funds. Authors would like to acknowledge the use of Servicio General de Apoyo a la Investigación-SAI, Universidad de Zaragoza

feb '18 Risk Assessment Research Assembly

BIOTEST FOR TOXICITY EVALUATION OF MIXTURES OF CONTAMINANTS FROM EMERGING FOOD PACKAGING MATERIALS

Marga Aznar, Cristina Nerín

Department of Analytical Chemistry, I3A, University of Zaragoza (Spain)

feb '18 Risk Assessment Research Assembly

PACKAGING MATERIALS

✓ CONVENTIONAL POLYMERS

- Polypropylene (PP)
- Polyethylene (PE)
- Polyethylene terephtalate (PET)
- Polycarbonate (PC)
- …

✓ BIOPOLYMERS

- Starch
- Polylactic acid (PLA)
- Polyhydroxybutyrate (PHB)
- …

✓ RECYCLED POLYMERS

- Recycled PET (PETr)
- Recycled polyolefins

✓ MULTILAYERS

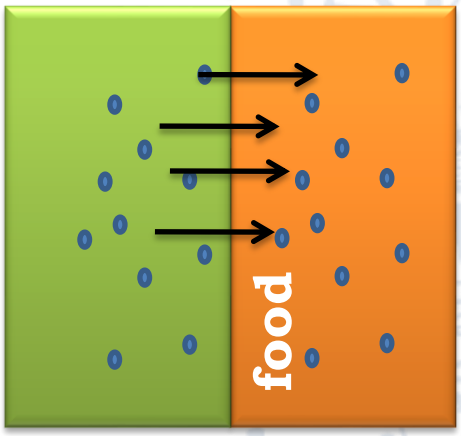
- Adhesives (polyurethane, hot melt,…)
- Printing inks
- Coatings

IAS (Intentionally Added Substances) + **NIAS** (Non Intentionally Added Substances)

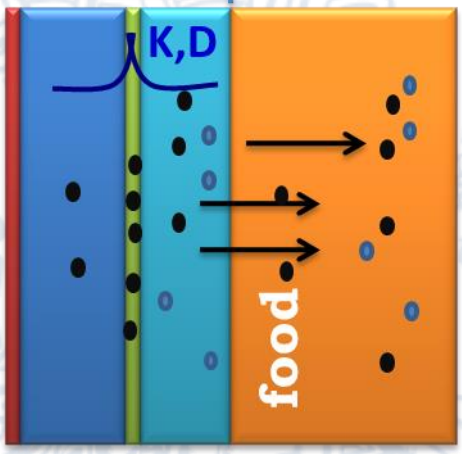
EMERGING CONTAMINANTS

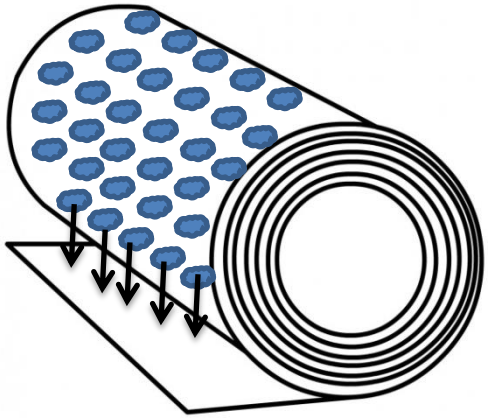
POTENTIAL RISK

Monolayer



Multilayer



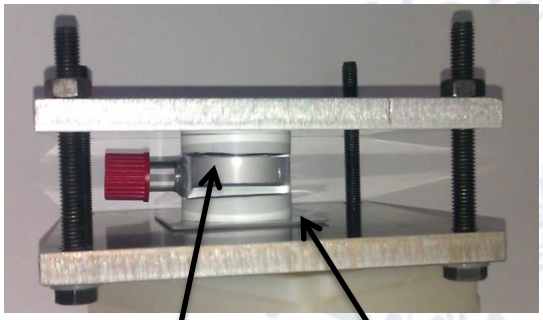


- ✓ DIFFUSION
- ✓ PARTITION
- ✓ SET-OFF

MIGRATION TO FOOD

WHAT WE DO

1. Migration test



Food simulant Polymer

2. Identification

- ✓ GC-MS (EI)
- ✓ APGC-HRMS
- ✓ UPLC-HRMS

3. Quantification

- ✓ GC-MS
- ✓ UPLC-MS/MS

RISK ASSESMENT

One by one

- ✓ European Legislation
- ✓ National Legislation
- ✓ EFSA opinion
- ✓ CRAMER rules (TTC)

- ✓ **Time consuming**
- ✓ **Unknown effects of mixtures**
- ✓ **Expensive**

WHAT WE HAVE FOUND

Example 1: **Non-volatile** compounds detected in migration from $[PET//PA//PP]_{FCS}$ multilayer material

	rt mass	Adduct	Candidate MF	QS	EtOH 95% µg/Kg	EtOH 10% µg/Kg	HAc 3% µg/Kg	SML mg/Kg	Remarks
1	2.52 249.1589	$[MNa]^+$	Caprolactam oligomer (n=2) $C_{12}H_{22}N_2O_2$	1	271 ± 40	<LOD	<LOD		Polyamide oligomer
2	2.74 114.0918	$[MH]^+$	Caprolactam✓✓ $C_6H_{11}NO$	1	69.9 ±14.6	129 ±10	122 ±29	15	Polyamide oligomer
3	3.25 362.2425	$[MNa]^+$	Caprolactam oligomer (n=3) $C_{18}H_{33}N_3O_3$	1	2600 ± 280	<LOD	<LOD		Polyamide oligomer
4	3.72 475.3268	$[MNa]^+$	Caprolactam oligomer (n=4) $C_{24}H_{44}N_4O_4$	1	3450 ± 317	<LOD	<LOD		Polyamide oligomer
5	4.05 588.4082	$[MNa]^+$	Caprolactam oligomer (n=5) $C_{30}H_{55}N_5O_5$	1	169 ± 34	<LOD	<LOD		Polyamide oligomer
6	4.31 259.0588	$[MNa]^+$	PA-DEG $C_{12}H_{12}O_5$	2	779 ± 142	240 ± 28	222 ± 39		Polyurethane oligomer
7	5.22 495.1267	$[MNa]^+$	PA-DEG-PA-DEG $C_{24}H_{24}O_{10}$	3	71.5 ± 7.9	32.3 ± 5.8	28.9 ± 7.3		Polyurethane oligomer
8	5.60 269.0617	$[MNa]^+$	Anhydride of monomethyl succinate $C_{10}H_{14}O_7$	6	57.7 ± 2.0	6.55 ± 2.89	<LOD		
9	6.02 311.2203	$[MNa]^+$	Glycerol monotridecanoate✓ $C_{16}H_{32}O_4$	6	3.59 ± 0.11	<LOD	<LOD		Lubricant
10	6.38 233.1536	$[M-H]^-$	3,5-di-tert-butyl-4-hydroxybenzaldehyde✓✓ $C_{15}H_{22}O_2$	10	2.89 ± 0.56	<LOD	<LOD		
11	6.46 383.2782	$[MNa]^+$	Erythriol monopalmitate $C_{20}H_{40}O_5$	6	9.28 ± 0.33	<LOD	<LOD		
12	6.84 425.2158	$[MNa]^+$	Tributyl acetylcitrate✓✓ $C_{20}H_{34}O_8$	5	29.8 ± 1.0	<LOD	<LOD	60	Plastizicer
13	7.19 679.4187	$[MNa]^+$	Irganox 1010✓✓	9	1602 ± 358	<LOD	<LOD	No SML	Antioxidant
14	7.63 391.2831	$[MH]^+$	Dioctil phthalate✓✓ $C_{24}H_{38}O_4$	8	53.3 ± 3.7	<LOD	<LOD		Plastizicer
15	7.88 367.2822	$[MNa]^+$	Glycerol monoheptadecanoate✓ $C_{20}H_{40}O_4$	6	19.5 ± 3.3	<LOD	<LOD		Lubricant
16	8.11 393.2999	$[MNa]^+$	Bis(2-etilhexil) adipate✓✓ $C_{22}H_{42}O_4$	4	47.1 ± 2.3	<LOD	<LOD	18	Plastizicer
17	8.59 395.3137	$[MNa]^+$	Glycerol monononadecanoate✓ $C_{22}H_{44}O_4$	6	10.3 ±1.3	<LOD	<LOD		Lubricant

Sara Ubeda; Margarita Aznar; Cristina Nerin; Luis Henriquez; Laura Taborda; Claudia Restrepo.
Food Additives & Contaminants: Part A. Taylor and Francis, 2017

WHAT WE HAVE FOUND

Example 2: **Volatile** compounds detected in migration from [PE/aluminum/ paper/ink/ varnish]$_{FCS}$ multilayer material

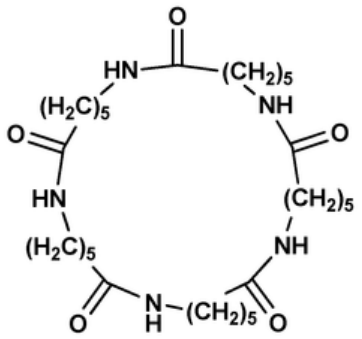
rt	Compound	Tenax®	Isooctane	EtOH 95%	EtOH 50%	Cramer
7,35	2-Pentanone-4-hydroxy [7]	0,151±0,011				I
9,51	2,3-Octanedione [7]	0,040±0,004				III
11,83	Cyclo propanecarboxylic acid, decyl ester [3]	0,019±0,004				II
12,18	1,5-Hexadien-3-ol [1]	0,041±0,004	0,253±0,169	0,384±0,112		I
13,23	2-Butoxyethyl acetate [3]					I
13,43	2,3-Dimethyldecane [12]		0,087±0,100	0,033±0,006		I
15,63	1,2,3-Propanetriol, monoacetate [3]				2,213±0,410	I
15,80	Cyclohexanol,2-methyl-5-(1-methylethyl)- [1]	0,352±0,052	0,214±0,044	0,620±0,105		I
16,48	Succinic acid, butyl undecyl ester [3]		0,339±0,023			I
17,01	1,2,3-Propanetriol,triacetate [3]	0,454±0,104	8,757±0,556	6,146±0,780	9,357±0,644	I
17,46	1-Dodecanol,3,7,11-trimethyl [1]		0,349±0,033	0,772±0,126		I
17,52	Azocine,octahydro-1-nitroso [6]			0,156±0,005	0,855±0,206	III
17,74	Cyclo octane methyl [8]		0,461±0,037	0,728±0,107		I
18,50	Oxazolam [10]	0,013±0,001	0,116±0,012	0,149±0,016	0,699±0,156	III
18,66	alkane > 12 C [12]	0,021±0,000	0,439±0,024	0,542±0,096		-
18,77	2,5-cyclohexadiene-1,4-dione,26,-bis-(1,1-dimethylethyl) [6]	0,045±0,001	0,174±0,011	0,113±0,018		II
19,03	Eicosene [12]	0,004±0,000	0,258±0,029	0,405±0,042		I
19,25	Phenol,2,4-di-tert-butyl [10]	0,021±0,002	0,415±0,027	0,695±0,065		I
19,85	2-Thiophenecarboxylic acid, 2-butyl Ester [3]	0,025±0,001	1,769±0,042	1,167±0,113	2,124±0,095	III
19,91	1,6-Dioxacyclododecane-7,12-dione [11]	0,398±0,068	7,441±0,470	10,929±1,357		I
20,27	Dibutyl itaconate [3]				0,309±0,051	I
20,95	n-capric acid n-heptyl ester [3]			0,158±0,013	0,294±0,003	I
21,47	alkane > 12 C [12]	0,040±0,003	0,556±0,023	0,653±0,122		-
22,03	alkyl alcohol > C8 [1]			0,977±0,192		-
22,26	3,5-di-tert-butyl-4-Hydroxybenzenaldehyde [10]		0,243±0,013	0,320±0,077	0,128±0,016	II

Isabel Clemente; Margarita Aznar; Cristina Nerin; Osvaldo Bosetti.
Food Additives & Contaminants: Part A. 33, pp. 703 - 714. Taylor & Francis, 2016.

WHAT WE HAVE FOUND

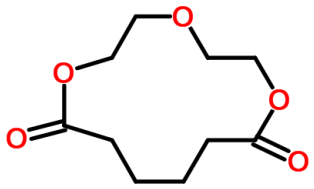
Example 3: **Oligomers**

POLYAMIDE



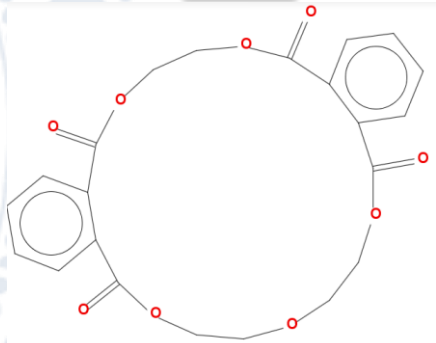
PA6 (n=5)

POLYURETHANE



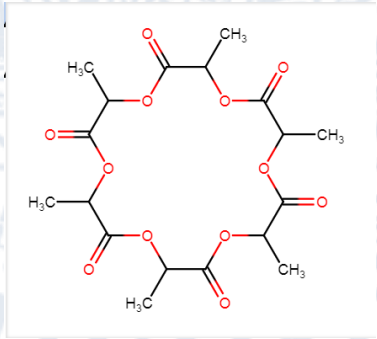
AA-DEG

PET



PhA-DEG-PhA-EG

PLA (POLYLACTIC ACID)



$[LA]_{n=6}$

WHAT WE NEED

Evaluation of the **migrants mixture** toxicity instead of an individual evaluation of each component.

Collaboration

Toxicity research :

- ✓ Development of **biotests** able to be applied to mixtures of compounds

Analytical research:

- ✓ Identification of compounds
- ✓ Quantification of compounds

Improve risk assesment in food packaging materials

Thanks for your attention!

Environmental risks to groundwater ecosystems related to the use of feed additives

Dr. Boris Kolar, Aleš Gutmaher

National Laboratory of Health, Environment and Food
Prvomajska ulica 1, 2000 Maribor, Slovenia

Problem identification

Extensive use of manure burdens the environment not only with nitrogen but also with residues of feed additives and veterinary medicinal products.

- **Persistence in the environment.** Feed additives such as metals and some coccidiostats do not degrade or show a little biodegradation under laboratory conditions; thus, they might accumulate in the environmental compartments over the years.
- **Limited information on the imission concentrations of active ingredients (AIs).** The introduction of AIs into the environment is not controlled, AIs are not regularly monitored in the EU member states, the knowledge on the fate and behaviour of the AIs in the environment under different climatic conditions is scarce.
- **High production volumes.** In the EU, approximately 20 million tons of feed containing coccidiostats are produced every year.
- **The need for a re-evaluation of the environmental risk assessment within authorization procedure for feed additive.** The default values that support the exposure assessment scenarios may not represent actual agricultural practice in the 28 MS, leading to a possible serious underestimation of risk, or to over-conservative conclusions on environmental safety.
- **The need to consider additional protection goals in the environmental risk assessment.** Protection goals should be extended the groundwater ecosystems due to its vulnerability and unfavourable conservation status of several species. Aquatic species might be more sensitive to contaminants than humans.

Objectives

- Estimation of the level of contamination of the soil and groundwater with selected AIs used as feed additives at selected project sites in MS from different climatic and geographic regions.
- Assessment of the risk to the receiving compartments and groundwater ecosystems related to the use of selected AIs in feed additives in different member states.
- Assessment of possible impacts related to the use of selected AIs on the receiving compartment and on the groundwater ecosystems.
- The re-evaluation and review of the default parameters used in the assessment of the environmental exposure to feed additives in relation to manure application practice on agricultural land in MS.

Foreseen impact and benefit of implementation of the proposed project idea

The main beneficiaries from the implementation of the proposed idea will be:

- Risk managers: the information on imission of feed additive will enable better managing of potential risks in exposed compartments on the level of EU as well as in individual member states.
- Regulatory bodies responsible for authorization feed additive: due to exposure assessment based on realistic scenarios based on the representative data and agricultural practice in different geographic regions of EU.
- Regulatory bodies responsible for authorization veterinary medicines products as these pharmaceuticals share the same exposure routs as feed additives.
- Applicants and marketing authorization holders of feed additives (and veterinary medicinal products) due to reduced over-conservative exposure scenarios.
- Farmers: reduction of the risk on the adverse, long-term effect on the plants (crop, grassland plant composition), permanent contamination of the soil.

The expected impact of the study the implementation of the proposed idea is:

- Increased safety and sustainability of use of feed additives in relation to the groundwater ecosystems.
- Improved safety for the terrestrial environmental compartment in EU member states due to updated realistic exposure assessment.

Why this idea needs to be funded from public sources

In EU feed additives are authorized via centralized procedures. Some groups of feed additives may potentially have a harmful impact on the environment. Feed additives are used in large quantities and emitted via manure into the soil as a primary receiving compartment.

As a consequent, the Community is expected to:

- **Identify and provide information on AIs and compartments of concern** (due to persistence, toxicity and lipophilicity of AIs) as support for the monitoring of these substances.
- **To introduce the groundwater ecosystem as a protection goal of environmental risk assessment.** Several groundwater species are endangered; thus, it is in the public interest to protect them.
- **Provide efficient and regularly updated guidance on the regulatory assessment of the environmental risk of feed additives.** The update should be based on the survey on the use of feed additives according to agricultural practices in different MS, due to climate changes, considering the landscape in different regions and considering different protection goals.

Potential partners in the project

Partners from the Mediterranean region, with a mainly karst landscape, partners from the Baltic countries and partners from central European MS would be particularly welcome to participate and contribute to the execution of the project.

Partners from the MS that have already expressed their interest in participating in the project

- Boris Kolar, **Slovenia**
- Martin Danaher, **Ireland**
- Ludek Blaha, **Czech Republic**
- Dimitris Tsaltas, **Cyprus**
- Antonio Finizio, **Italy**
- Angelina Pena, **Portugal**

Environmental risks to groundwater ecosystems related to the use of feed additives

Dr. Boris Kolar; Aleš Gutmaher
National Laboratory of Health, Environment and Food
Prvomajska ulica 1, 2000 Maribor,
Slovenia

Problem identification

An extensive use of manure burdens the environment not only with nitrogen and phosphorous but also with residues of veterinary medicinal products (VMPs) and feed additives.

- **Persistence in the environment.** Feed additives such as metals and some coccidiostats do not degrade or show a little biodegradation under laboratory conditions; thus, they might accumulate in the environmental compartments over the years.

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- **High production volumes.** In the EU, approximately 20 million tons of feed containing coccidiostats are produced every year.

- **The need for a re-evaluation of the environmental risk assessment within authorization procedure for feed additive.** The default values that support the exposure assessment scenarios may not represent actual agricultural practice in the 28 MS, leading to a possible serious underestimation of risk, or to over-conservative conclusions on environmental safety.

- **The need to consider additional protection goals in the environmental risk assessment.** Protection goals should be extended the groundwater ecosystems due to its vulnerability and unfavourable conservation status of several species. Aquatic species might be more sensitive to contaminants than humans.

The aim of the project is to

Estimate the level of contamination of the soil and groundwater with selected AIs used as feed additives at selected project sites in MS from different climatic and geographic regions.

Assess the risk to the receiving compartments and groundwater ecosystems related to the use of selected AIs in feed additives in different member states.

Assess possible impacts related to the use of selected AIs on the receiving compartment and on the groundwater ecosystems.

The re-evaluation and review of the default parameters used in the assessment of the environmental exposure to feed additives in relation to manure application practice on agricultural land in MS.

The proposed duration of the project: 4 years

Potential partners in the project

Partners from the MS that have already expressed their interest in participating in the project

- Boris Kolar, **Slovenia**
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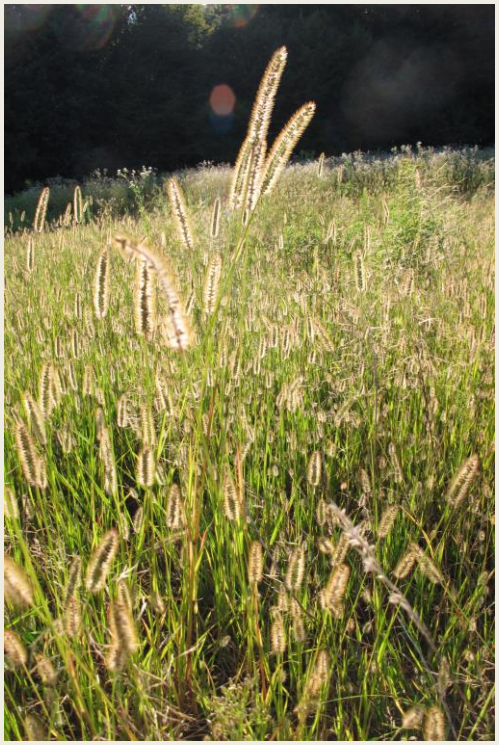


Partners from the Mediterranean region, with a mainly karst landscape, partners from the Baltic countries and partners from central European MS would be particularly welcome to participate and contribute to the execution of the project.

Why this idea needs to be funded from public sources

Centrally authorized feed additives are chemical substances with a potentially harmful impact on the environment. Some groups of feed additives are used in large quantities and emitted via manure into the soil as a primary receiving compartment.
As a consequent, the Community is expected to:

- Identify and provide information on AIs and compartments of concern (due to persistence, toxicity and lipophilicity of AIs) as support for the monitoring of these substances.
- To introduce the groundwater ecosystem as a protection goal of environmental risk assessment. Several groundwater species are endangered; thus, it is in the public interest to protect them.
- Provide efficient and regularly updated guidance on the regulatory assessment of the environmental risk of feed additives. The update should be based on the survey on the use of feed additives according to agricultural practices in different MS, due to climate changes, considering the landscape in different regions and considering different protection goals.

Thank you for your attention

European Food Safety Authority

Area of priority:
The impact of chemicals on the ecosystem (release of chemicals into the environment)

feb '18 Risk Assessment Research Assembly

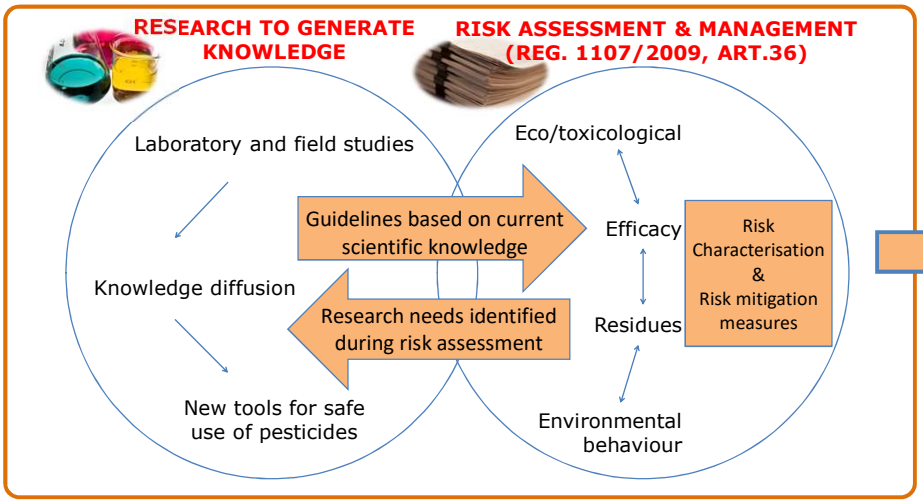
SOIL AMMENDMENTS AND ITS EFFECT ON THE PESTICIDE BEHAVIOUR IN SOIL

GOBIERNO DE ESPAÑA · MINISTERIO DE ECONOMÍA, INDUSTRIA Y COMPETITIVIDAD · INIA Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria

P. Sandín-España, C. López-Goti, E. Alonso-Prados, A.P. Fernández-Getino and J.L. Alonso-Prados*

***prados@inia.es Plant Protection Products Unit -INIA, Madrid (Spain)**

INIA PLANT PROTECTION PRODUCTS UNIT



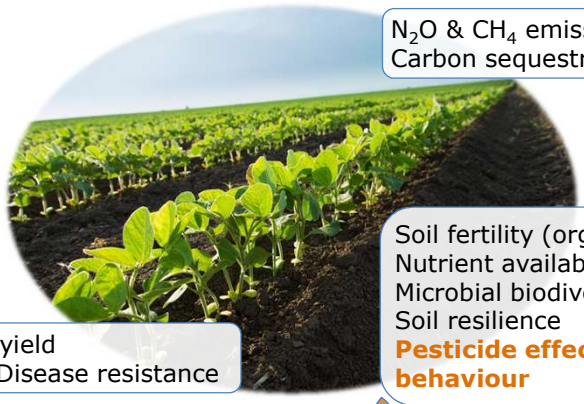
- The implementation of appropriate risk mitigation measures contribute to reduce human and environmental exposure and risks associated with pesticide application.
- In this sense, the use of organic soil amendments (e.g. biochar, compost, etc.) is having very promising results as risk mitigation measure for pesticides.
- However, the effect of organic amendment on pesticide efficacy and behaviour in the environment are poorly studied.

BACKGROUND

Effects of organic amendment on soil

Different types of **organic soil amendments** with different physicochemical properties

Effects on



N_2O & CH_4 emissions
Carbon sequestration

Soil fertility (organic matter)
Nutrient availability
Microbial biodiversity/activity
Soil resilience
Pesticide effectiveness, fate and behaviour

Crop yield
Pest/Disease resistance

PROPOSAL

INFLUENCE ON….?

Influence of organic amendment on pesticide behaviour

Mobility

Adsorption/desorption
Leaching
Volatilisation

Efficacy on control

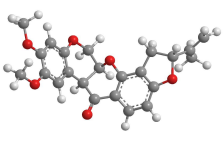
affects

Safe use & Guarantee crop production

Degradation

Chemical degradation (hydrolysis, …)
Biological degradation (bacteria, fungi, …)
Photodegradation (direct/indirect)

Identification of degradation products



Eco/toxicological effects on non-target organism

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Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria

Unit of Plant Protection Products

Dr. Jose Luis Alonso Prados

General Deputy of Foresight and Program Coordination

prados@inia.es

Technical Directorate for Evaluation of Plant Varieties and Plant Protection Products

The National Institute for Agricultural and Food Research and Technology

INIA, Madrid

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MAIN ACTIVITIES IN RESEARCH

1. Chemical behaviour of pesticides residues in the environment
2. Structural elucidation and isolation of unknown transformation products (TPs) as emerging pollutants
3. Development and validation of analytical methods of pesticides and their TPs
4. Studies of biological activity of TPs
5. Environmental risk assessment of pesticides

HUMAN RESOURCES

J.L. Alonso-Prados (PhD. Agronomy)
Pilar Sandín-España (PhD. Chemistry)
Carmen López-Goti (PhD. Chemistry)
Elena Alonso-Prados (Biologist)
Beatriz Sevilla-Morán (PhD. Chemistry)
Mercedes Villarrolla (Chemist)
Evaluation group of Plant Protection Products

EQUIPMENT & FACILITIES

Laboratory of Chemistry

LC-MS/MS; solar simulator.
NMR; LC/QtoF

Other facilities

Greenhouses, growth chambers, field falicities, molecular biology laboratory

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RESEARCH IDEA

Area of priority: The impact of chemicals on the ecosystem (release of chemicals into the environment)

SOIL AMMENDMENTS AND ITS EFFECT ON THE PESTICIDE BEHAVIOUR IN SOIL

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- **Availability of PPP in the market has been reduced**
- **The availability of PPP depends on a correct risk management that guarantee a sustainable and safe use of pesticides**
- **Reduction of plant protection products (PPP) in the market could contribute to an increase of nº of cases of resistance**

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PROPOSAL

Application of RISK MITIGATION MEASURES to reduce the problems associated with the use of PPP

Use of organic soil amendment (biochar…) as a risk mitigation measure

- **change the environmental behavior of pesticides (adsorption, biodegradation…)**
- **reduction of contamination of water**

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OUR ADDED VALUE TO THE TOPIC:

❑ Experience of the Plant Protection Products Unit (PPPU):

- The group has expertise on environmental risk assessment, bio- and chemical behaviour of pesticides in the environment, field trials and bioassays with pesticides for the assessment of environmental fate.
- INIA and PPPU is the acredited entity by the Spanish Ministry of Agriculture for the assessment of pesticides under Regulation 1107/2009/EU.

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- Members of our group belong to the National expert group for the evaluation of pesticides.
- Members of our group participate on the evaluation coordinated by EFSA of pesticides and on the development of guidance documents for their risk assessment.
- Our group participate on the zonal evaluation of pesticides

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Many thanks for your attention

Jose Luis Alonso Prados

Unit of Plant Protection Products

Technical Directorate for Evaluation of Plant Varieties and Plant Protection Products

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Biosensing Devices as a Tool to Refine the Routine Analysis of Organophosphate Pesticides

Janis Rusko, Ferdinando Febbraio, Giuseppe Manco

IBP - Institute of Protein Biochemistry, CNR, Naples, Italy

General description:

The presence of pesticide residues and metabolites is one of the major issues in food and environmental safety research. Quantitative analysis of pesticides by common chromatographic and spectroscopic technologies are limited by the time and cost required to analyze a high number of samples.

However, to perform food safety risk assessment a lot of data is needed , which is derived from large quantities of samples and a methodology which enables rapid quantitative analysis.

To propose a solution for the foreseen issue, we are in process of developing specific enzymes for the detection of selective organophosphate (OP) pesticides and implementing the designed biosensing devices in a robotic system in combination with fluorescence and mass spectrometric (MS) detection. Analysis time for multiple samples by fluorescence measurement takes about one minute, which is at least ten times faster than common quantification methods.

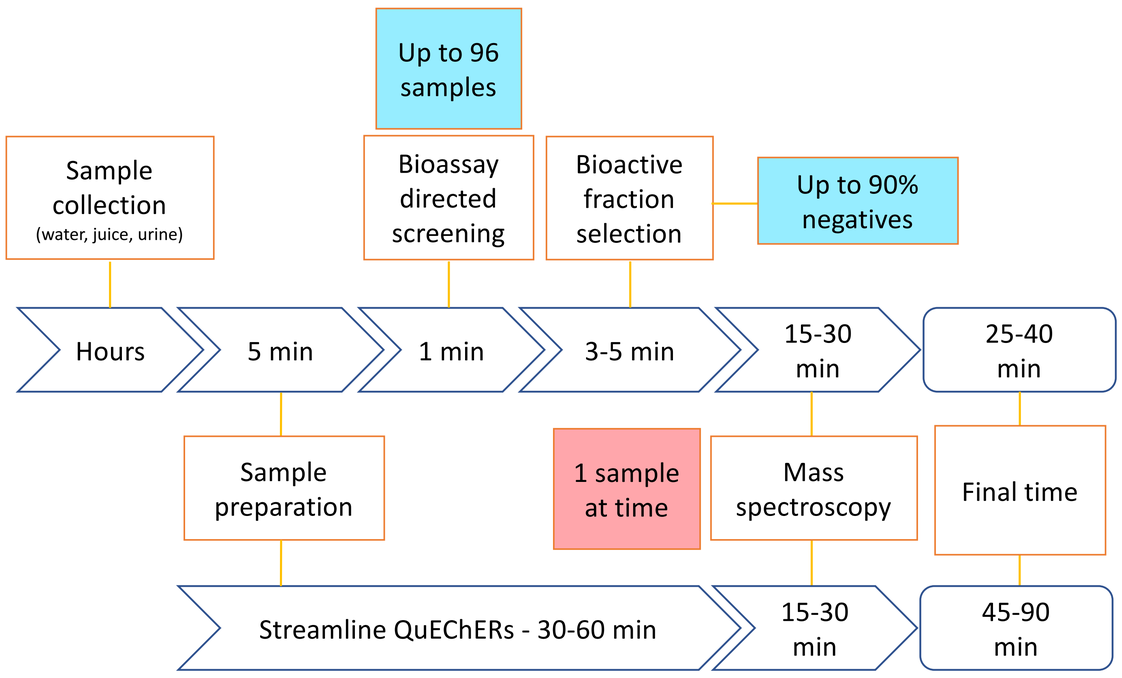

Fig. 1. Analysis method process, in comparison with a conventional pesticide analysis method (QuEChERs + mass spectroscopy)

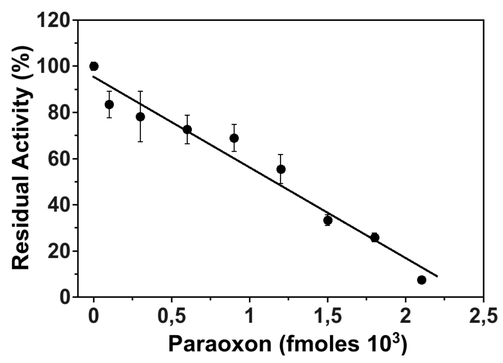

Fig. 2. Sensitivity achieved by a bioassay measurement

Why the idea needs to be sustained through public funding:

- Decisions regarding environmental health and food safety risks include both science and broader public communication on that science. Although public discourse can be belligerent at times, successful dialogue and decision making are improved only with broad scientific engagement.
- Collaborative engagement is important to ensure that diverse, and in some cases novel, scientific knowledge and perspective are considered in the improvement of public and food safety and risk assessment.
- Public funding can benefit further research to enable the commercialization of biosensors to achieve the monitoring of contaminants at the household level, broadening the surveillance scheme. In particular, pesticides are ranked #1 food safety concern in most EU member states by Eurobarometer, thus the society is very interested in the evaluation and monitoring of the risk. Moreover, this topic is also relevant to public because of common misconceptions and perseverance of media related to pesticide use.

EU-FORA Fellowship Programme

Acknowledgement:

J.R. is supported by the European Food Risk Assessment Fellowship Programme (EU-FORA) granted from the European Food Safety Authority (EFSA), number GP/EFSA/AFSCO/2016/02-Ga7.

Foreseen impact/benefit:

– Biosensing devices are a rapid and cost effective pre-screening tool for sample diagnostics. Pre-screening allows for the reduction of samples subjected to costly instrumental analysis, by filtering a significant number of negative samples.

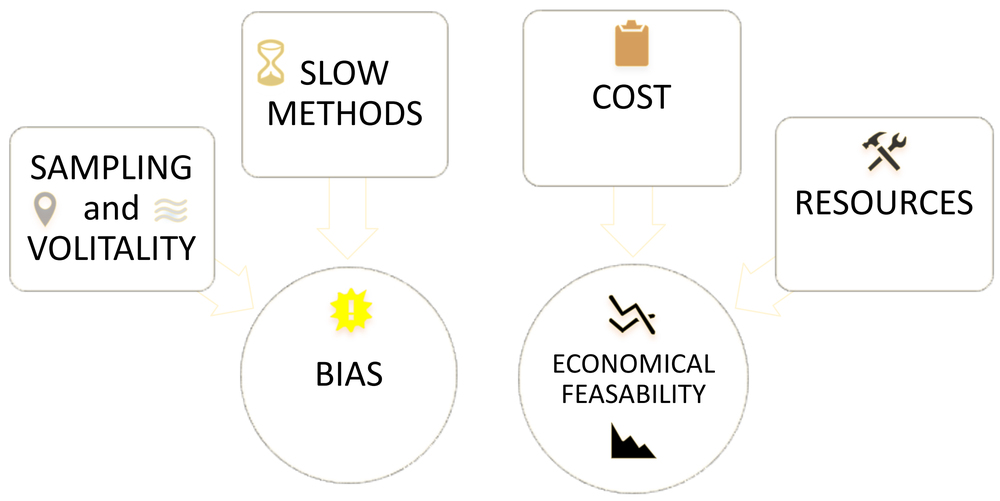

Fig. 3. Underlying issues in common pesticide analysis methods

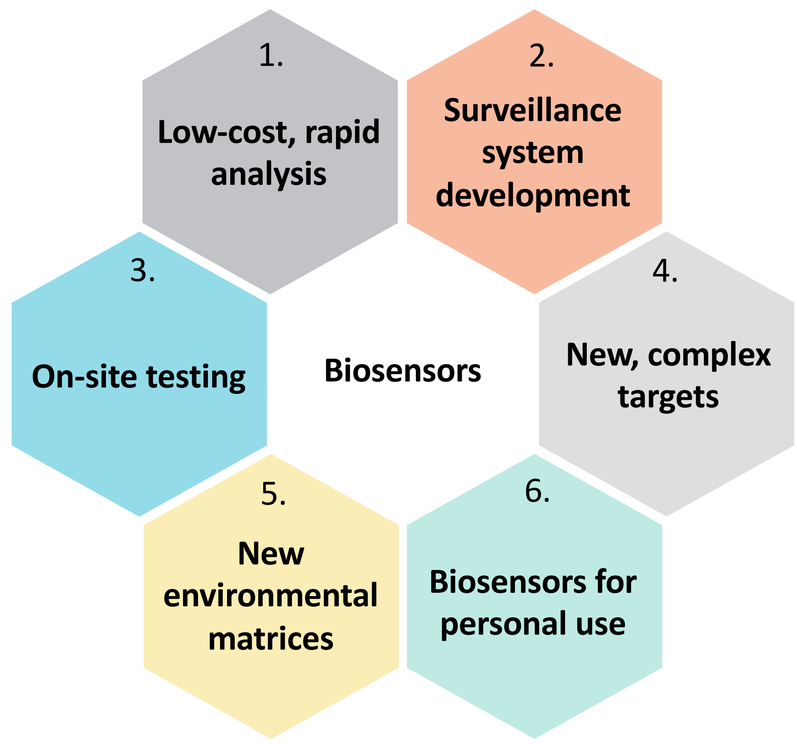

Fig. 4. Future goals and impact on society

What do we need to make our idea happen:

– We are looking for partners which could help us establish this research and employ and adapt the surveillance scheme.

– Funding would enable us to move towards the set research goals and make the project more appealing by improving the quality of methods.

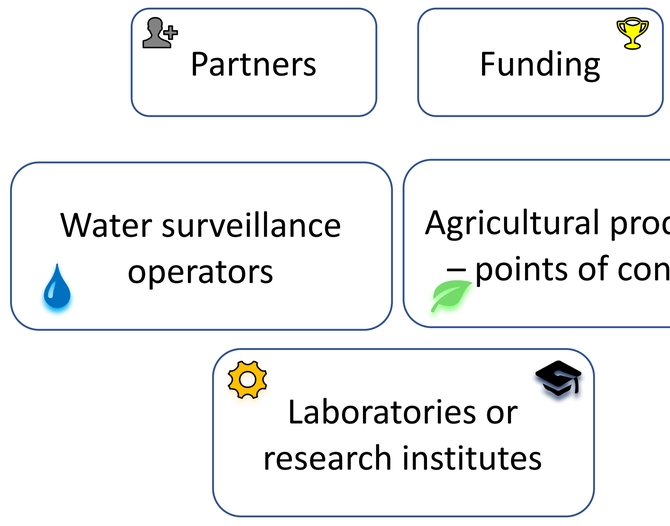

Fig. 5. Our needs and types of partners

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Biosensing Devices as a Tool to Refine the Routine Analysis of Organophosphate Pesticides

Janis Rusko, Ferdinando Febbraio, Giuseppe Manco
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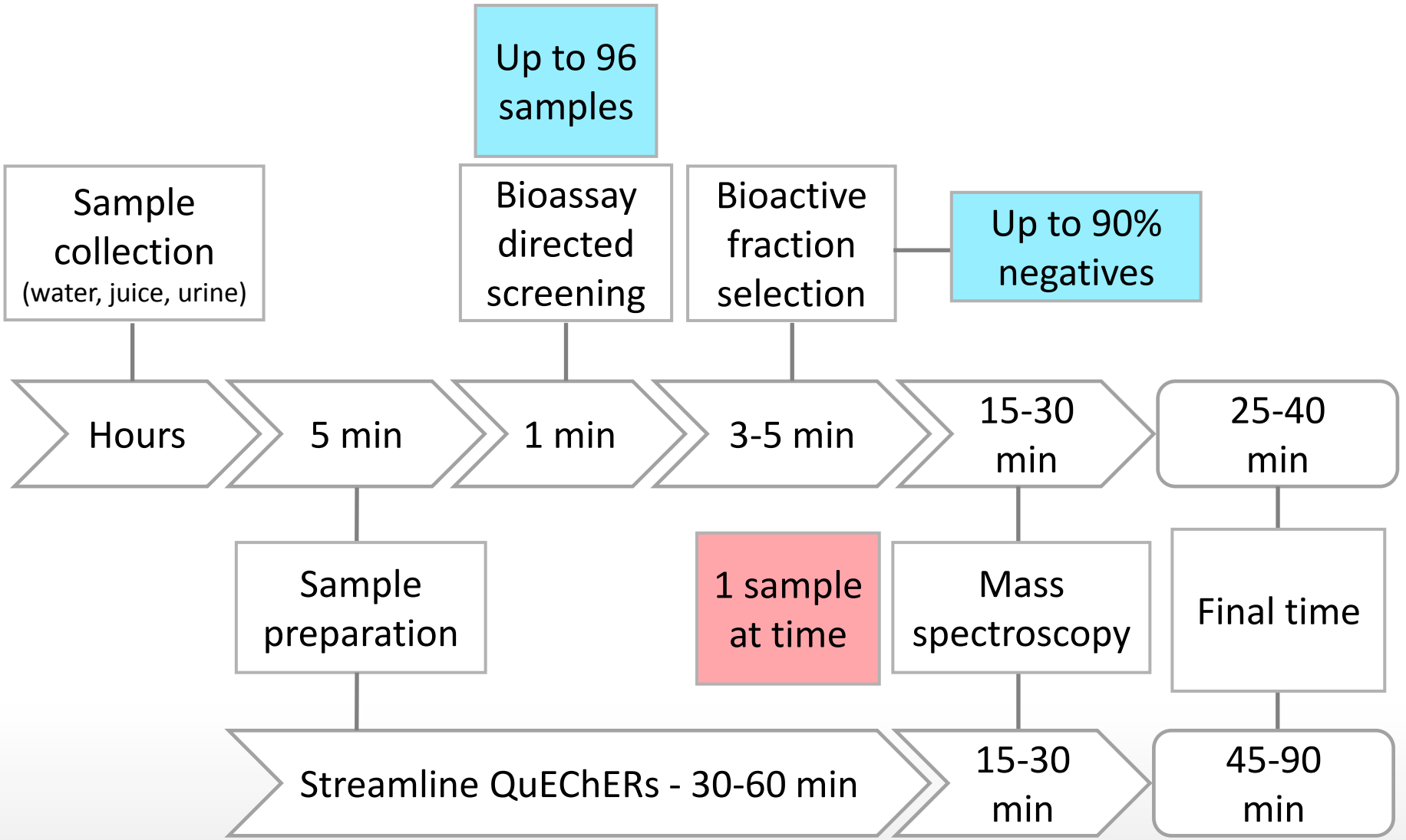
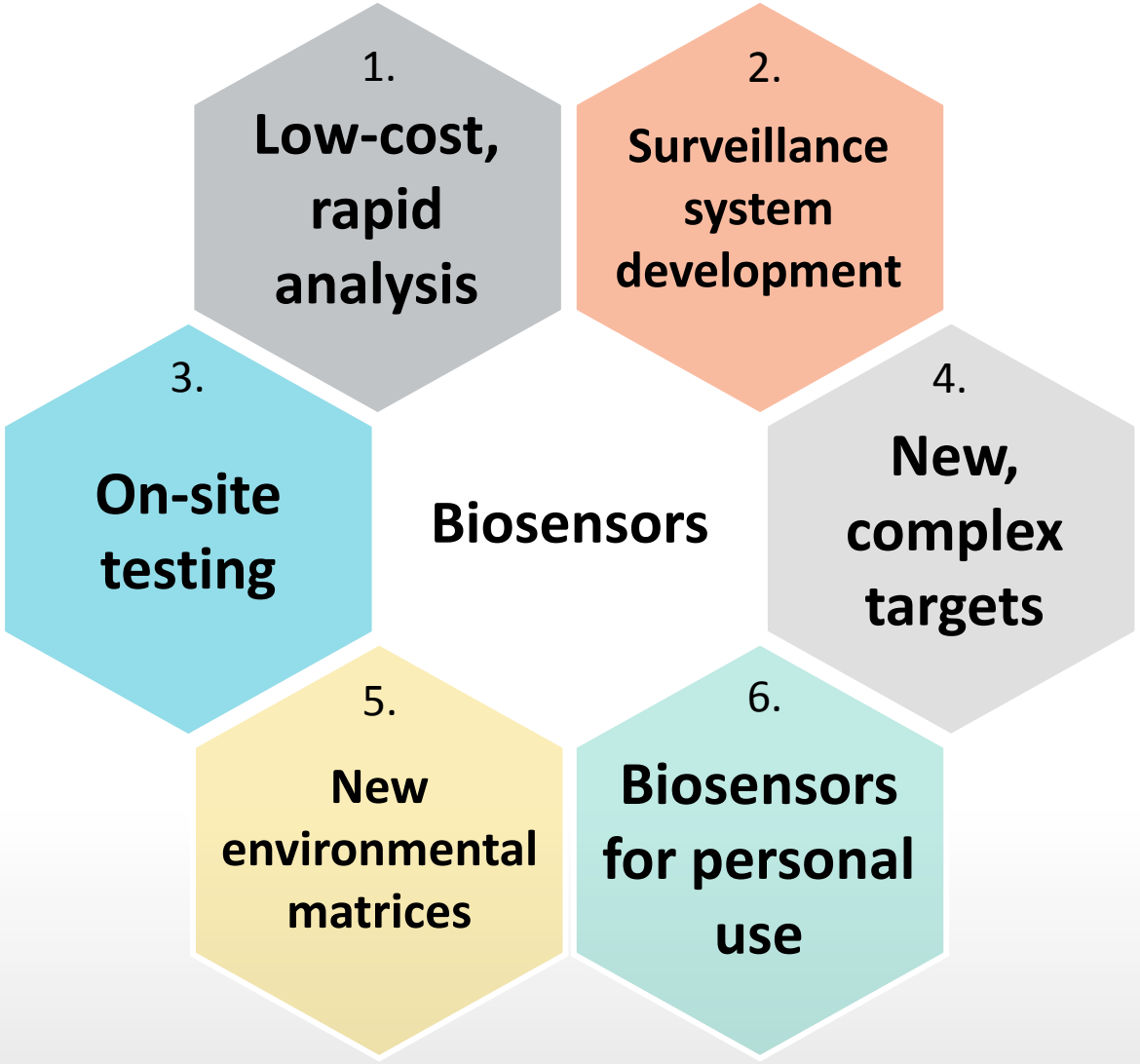
Underlying issues

Current process



Future goals and impact on society



Our needs

Partners

Funding

Water surveillance operators

Agricultural producers – points of concern

Laboratories or research institutes

Thank you

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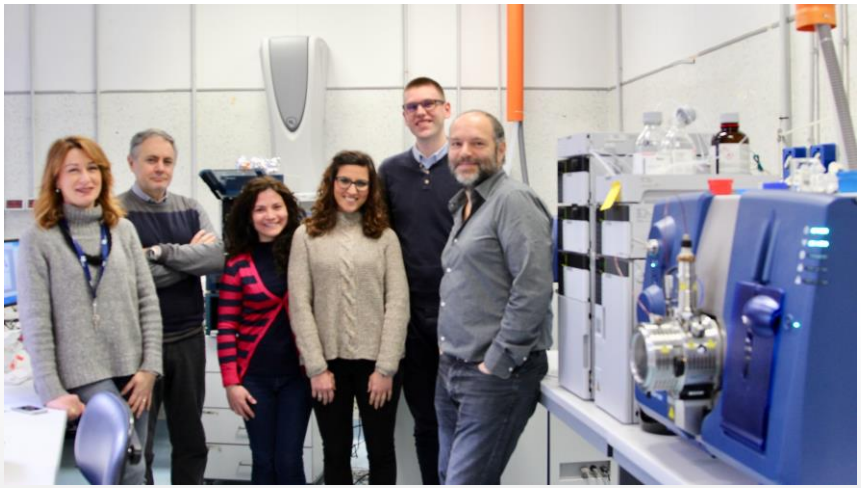
@ruskojanis



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DE MONTFORT UNIVERSITY
LEICESTER

Safety of Imported Ethnic Foods Within Europe

Professor Dr Parvez I. Haris
Faculty of Health & Life Sciences
De Montfort University
Leicester, UK
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Definition of Ethnic Foods

There are several different definitions but one is as follows:

"foods from countries other than the home market, thus including also many imported foods, contributing to a different food culture than the traditional cuisine of the host country " *Marletta et al. 2010.*

Demand for Ethnic Foods Increasing Within Europe

In an ever increasing globalised world international trade and migration is increasing.

- *This is leading demand for imported foods*
- *Imported foods are not only popular with migrant populations but also with mainstream population*
- *Rise in popularity of ethnic foods (for e.g. Chinese & Indian foods in the UK)*
- *Tourism*
- *Ethnic food sales in Europe is rising at ca. 14% per year (Fusco et al. 2015, Curr. Op. Food. Sci.).*

Limited Research on Toxicological analysis of imported foods

- We have been analysing ethnic foods sold in the UK market for over a decade (e.g. Al Rmalli, et al, 2005. *Science of the Total Environment*, *337*(1-3), pp.23-30.)

- High levels of arsenic, lead, cadmium have been detected in foods imported from Asia and sold in UK markets.

- Our study has recently revealed that Bangladeshis living in the UK have higher exposure to arsenic and other heavy metals which could be due to their higher consumption of rice and other imported foods (*Cascio, C., Raab, A., Jenkins, R.O., Feldmann, J., Meharg, A.A. and Haris, P.I., 2011. The impact of a rice based diet on urinary arsenic. Journal of Environmental Monitoring, 13(2), pp.257-265.*)

- More research and collaboration in this area is needed.

Our experience of studies on imported foods in the UK

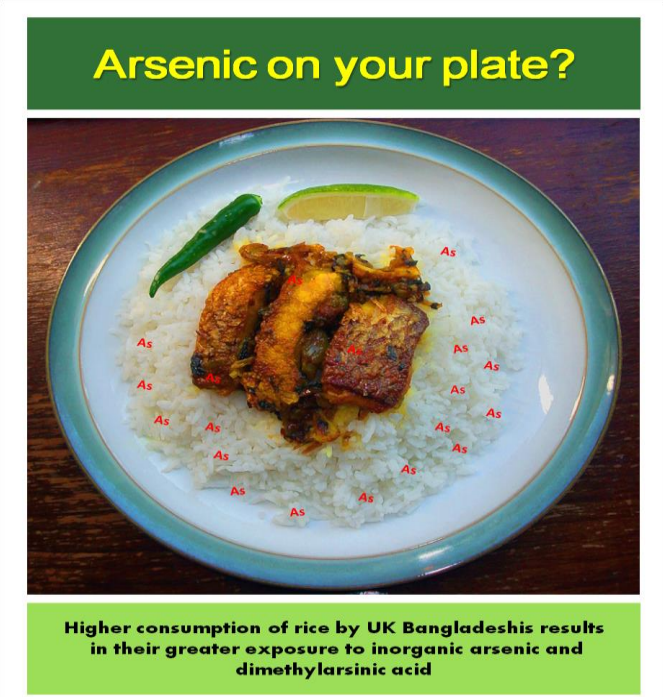
Asians make up 6.1% of the population of England.

Asian food is not only popular amongst Asians but also White British population (curry is considered a national dish of Britain).

Asians have higher incidence of certain diseases including diabetes and certain types of cancers (for example oral cancer).

These may have links to their consumption of certain imported foods that increases their exposure to toxic chemicals.

Exposure to Arsenic from rice in the UK – higher rice consumers are at greater risk of exposure to inorganic arsenic



Front Cover of Journal Environmental Monitoring: Cascio, C., Raab, A., Jenkins, R.O., Feldmann, J., Meharg, A.A. and Haris, P.I., 2011. The impact of a rice based diet on urinary arsenic. *Journal of Environmental Monitoring*, *13*(2), pp.257-265.

Diversity of imported foods is immense and health risks are high: Example: Baked Clay (known as Sikor) that are consumed by women, especially pregnant women

Our research shows clay consumption can be a significant source of heavy metal exposure.

Diversity imported foods is immense and health risks are high: Example: Betel quid and its components (areca nut, piper betel leave, lime and zarda) are popular amongst some South Asians in the UK

Our research has shown that betel quid, especially its tobacco component, contain high concentration of heavy metals.

What needs to be done?

- Research needed to determine safety of imported ethnic foods in different EU countries
- Develop a EU-wide database of key imported foods and their toxic chemical contents
- Identify and rank risk factors
- Human biomonitoring studies of groups with high consumption of certain imported foods
- Develop strategies for risk management & mitigation
- Greater co-operation between food safety researchers, food safety agencies, food importers, producers and consumers

Acknowledgements

Dr Claudia Cascio

Professor Richard O. Jenkins

Dr Shaban Al-Rmalli

Risk Ranking of chemical and microbiological hazards in food

Salomon Sand
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Livsmedelsverket
National Food Agency

Evira

University of Maribor

Research idea

Interpretation of risks in a relative context can improve decision making and risk communication

Overarching scientific objective

A general approach for estimation of public health burden

Impact

Helps prioritize the use of resources

Can direct food control, legislation, and dietary advice

Chemical	SAMOE	Risk class
dioxin	**0.14**	**3**
Al	**0.17**	**3**
Hg	**0.17**	**3**
Pb	**0.22**	**3**
Ni	**0.45**	**3**
Cd	**0.63**	**3**
iAs	1.3	2
3-MCPD	1.6	2
Deoxynivalenol	2.6	2
zearalenone	2.6	2
T2 and H2	3.1	2
glycidol	5.2	2
BDE-99	5.5	2
I-PFOS	7.0	2
fumonisins	8.3	2
I-PFOA	8.9	2
ochratoxin a	15	1
BDE-153	19	1
ndl-PCB	24	1
BDE-47	29	1
PAH4	33	1
BaP	34	1
HCB	74	1
Cu	88	1
Cr III	530	1
DDT	930	1
HBCD	982	1
CP (sum)	2436	1
TCDPP	4743	1
Ag	6182	1
TCEP	13126	1
TPHP	26042	1
BDE-209	26443	1
TCPP	33731	1

Impact

Helps prioritize the use of resources

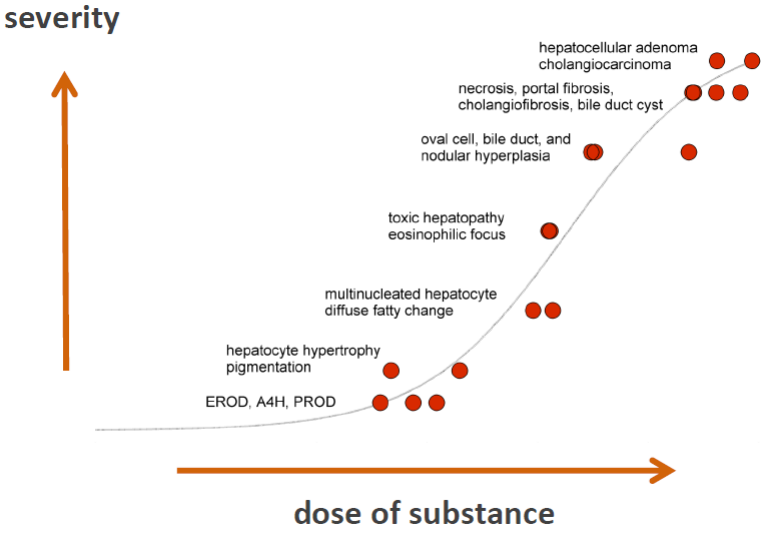
Can direct food control, legislation, and dietary advice

Can support risk communication, illustrating the overall result

Livsmedelsverket
National Food Agency

How to make it happen

A generalized risk metric "fraction of disease"?



Consumer risk perception, graphical design

Interactions across sectors involved in risk analysis

Livsmedelsverket
National Food Agency

Importance of public funding

Risks in the food chain renders debate

Public funding supports a scientifically sound process

Risk assessment method development falls between funding sources

Livsmedelsverket
National Food Agency

Using Big Data" gathered in Food production, to be used for food safety/food quality Risk Assessment

Dr. Len Lipman, Institute for Risk Assessment Sciences,
Division of Veterinary Public Health, Utrecht University

l.j.a.lipman@uu.nl

Production of food of animal origin

Food Safety/Food quality

Meat inspection and zoonoses control

- Most countries of modern world
- Regulation by legislation.
- By governmental veterinarians and industry quality assurance employees

Examples of extinction of zoonotic infections due to proper veterinary infrastructure

Tuberculosis

Trichinellosis

Brucellosis

Leptospirosis

What is Safe Food /optimal Quality Food nowadays?

Definition of food quality?

- Healthy feed – healthy animals – healthy food
- Animal welfare
- Environment protection
- Novel food, fast food, neutroceuticals, genetically modified
- Safety

It is a consumer market! And consumers demand asurances by industry, goverment

Food related problems (Food safety???):

- Overweight
- Food infection and Food intoxication
- Allergies
- Other problems AB residues in food?, Toxins of fungi (aflatoxins), chemical residues

Big Data in Food of Animal origin production

- Individual animal data: feed consumption, movement indicators, heart rate, antibody levels against, carrier levels of pathogens, …..
- Animal welfare indicators: cortisol levels, animal sound production……
- Environment protection: Co2 production, fine dust production….
- Slaughter house data: fat/protein levels, lesions on skin….

Risk assessment for Food quality/ food safety using Big Data in Food of Animal origin production

- Give assurance to consumer on animal welfare, environmental protection.
- Status of animals concerning food safety when they arrive at slaughterhouse (level green ,orange or red)
- Total quality assurance from farm to fork

Risk assessment for Food quality/ food safety using Big Data in Food of Animal origin production

We need a consortium of interested parties including farm animal specialists, food quality control specialists, risk assessors etc etc but also innovative (out of the box thinkers) animal and ict/mathematical specialists which can create/measure robust data which relates animal information with food quality/food safety.

Questions?

"If I had wanted you to understand it, I would have explained it much better".

(Johan Cruijff)

DTU Food
National Food Institute

Development of Risk-Benefit Assessment of foods in the EU: from methodology to application

Maarten Nauta, Géraldine Boué, Morten Poulsen and proponents
maana@food.dtu.dk; geraldine.boue@oniris-nantes.fr; morp@food.dtu.dk

What is Risk-Benefit Assessment?

A comparative assessment of human health risks and benefits of diets, foods and food compounds, based on a common scale of measurement. It combines risk assessment with benefit assessment and requires a multidisciplinary approach including Nutrition, Toxicology, Microbiology, Epidemiology, Mathematical Modelling, Public Health Sciences and more.

Background

Methods for Risk-Benefit Assessment in foods (RBA) have been developed and proposed in past European research projects. However, performing an RBA remains challenging. To further develop the RBA methodologies, case studies that address the challenges related to RBA are needed.

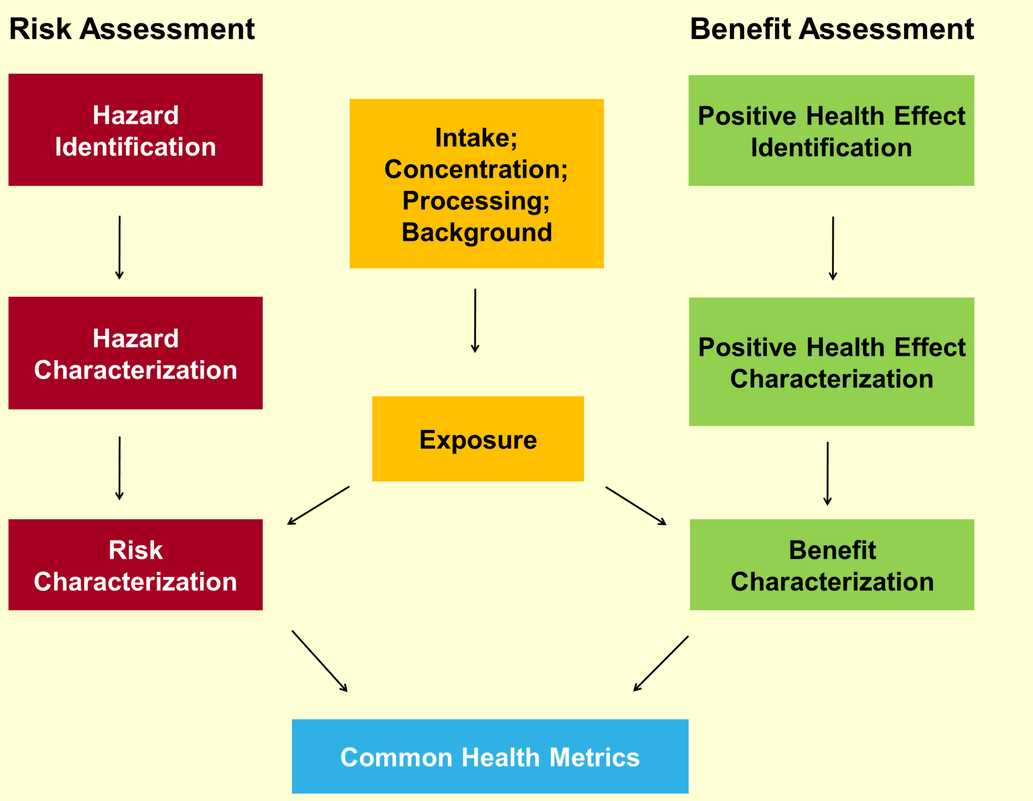
Our research idea is based on an EFSA sponsored RBA workshop with 28 participants from 17 organizations in and outside the EU (Copenhagen, May 2017).

Research Strategy

Our research idea should be performed in a collaborative project that combines two strategies:

1. **Method development:** construction of an RBA typology, modelling approaches and software tools,
2. **Practical case studies** to test the proposed methods partly by re-analyzing and expanding previously performed case studies, using new data and new methods.

Relevant **stakeholders** should be included to ensure that RBA meets the societal requirements. The research will result in **standardized tools** that allow an integrative approach to perform risk-benefit assessment of foods.



Are you a public funding body representative?
Do you want to make a change?

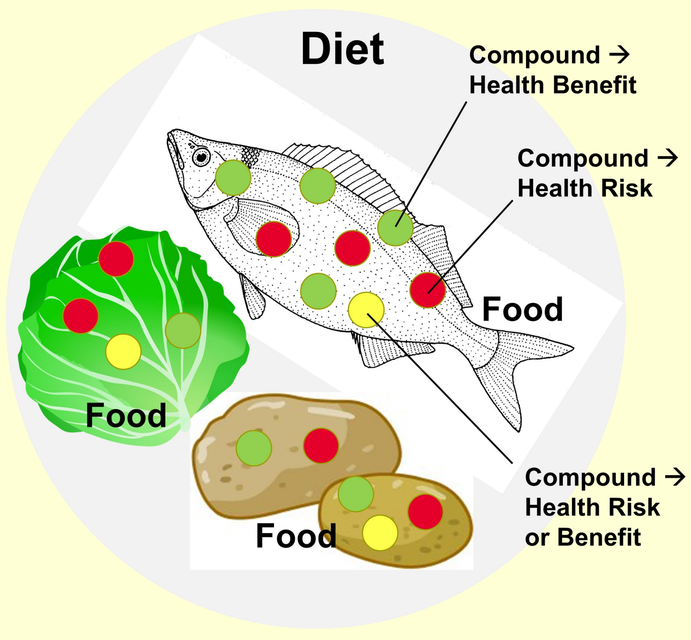
Do not miss this opportunity to be part of our initiative, which will improve food safety and public health!

Impact on food safety and public health

By developing a transparent methodology for an integrated assessment of risks and benefits associated with food consumption, food safety authorities can give sound and consistent dietary advices and consumers can make well-informed dietary choices, for the benefit of all.

Main Challenges

- **Evidence synthesis**, the imbalance between scientific evidence required for risk and benefit assessment;
- **Data** availability, data needs and the development of shared databases, including the development of novel harmonized consumption surveys for nutritional, chemical and microbiological exposure assessment with coverage of the respective relevant subpopulations;
- The consideration and quantification of **uncertainty** in RBA;
- The selection of **integrated health metrics** and the potentials for quantitative RBA;
- Risk-benefit **communication** to food safety authorities and consumers;
- RBA **beyond human health** effects: inclusion of sustainability, (health) economy and variation between consumer groups.



To make this happen…

Our RBA research idea requires **international and multidisciplinary collaboration** because the challenges are large and demanding, and not restricted to national borders. A new harmonized and standardized RBA research methodology will therefore need broad international support (incl. financing) to make it sustainable within Europe.

Our research idea includes the performance of **case studies** and requires development and discussion of methods. Hence, a variety of research partners, in terms of expertise, geographical spread and stakeholder status is important.

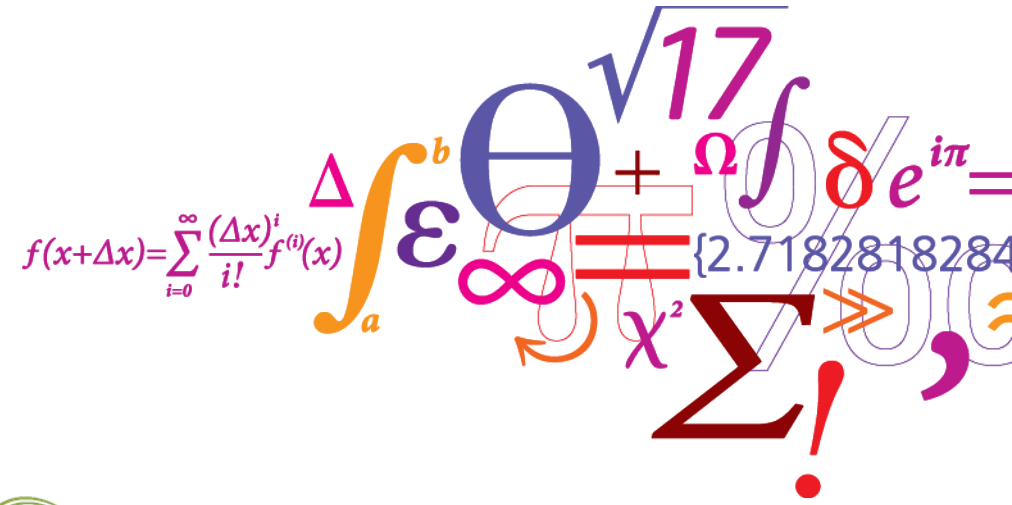
Join our recently started International Network on Risk-Benefit Assessment of Foods!
Mail to maana@food.dtu.dk

Development of Risk-Benefit Assessment of foods in the EU: from methodology to application

Maarten Nauta
Géraldine Boué
Morten Poulsen

and proponents

DTU Food
National Food Institute



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Food Safety & Microbiology
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Oniris

Why is Bread Bad For You? The Shocking Truth

By Kris Gunnars | 381,111 views

"The Whiter The Bread, The Sooner You're Dead."

It has been known for a long time that white bread and refined grains in general aren't particularly nutritious.

Nutritionists and dietitians all around the world have encouraged us to eat whole grains instead.

But grains, especially gluten grains like wheat, have been under intense scrutiny in recent years.

IS ALL FOOD DANGEROUS?

Fruit and Vegetable Inta… Chronic Disease

Hsin-Chia Hung, Kaumudi J. Joshipura, Rui Jiang, Frank B. Hu, David Hunter, Stephanie A. Smith-Warner, Graham A. Colditz, Bernard Rosner, Donna Spiegelman and Walter C. Willett

+ Author Affiliations

Correspondence to: Walter C. Willett, MD, Department of Nutrition, Harvard School of Public Health, 651 Huntington Ave., Boston, MA 02115 (e-mail: walter.willett@channing.harvard.edu)

Received April 3, 2004.
Revision received August 26, 2004.
Accepted September 1, 2004.

Abstract

Background: Studies of fruit and vegetable consumption in relation to overall health are limited. We evaluated the relationship between fruit and vegetable intake and the incidence of cardiovascular disease and cancer

Risk Assessment

…cancer and

A diet high in red meat can … expectancy, according to researchers at Harvard Medical School.

The study of more than 120,000 people suggested red meat increased the risk of death from cancer and heart problems.

Substituting red meat with fish, chicken or nuts lowered the risks, the authors said.

The British Heart Foundation said red meat could still be eaten as part of a balanced diet.

The researchers analysed data from 37,698 men between 1986 and 2008 and 83,644 women between 1980 and 2008.

They said that during the study period, adding an extra portion of unprocessed red meat to someone's daily diet would increase the risk of death by 13%, of fatal cardiovascular disease by 18% and of cancer mortality by 10%. The figures for processed meat were higher, 20% for

Experts advise to choose leaner cuts of red meat

Related Stories

- Red meat study: Risks 'very clear'
- Cut red meat to lower cancer risk
- How much red meat should we eat?

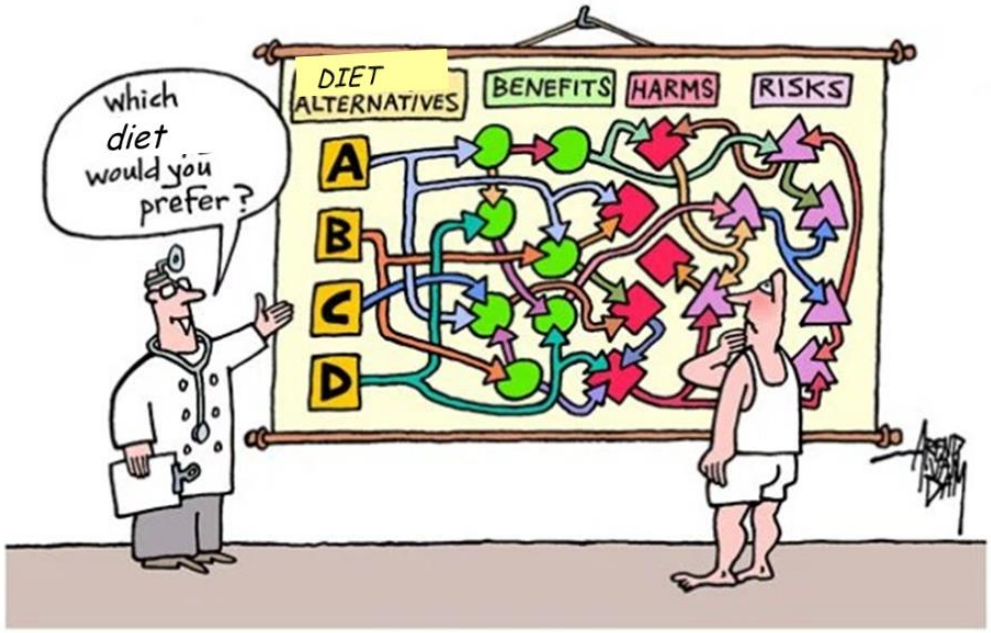

Healthy Life
35 Calories Per Slice
White
High Fiber
Reduced Sodium
No High Fructose Corn Syrup
35 Calories Per Slice
White
High Fiber


Benefits of Fruits
Pineapples help digest food and build strong bones
Natural oil in oranges keeps your skin young and fresh
Watermelons help the body get rid of excess ammonia and helps you heal wounds
Cherries contain antioxidants that protect the body from cancer cells
Drinking lemon water can help cure bad breath
HEALTH TOTAL
ANJALI MUKERJEE


EASONS
EAT
EAT
OR OPTIMAL
EALTH
healthylivinghowto.com

What is the issue?

- Food is associated with risks *and* benefits
  - Focus should not only be on risk
  - Integrated analyses are needed: Risk-Benefit Assessment (RBA)



What is needed?

- RBA is being done, but there are challenges
  - Scattered expertise
  - Multidisciplinarity
  - Data and knowledge gaps
  - Incomplete methodological toolbox
  - Risk-Benefit Communication
  - More than health?

- We have to take this up together and build up RBA!

  Conclusion from EFSA sponsored workshop on RBA, Copenhagen 2017

  - Harmonised methodological tools
  - Case studies: learning by doing
  - Shared databases

All stakeholders will benefit from RBA

- Governments / authorities
  - Balanced and harmonized advise
  - Improved dietary guidelines
- Industry
  - Improved harmonized knowledge base on benefits and
  - sta
- Co
  - choices

What's needed?

- Opportunities to do RBA **case studies**
  - Proof of principle
  - Learn from them

- **Collaboration**
  - European
  - Multidisciplinary

- **Public funding**
  - Consumers are the ultimate food managers
  - Societal trust: potential conflicts of interest may kill the message

Support team

- Maarten Nauta and Morten Poulsen, DTU, Denmark
- Géraldine Boué, INRA-Secalim, France
- Jacob van Klaveren, RIVM, the Netherlands
- Matthias Greiner, BfR, Germany
- Salomon Sand, National Food Agency, Sweden
- Helga Gunnlaugsdottir, Matis, Iceland
- Inger Therese Lillegaard, VKM, Norway
- Francesco Cubadda, ISS Rome, Italy
- Paulo Alvito, INSA, Portugal
- Brecht de Vleesschauwer, WIV-ISP, Belgium
- Annemarie Pielaat, Unilever, the Netherlands

- **You!**

IMPLEMENTATION OF HEALTH TECHNOLOGY ASSESSMENT METHODOLOGY IN FOOD SAFETY RISK ANALYSIS CASE STUDIES

EFSA Risk Assessment Research Assembly (RARA) – Utrecht, 7 February 2018

János G. Pitter[1], Ákos Józwiak[2], Zoltán Vokó[1,3], Zoltán Kaló[1,3]

[1]Syreon Research Institute, Budapest, Hungary; [2]National Food Chain Safety Office, System Management and Supervision Directorate, Hungary; [3]Department of Health Policy and Health Economics, Faculty of Social Sciences, Eötvös Lóránd University, Hungary.

BACKGROUND

Food Safety Risk Analysis (RA) and Health Technology Assessment (HTA) are two different paradigms sharing multiple common features. Decision makers in both fields have the responsibility to promote the health of society deciding on intervention opportunities based on disease burden, intervention feasibility, effectiveness and cost, equity and ethical considerations. The evolution of HTA in the last two decades has resulted in the establishment and widespread use of quantitative tools to support and justify evidence-based decisions. In contrast, decision making in the food safety domain is still a qualitative process rendering ad hoc weights to all aspects considered[1].

In our previous paper[1] we proposed that **cost-utility analysis (CUA)** could better serve the priority settings in food safety risk management than the currently (rarely) applied cost-benefit analysis (CBA), considering either broad resource allocation or specific safety measure decisions. Moreover, development of **multi-criteria decision analysis** tools could help the introduction of consistent and explicit weighting among cost and health impacts, equity and all other relevant aspects[2]. **Risk sharing schemes** established in performance based agreements of health technology reimbursement decisions may also contribute to the success of food safety interventions requiring cooperation of various stakeholders[1,3].

RESEARCH IDEA

The proposed research idea is **to evaluate the added value of cost-utility analyses, MCDA, and/or risk sharing schemes in food safety risk analysis, by applying them in selected Food Safety Risk Assessment case studies.**

FORESEEN IMPACT / BENEFIT

Improve the food safety decision process in case studies
Analysis of risks and potential benefits in one framework ➢ health gains not monetized (unlike in cost-benefit analyses) ➢ a bridge between risk assessment and risk management ➢ systematic and transparent methods Better and more justifiable decision with higher societal values and gains
Smooth the implementation process of selected measures
A place for risk sharing agreements?

NEED FOR PUBLIC FUNDING

Public funding is justified by the expected public benefits, and by the marginal availability of private funds for the proposed research.

WE LOOK FOR:

- **Partners** who are involved in Food Safety Risk Assessment and are interested in the benefits of applying HTA methodology (e.g. CUA, MCDA, and/or risk sharing schemes) in **selected case studies**;
- **Funding** for the above collaborative research.

REFERENCES

[1] Pitter, J. G., Józwiak, Á. B., Martos, É., Kaló, Z., & Vokó, Z. Next steps to evidence-based food safety risk analysis: opportunities for health technology assessment methodology implementation. Studies in Agricultural Economics, 2015, 117(3), 155-161.

[2] Baltussen, R., Niessen, L. Priority setting of health interventions: the need for multi-criteria decision analysis. Cost Effectiveness and Resource Allocation, 2006, 21(4), 14.

[3] Pitter, J. G., Vokó, Z., Halmos, Á., & Józwiak, Á. Cost-utility analysis of potential campylobacter control measures in the food chain of indoor broiler chicken in the Eu. Value in Health, 2015, 18(7), A649.

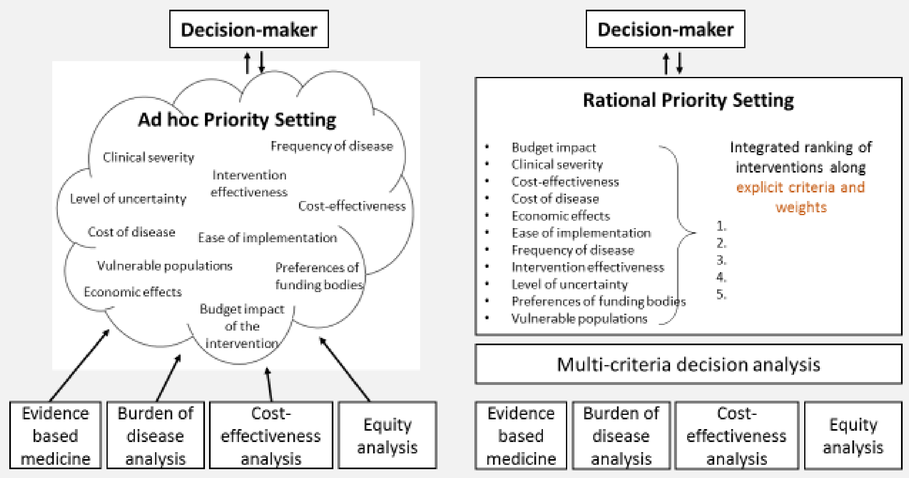
Full economic analyses in food safety risk analysis

Type of analysis	Unit of health gain	Applicability in HTA*	Applicability in food safety risk analysis
Cost-minimisation	Not specified (equal health gain)	Comparison of medical procedures with equal health gain.	Compare two measures both achieving the ALOP, or the respective FSO in a threshold approach.
Cost-effectiveness	Natural units	Comparison of medical procedures with non-equal health gain measurable in the same health dimension.	Compare two measures against the same risk in an ALARA approach.
Cost-utility	QALY	Comparison of any medical procedures.	Compare any kind of food safety measures and/ or healthcare interventions (prioritisation among health-related investments).
Cost-benefit	Monetary value	Comparison of any medical and non-medical procedures and investment options.	Prioritisation of health-related versus not health-related investments.

ALARA, as low as reasonably achievable;
ALOP, appropriate level of protection;
FSO, food safety objective;
QALY, quality adjusted life years.

Source: Studies in Agricultural Economics, 2015; 117: 155-161.

Multicriteria decision analysis (MCDA)

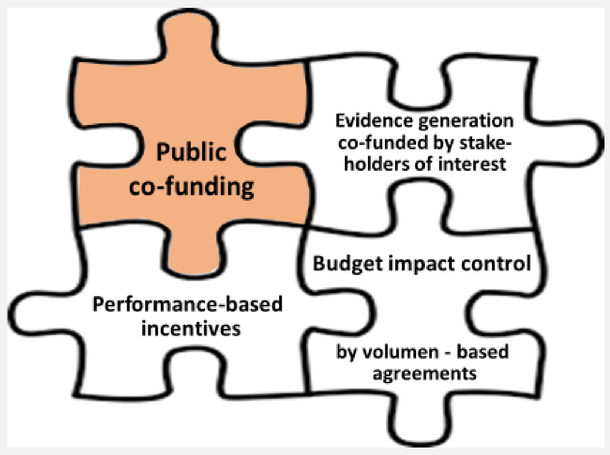


Adapted from: Baltussen R, Niessen L. Priority setting of health interventions: the need for multi-criteria decision analysis. Cost Eff Resour Alloc. 2006. 21;4:14.

Risk sharing schemes across stakeholders

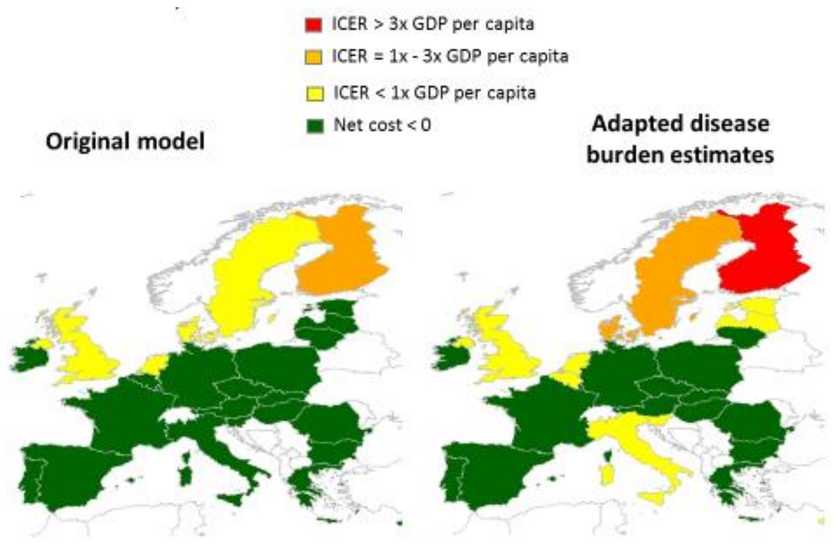
- Uncertainty in expected benefits / in assumptions on disease burden, efficacy of interventions, real-world uptake, etc.
- Costs and expected benefits occur at different stakeholders;

⇒ **Smooth the implementation phase by risk sharing schemes?**
- public co-funding
- performance-based co-payments
- public budget impact control

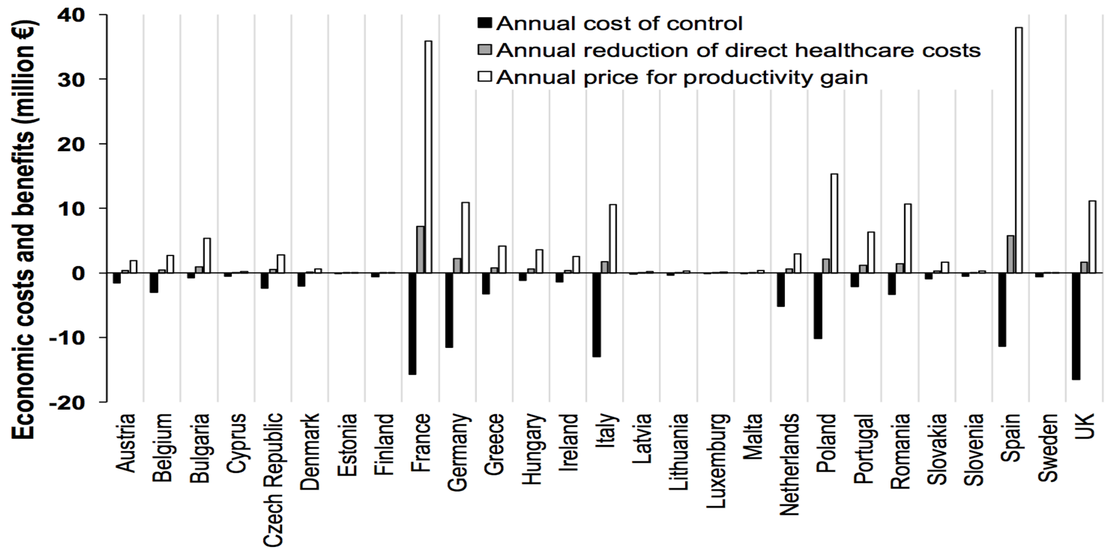


EXAMPLE:

CRITICAL REVIEW OF A COST-UTILITY ANALYSIS OF AN AVAILABLE CAMPYLOBACTER CONTROL STRATEGY OF GOOD CONSUMER ACCEPTANCE IN THE BROILER CHICKEN FOOD CHAIN



EU-27 net cost	-353 million EUR / year	-85 million EUR / year
EU-27 health gain	-67 300 DALY / year	26 400 QALY / year



HEALTH IMPACTS: QALY VERSUS DALY ESTIMATES

	DALY	QALY
Changes in life expectancy	Lost years are assumed	Gained years are directly observable
Disability weight determination	Expert panel preferences	Societal preferences (tax payers)
Use in HTA in the EU	Marginal	Extensive
Explicit CEA threshold	In theory (WHO)	In practice (in some countries; alone or as part of MCDA)

Implementation of health technology assessment methodology in food safety risk analysis case studies

János G. Pitter, Ákos Jóźwiak, Zoltán Vokó, Zoltán Kaló

Development of standard risk-benefit assessment methods of foods, Risk Assessment Research Assembly, Utrecht, 2018.

syreon Research Institute

Research idea

Food Safety Risk Analysis	Health Technology Assessment
Still a qualitative process rendering *ad hoc* weights to all aspects considered; Apparent lack of risk sharing schemes in practice.	Quantitative tools to support and justify evidence-based decisions: - Full economic analyses - Multicriteria Decision Analysis (MCDA) Established risk sharing schemes across stakeholders

In both fields, policymakers decide on intervention opportunities based on **multiple competing aspects***, with an **impact on multiple stakeholders**

⇒ **investigate the applicability of established HTA tools and practices in Food Safety Risk Analysis case studies**

*disease burden; intervention feasibility, effectiveness, cost; stakeholder interests; equity and ethical considerations; etc.

Full economic analyses in food safety risk analysis

Type of analysis	Unit of health gain	Applicability in HTA*	Applicability in food safety risk analysis
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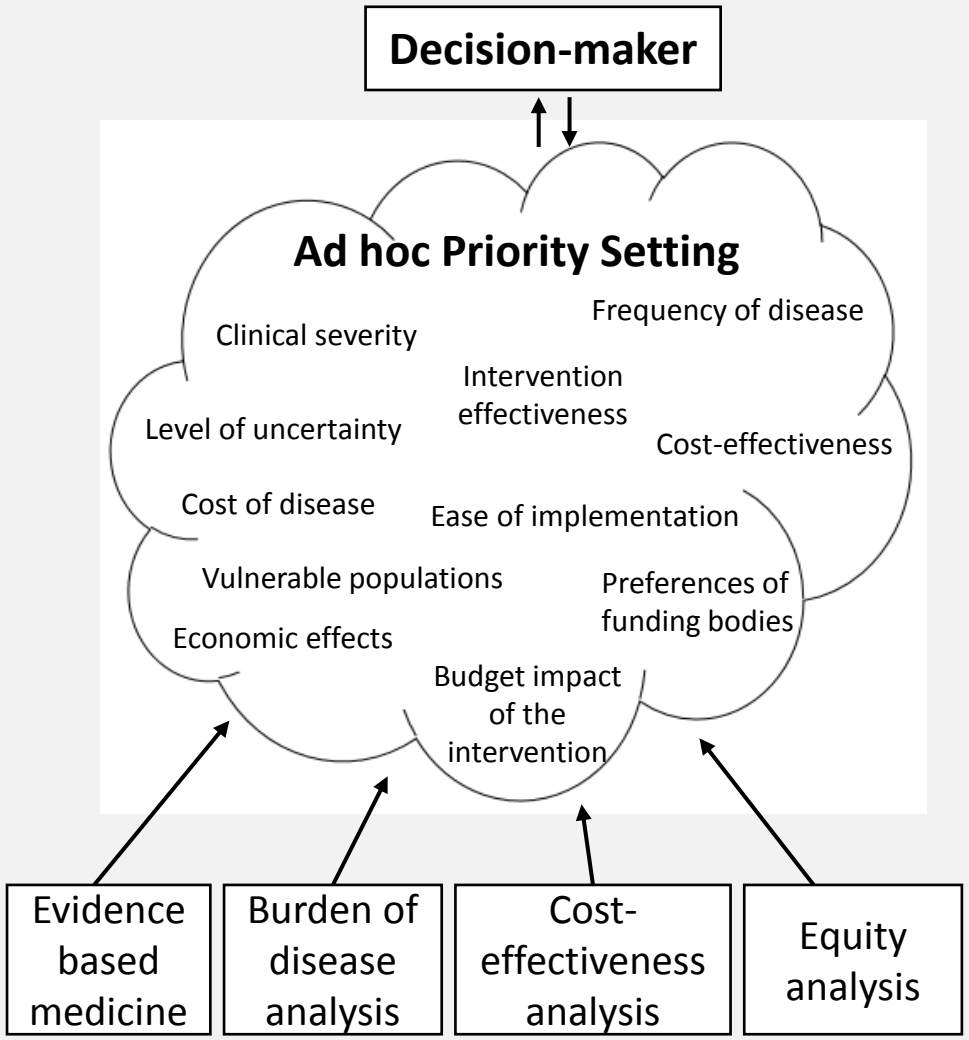

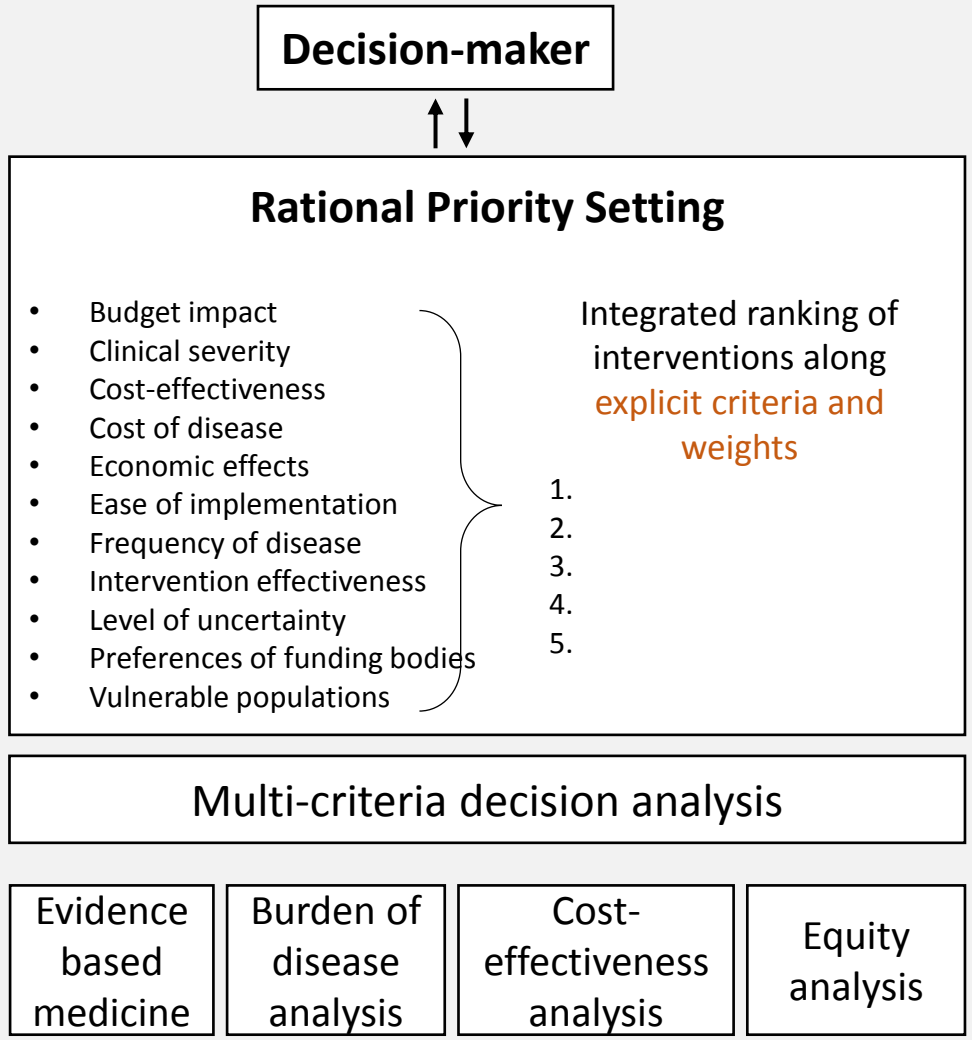

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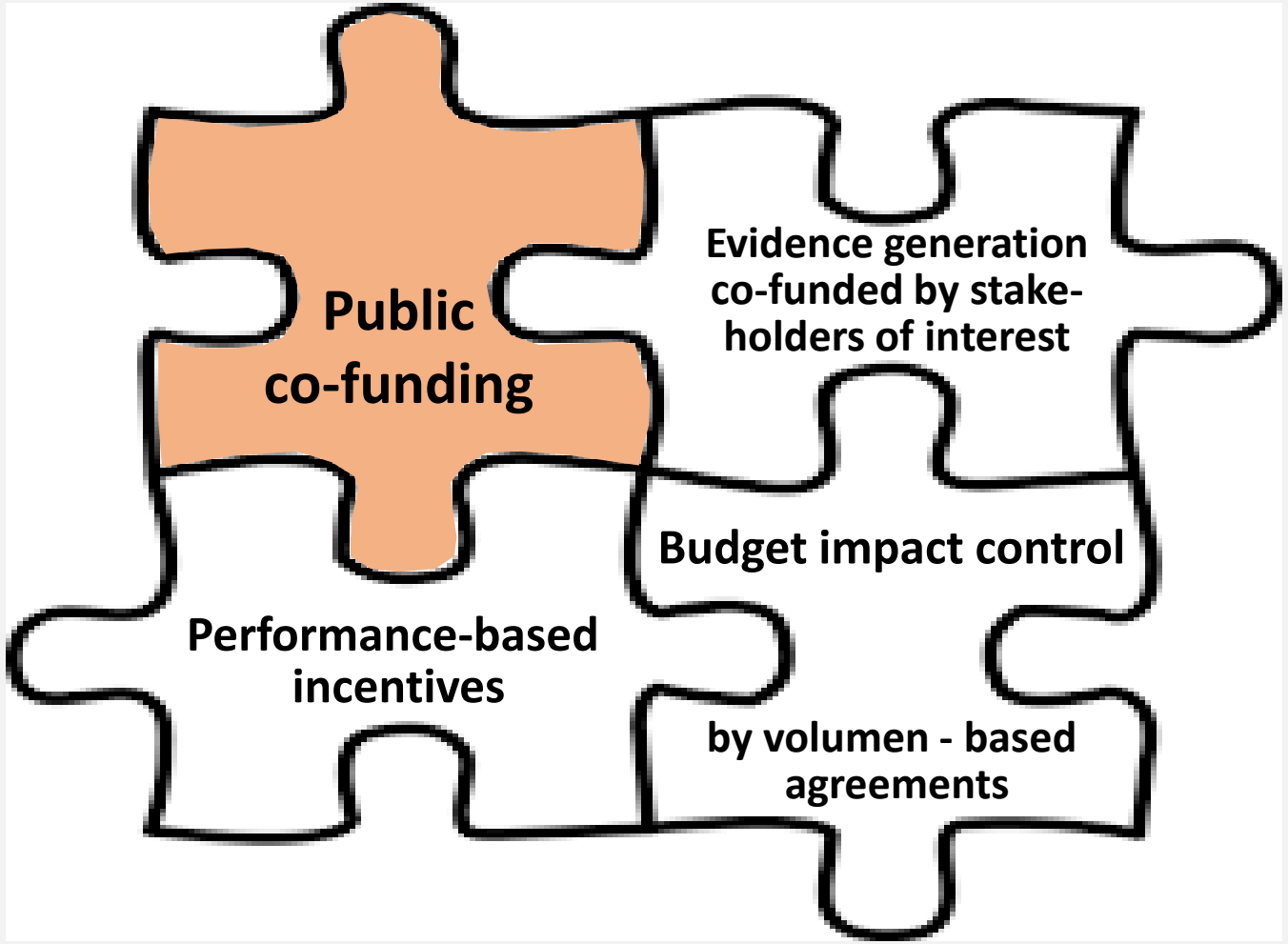

Foreseen impacts/benefit

Improve the food safety decision process in case studies
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Smooth the implementation process of selected measures
A place for risk sharing agreements?

We seek for:

- **Partners** who are involved in food safety risk assessment and are interested in the benefits of applying HTA methodology (e.g. cost-utility analyses, MCDA development, and/or risk sharing schemes) in **selected case studies**

- **Public funding** for the above collaborative research

Public funding is justified by the expected public benefits, and by the marginal availability of private funds for the proposed research.

THANK YOU FOR YOUR ATTENTION!

Comparing apples and oranges: A generic risk-benefit assessment approach to determine optimal beneficial and safe dose levels of food intake

Jolanda H.M. van Bilsen, PhD, ERT

TNO, Zeist, the Netherlands; j.vanbilsen@tno.nl

TNO innovation for life

INTRODUCTION

To date there is no methodology available to decide whether beneficial effects of a food (additive) outweigh possible side effects. Therefore, it would be extremely helpful to address this issue by developing a generic, pragmatic, flexible and science-based risk-benefit assessment approach.

THE RISK-BENEFIT ASSESSMENT APPROACH

Recently, we adapted the risk-benefit approach published by Renwick et al. (2004) and Krul et al., (2016), to develop a generic framework that is fit for the risk-benefit assessment of immune nutrition. To this end, all possible hazardous and beneficial effects were redefined into generic severity-based health effect categories (Table 1). The incidence at which health effects in each category may be considered 'acceptable' form the basis to calculate the optimal balance between optimizing a beneficial effect while complying to safety standards (Figure 1). This way, the approach enables the comparison and weighing of the risks and beneficial effects of food intake.

IMPACT ON FOOD SAFETY AND PUBLIC HEALTH

This novel risk-benefit assessment approach enables risk assessors to take the multitude of different types of data covering toxicity and efficacy studies into account, by ranking and weighing all available data. Ultimately, this assessment will form the basis to derive the optimal dose levels of intake.

NEXT STEPS

A process needs to be developed to i) work out the approach, ii) test and validate it in case studies, iii) discuss the approach and validation outcomes with stakeholders and iv) to identify further actions needed to implement it.

REFERENCES

– Renwick AG et al., Risk-benefit analysis of micronutrients. Food Chem Toxicol. 2004 Dec;42(12):1903-22. DOI: 10.1016/j.fct.2004.07.013
– Krul L et al., Quantifiable risk-benefit assessment of micronutrients: from theory to practice. Crit Rev Food Sci Nutr. 2017 Nov 22;57(17):3729-3746. DOI: 10.1080/10408398.2016.1162765

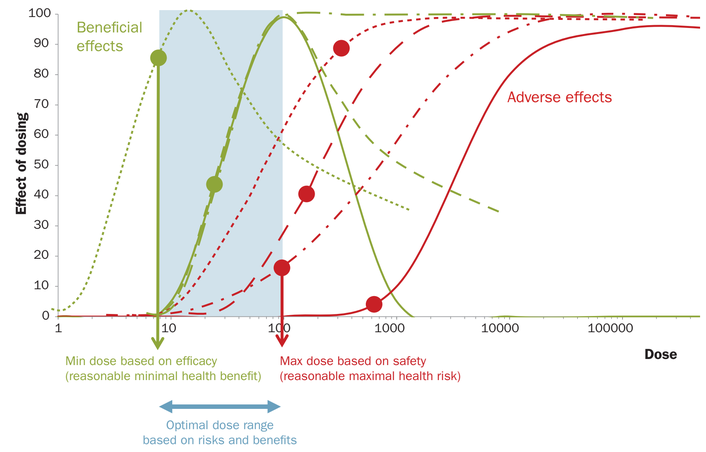


***Figure 1**. Conceptual approach for risk-benefit assessment of nutritional interventions. Dose-response curves for beneficial (green) and adverse (red) effects are used to weigh the benefits and risks of nutritional interventions based on the reasonable/acceptable incidences of the risks and benefits (big dots), resulting in an optimal dose range of acceptable intakes.*

FUNDING

This work was supported financially by the Dutch Ministry of Economic Affairs, as part of the 'Toeslag voor Topconsortia voor Kennis en Innovatie (TKI's)' program on Agriculture and Food, and by Danone Nutricia Research.

ACKNOWLEDGEMENT

The author is a member of the Utrecht Center for Food Allergy (www.ucfa.nl) and the TNO Shared Research Program Food Allergy, a non-profit open innovation initiative funded by its participants and Dutch Governmental TNO Research Investment Funds.

NUTRICIA RESEARCH | DANONE NUTRICIA RESEARCH

SRP food allergy

CFA UTRECHT CENTER FOR FOOD ALLERGY

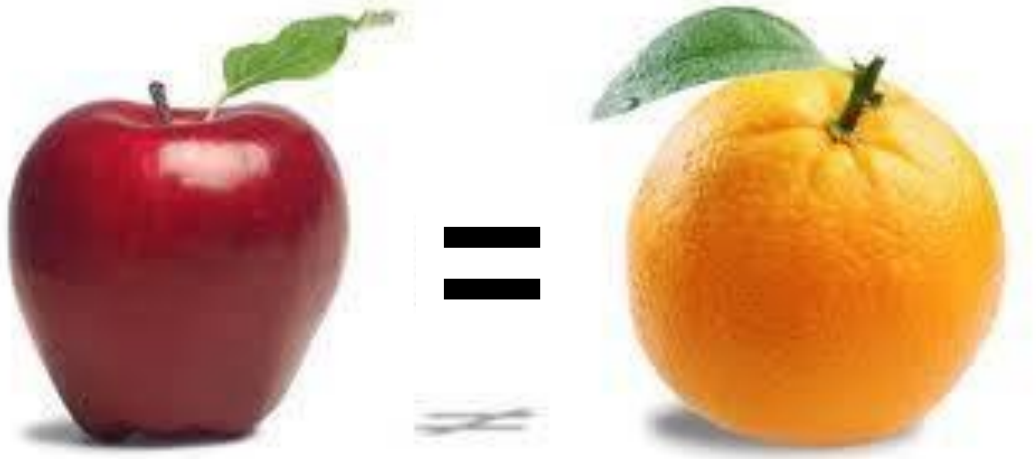
	Health effects	'Acceptable' incidence
1	Biochemical changes within or outside the homeostatic range and without known consequences	1/10
2	Biochemical changes outside homeostatic range which represent a biomarker of potential adverse effects	1/100
3	Clinical symptoms indicative of a minor but reversible change	1/1,000
4	Clinical symptoms of significant but reversible effects	1/10,000
5	Clinical signs indicative of significant but reversible organ damage	1/100,000
6	Clinical signs indicative of irreversible organ damage	1/1,000,000

***Table 1.** Preliminary classes of health effects and their proposed acceptable incidences based on Renwick et al., (2004) and Krul et al., (2017).*

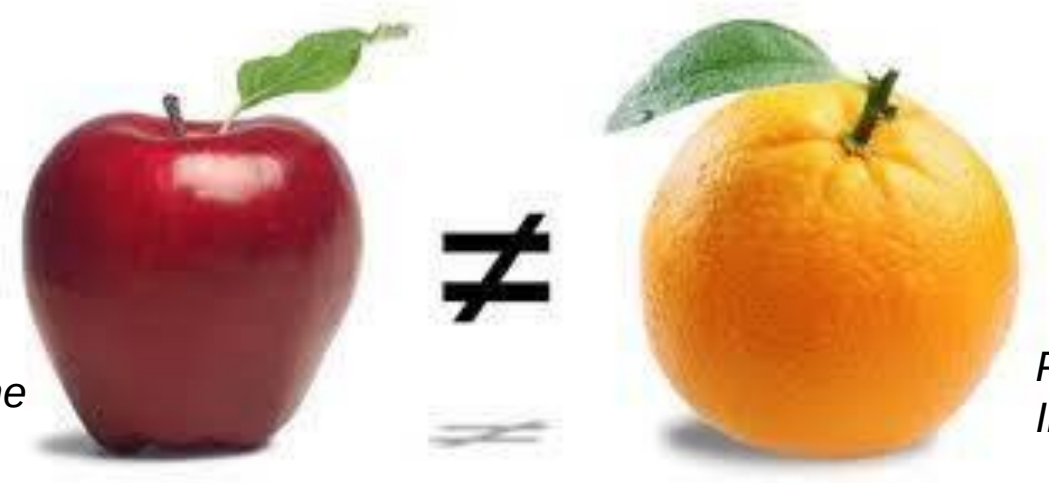
COMPARING APPLES AND ORANGES

A GENERIC RISK-BENEFIT APPROACH TO DETERMINE OPTIMAL DOSE OF FOOD INTAKE

Jolanda van Bilsen, PhD, ERT



RISK ASSESSORS:
A COLLECTION OF SAFETY AND EFFICACY DATA



Belly ache

Safety

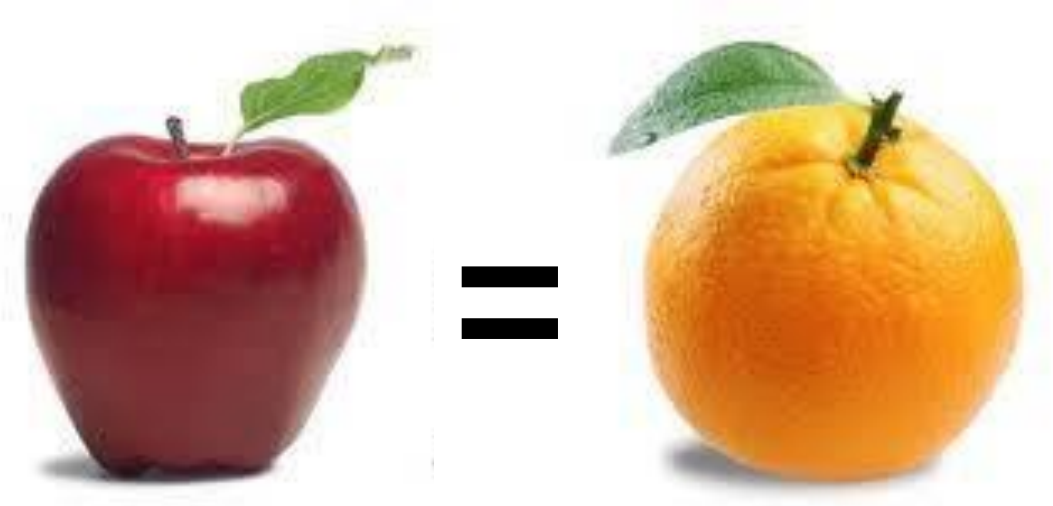
Efficacy

Protection against Influenza infection

ISSUE:
WHAT IS OPTIMAL EXPOSURE DOSE BECAUSE IT IS UNKNOWN HOW TO COMPARE THOSE TWO ENTITIES?

SOLUTION:

Redefine all possible hazard and beneficial effects into generic severity-based health effect categories



Safety = Efficacy

PRELIMINARY CLASSES OF HEALTH EFFECTS AND ACCEPTABLE INCIDENCES

	Health effects	'acceptable' incidence
1	Biochemical changes within or outside the homeostatic range and without known consequences	1/10
2	Biochemical changes outside homeostatic range which represent a biomarker of potential adverse effects	1/100
3	Clinical symptoms indicative of a minor but reversible change	1/1,000
4	Clinical symptoms of significant but reversible effects	1/10,000
5	Clinical signs indicative of significant but reversible organ damage	1/100,000
6	Clinical signs indicative of irreversible organ damage	1/1,000,000

Cytokines

Calprotectin

Belly ache

Diarrhea

Pneumonia

Tumor

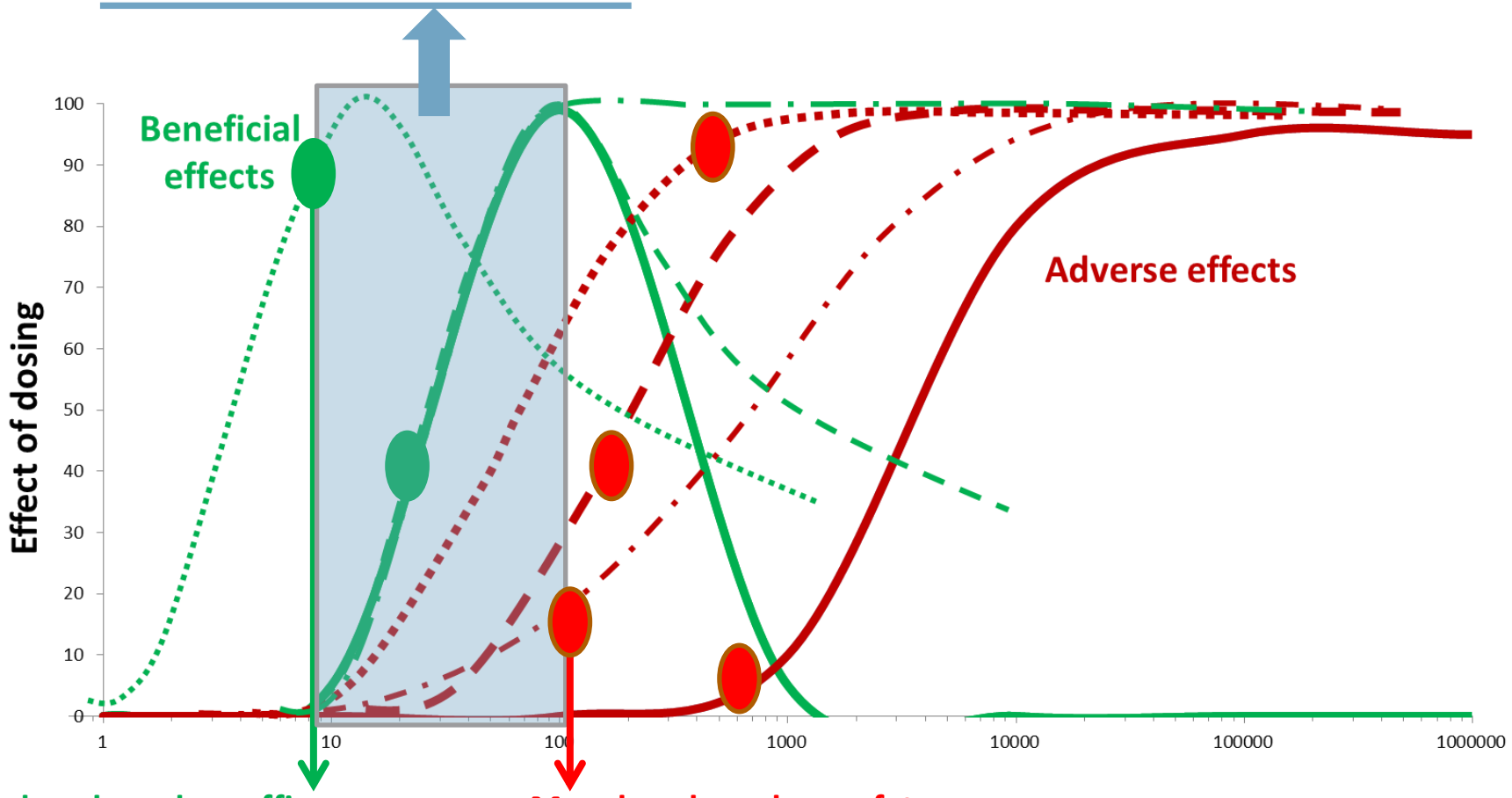
Renwick et al., 2004
Krul et al., 2017

RESULT FORMS THE BASIS TO CALCULATE THE OPTIMAL BALANCE BETWEEN BENEFICIAL AND ADVERSE EFFECTS

HOW TO COMPARE APPLES AND ORANGES?

TNO innovation for life

CONCEPTUAL APPROACH:
ACCEPTABLE INCIDENCES TO DETERMINE OPTIMAL DOSE RANGE



Min dose based on efficacy
(reasonable minimal health benefit)

Max dose based on safety
(reasonable maximal health risk)

Work in progress

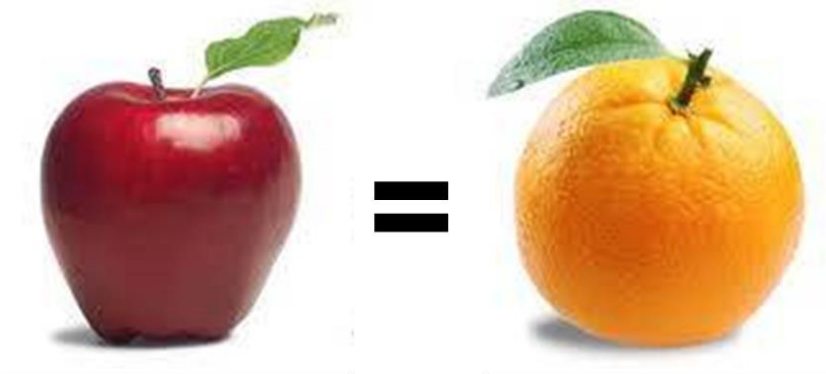
CONCLUDING

- Generic, pragmatic, flexible and science-based risk-benefit assessment approach
- All available data can be taken into account
- Calculates optimal balance between optimizing beneficial effects while complying to safety standards

WHAT IS STILL NEEDED?

- Funding for:
  - Testing/validation in case studies
  - Discuss with stakeholders
  - Implementation

THANK YOU FOR YOUR ATTENTION



- Take a look:
  - TIME.TNO.NL

TNO innovation for life

SRP food allergy

www.srpfoodallergy.com

CFA
UTRECHT CENTER FOR FOOD ALLERGY

j.vanbilsen@tno.nl

Implementing Network Science and Mathematical Modelling Tools into European Food Chain Safety Decision Making

Ákos Jóźwiak, NÉBIH, Hungary

BACKGROUND

- **Increasing volume and complexity** of food production and trade pose an increasing challenge to governmental stakeholders in their efforts to protect consumers from food-born disease outbreaks, food fraud or even bioterrorist attacks.
- On the other hand, **exponential growth of data available** on food products and commodity chains provides the potential of better informed decisions.
- Network science and mathematical modelling – as **decision support** tools – may have an important role in enhancing the safety of the consumers and the supply chain itself.

PROBLEM

- Raw trade and movement data are in the national domain: **many different data systems** (structure & content) co-exist
- **No common** network analysis nor epidemiological simulation **framework** or software
- Data analyses, simulations, visualizations are done mainly at a national level with the help of **ad hoc data analysis** scripts
- **Sharing** methodologies and results **is hard**
- '**Playing around**' the data by food chain science experts is **particularly hard** without a 'playground'

RESEARCH IDEA

- Food chain is a **complex embedded network** of different entities and/or processes
- Spreading of different hazards is happening via these **networks** and via **spatial spreading**

1. Using network analysis and spatial spreading simulations would provide a **better insight** into the epidemiological and other food safety processes
2. It would allow for a **better decision making** for authorities and other stakeholders

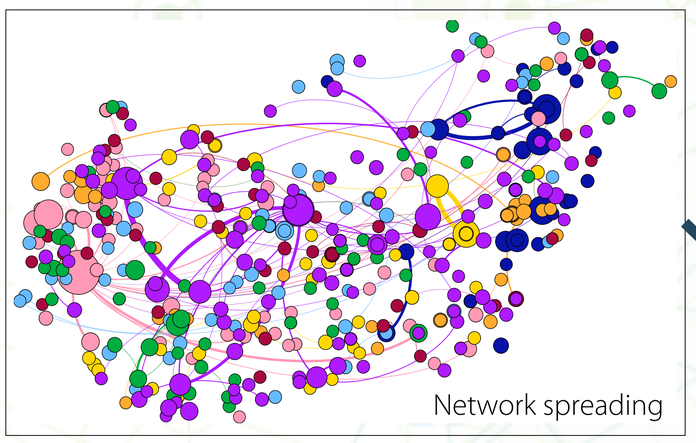
IMPACT

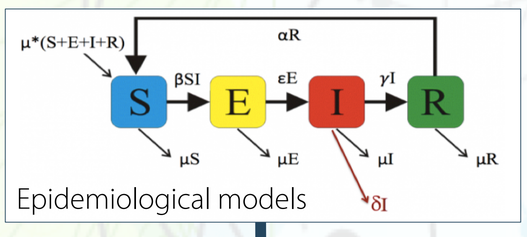
1. Possibility for a **quick** and for a **deep insight** into the connection of various entities of the food chain
2. More **profound disease modelling** possible
3. Subtle changes of the animal trade and movement network and their impact could be detected, making an **earlier intervention** possible
4. Possibility for **connecting animal**-related networks to **food** networks and **human** population network

SOLUTION

1. Code to data → framework to data
   Development of a static and dynamic network analysis framework for analysing various data sources
2. Epidemiological spreading playground
   Development of a framework capable of simulating different epidemiological situations (network based + spatial spreading)
3. Network based food chain safety playground
   Development of a framework capable of tracing and simulating spreading of various hazards on inter-connected networks

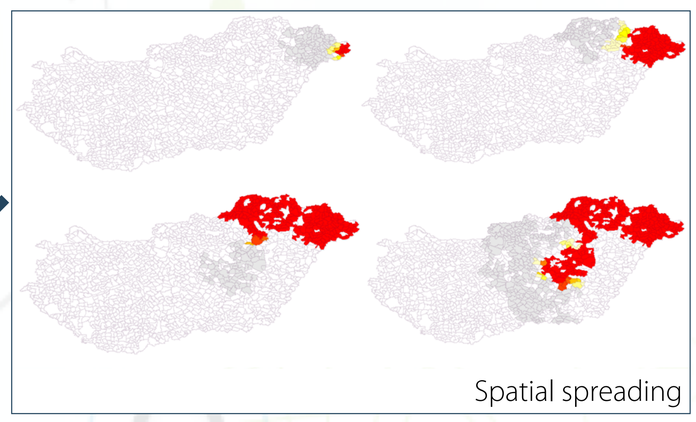
EXAMPLE


Network spreading



Epidemiological models

Develop a methodological and user framework for combining a network based disease spreading with a spatial spreading


Spatial spreading

WE SEEK FOR...

- **Partners** involved in animal disease modelling and interested in applying network analysis. Already expressed interest:
  Austria (AGES), Croatia (HAH), Denmark (KU), Finland, France (INSERM, INRA), Germany (BfR, TU, FU, FLI), Greece (EFET), Ireland (UCD), Italy, Netherlands (RIKILT Wageningen UR), Poland (NIZP-PZH), Romania (DJU), Slovenia (UL - Veterinary Faculty), Spain, Sweden (LU), Switzerland, UK
- **Funding** for the **collaborative research**
- **Funding** for developing a network analysis based epidemiological modelling **tool**

Contact
Ákos Jóźwiak @jozwi
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EFSA Risk Assessment Research Assembly (RARA) – Utrecht, 7 February 2018

nébih

Implementing **Network Science and Mathematical Modelling Tools** into European Food Chain Safety Decision Making

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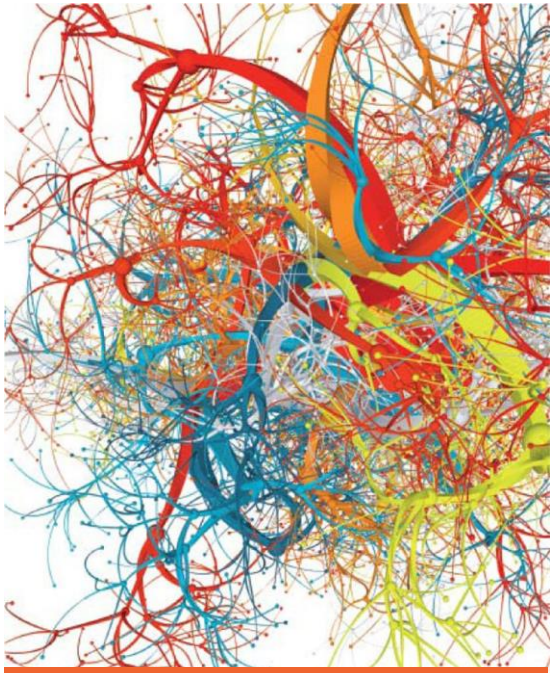
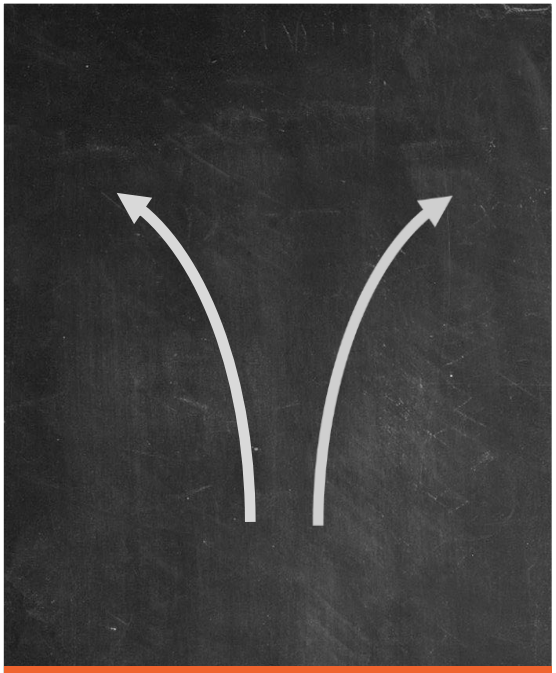
NÉBIH, Hungary



Increasing
volume & complexity
of the food chain

Growth of the amount
of **data available**
for analysis



Better evidence-based
decision making?

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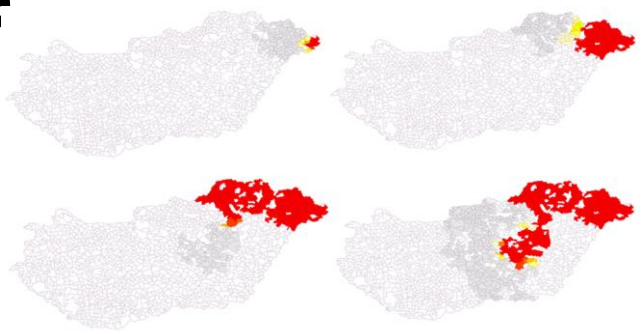
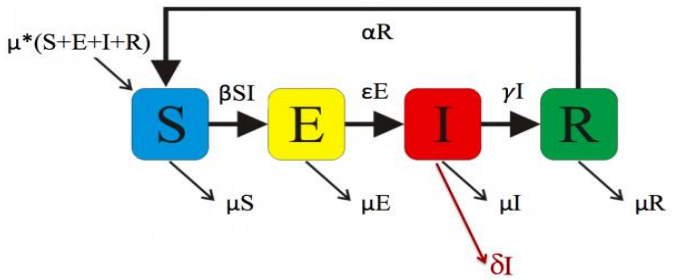
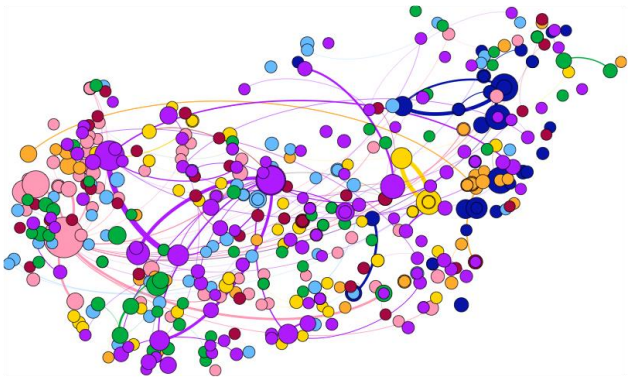
gleamviz.org

An **Example**







Impact

1. Possibility for a **quick** and for a **deep insight** into the connection of various entities of the food chain

2. More **profound disease modelling** possible

3. Subtle changes of the animal trade and movement network and their impact could be detected, making an **earlier intervention** possible

4. Possibility for **connecting animal**-related networks to **food** networks and **human** population network

We **seek for**

Partners involved in animal disease modelling and interested in applying network analysis

Already expressed interest:

- Austria (AGES)
- Croatia (HAH)
- Denmark (KU)
- Finland
- France (INSERM, INRA)
- Germany (BfR, TU, FU, FLI)
- Greece (EFET)
- Ireland (UCD)
- Italy
- Netherlands (RIKILT Wageningen UR)
- Poland (NIZP-PZH)
- Romania (DJU)
- Slovenia (UL - Veterinary Faculty)
- Spain
- Sweden (LU)
- Switzerland
- UK

Funding for the **collaborative research**

Funding for developing a network analysis based epidemiological modelling **tool**

Thank you!

Contact

Ákos Jóźwiak

NÉBIH, Hungary

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@jozwi

Microbiological and chemical risk assessment in bivalve mollusks. Environmental and sanitary linkage

Mario Latini*, Francesca Barchiesi*.
Istituto Zooprofilattico Sperimentale dell'Umbria e delle Marche ''Togo Rosati'', Perugia (Italy)

Description of the research idea

- ✓ Both uman/animal waste and environmental conditions represent risk factors for the contamination of mollusc production areas.
- ✓ Therefore, food safety legislation and international guidelines require collecting both sanitary and environmental data.
- ✓ Currently, that information is gathered individually.
- ✓ The aim of our proposal is to build a network where to share knowledge and information
- ✓ A unique database where sanitary and environmental data is united is necessary.

Foreseen impact/benefit

- ✓ A unique database including both sanitary and environmental data permits to have at disposal all the information necessary to evaluate the risk of shellfish production areas contamination.
- ✓ The output will be a more efficient surveillance scheme and a safer model for product control.

Necessity of public funding

- ✓ This idea needs to be sustained through public funding, because no immediate private producers advantages can be expected.
- ✓ Due to a better surveillance scheme, adapted to different shellfish and fish products, will provide benefit to private producers in terms of product compliance and less monitoring pressure.

What is necessary to make the idea happen

- ✓ In order to relize this idea it is necessary to have different expertises: microbiologists, chemists, oceanographers, meteorologists, epidemiologists, statisticians, computer scientists with experience in GIS and marine biologists.
- ✓ In addition public funds are requested in order to carry out the project over a period of minimum 3 years to be able to obtain statistically significant data.

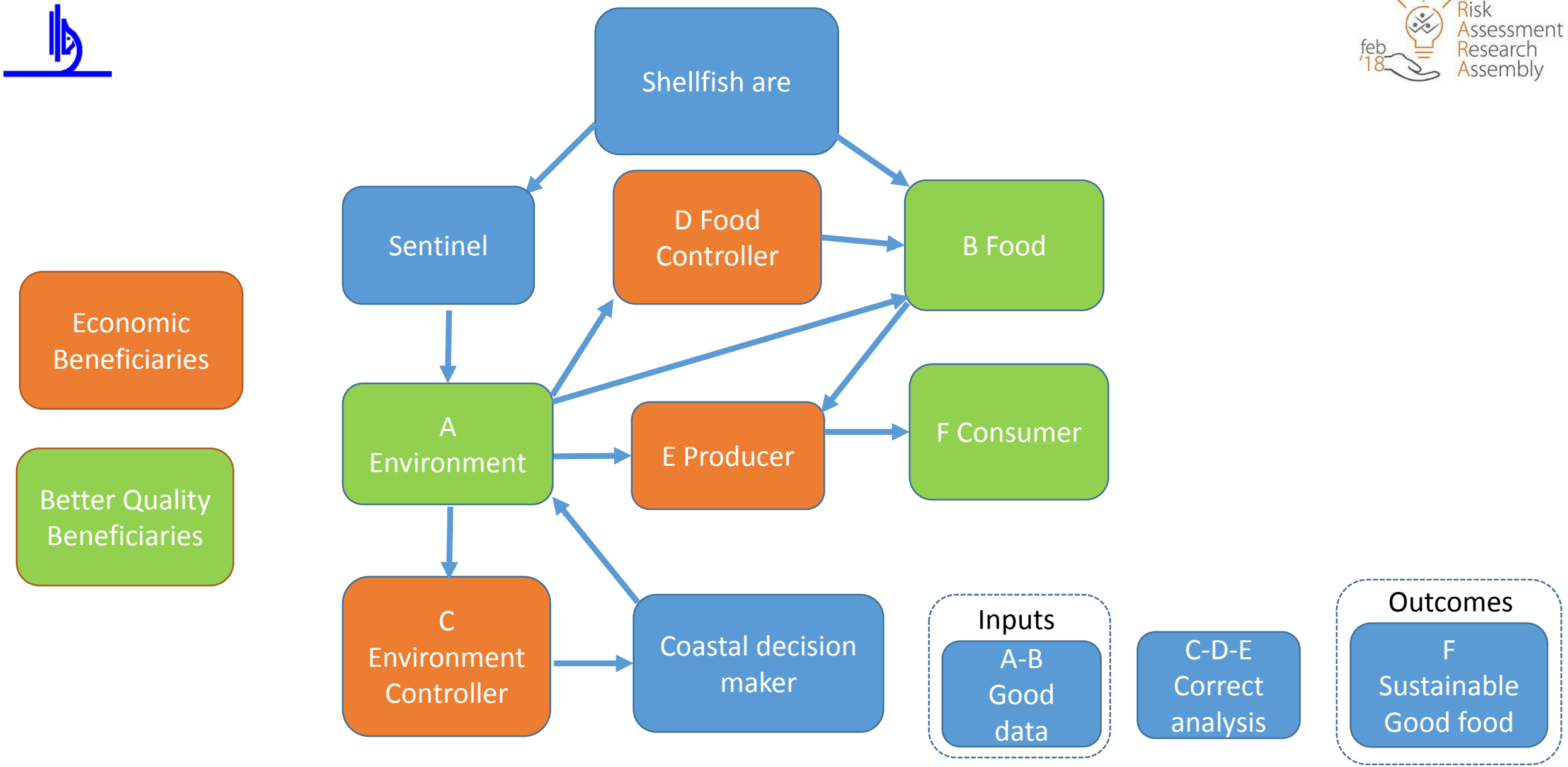
Microbiological and chemical risk assessment in bivalve mollusc. Environmental and sanitary linkage

Mario Latini – Francesca Barchiesi
LNR shellfish control (Italy)
m.latini@izsum.it

ENVIRONMENT AND HEALTH

Risk Assessment Research Assembly feb '18

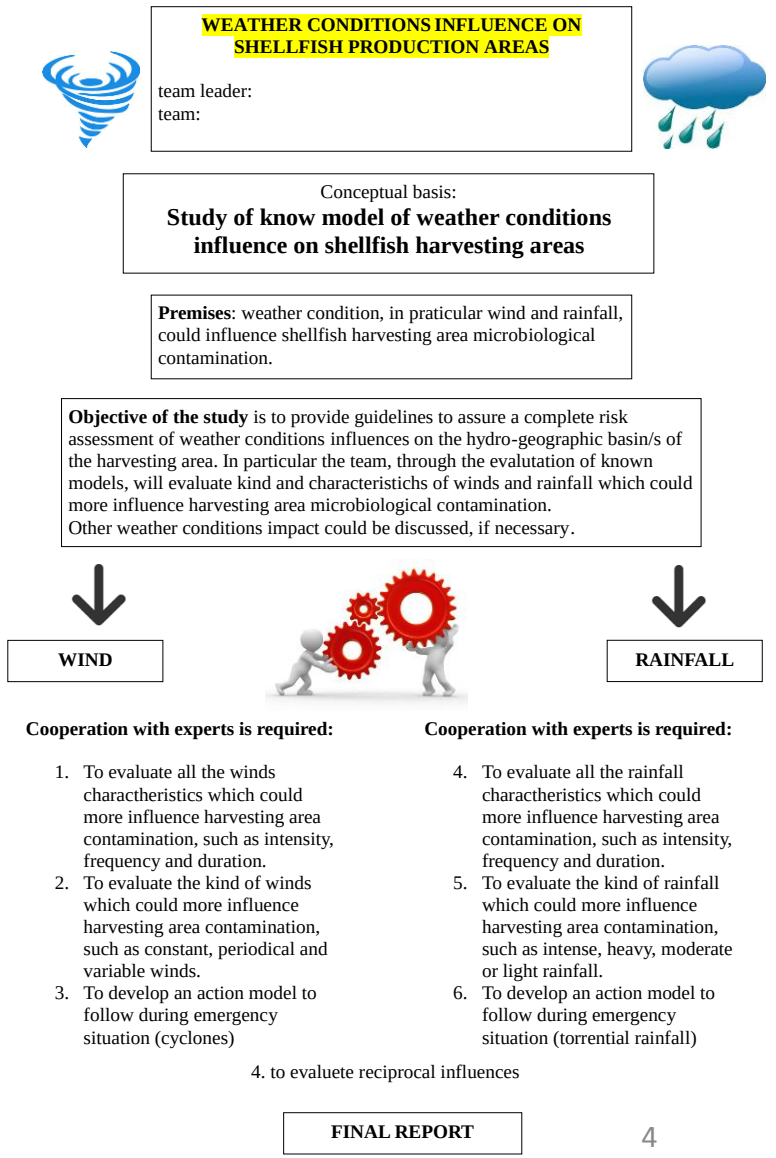
ARE THEY LINKED THROUGH FOOD?	**Of course they are**
AND WHAT ABOUT SHELLFISH?	**Wrong..ish question**
WHAT ABOUT ENVIRONMENT WHERE SHELLFISH GROW?	**Right question, no olistic control**
WHAT IS WRONG IN CONTROL?	**Dataset building and studying**
WHAT IS WRONG IN DATASET BUILDING AND STUDYING?	**Built as photo, no cooperation in studying**
WHAT DOES IT MEAN «BUILT AS PHOTO»?	**Environment is a movie, same picture can be in different movies**
WHAT IS YOUR SUGGESTION?	**Network to model a database for an EFFICIENT control**


Shellfish are
Sentinel
D Food Controller
B Food
Economic Beneficiaries
A Environment
E Producer
F Consumer
Better Quality Beneficiaries
C Environment Controller
Coastal decision maker
Inputs
A-B Good data
C-D-E Correct analysis
Outcomes
F Sustainable Good food

WHO YOU NEED?

Veterinarians
Biologists
Oceanographers
Meteorologists
Statisticians
Epidemiologist
GIS experts

RISK ASSESSORS



Why this idea **needs** to be funded from the public sources?

- **Private sector does not have immediate economic benefit**

- **Conflit of interest**

Effects of acceptance criteria on exposure and public health

Pirkko Tuominen and Johanna Suomi

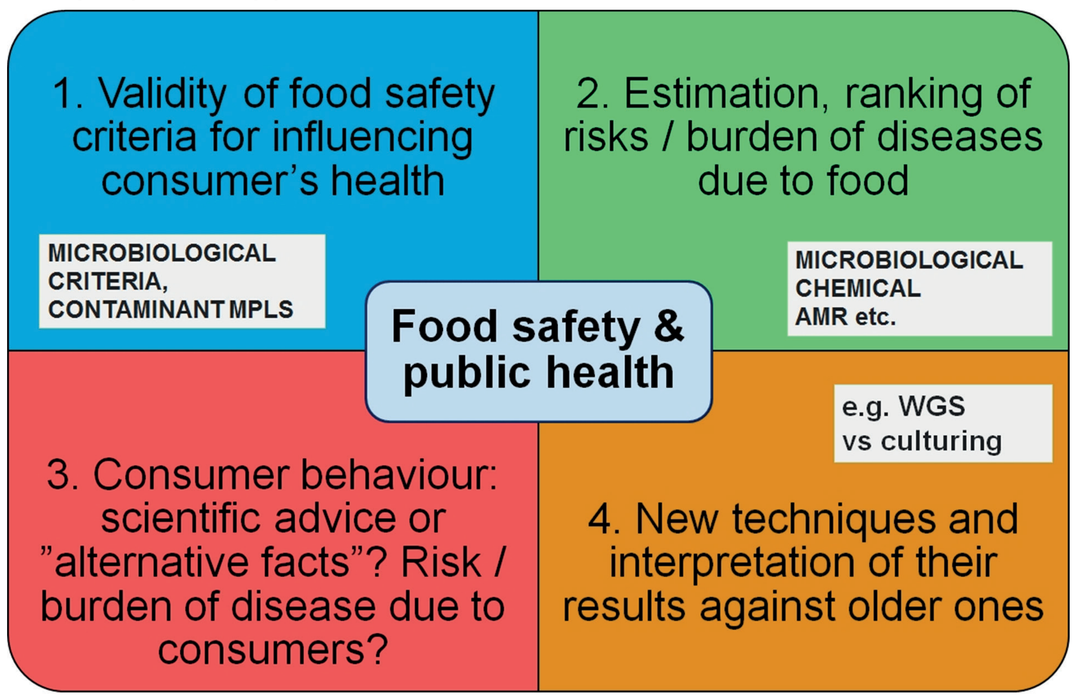
Finnish Food Safety Authority Evira, Risk Assessment Research Unit, Mustialankatu 3, FI-00790 Helsinki, Finland

Research idea

Do criteria in food safety management programmes influence consumer's health? Are the targets justified and reasonable? Or are they costly measures with little effect?

Studies inspecting EU-wide outcomes and legislation may dismiss national/regional problems, which may yet have high impact at national level. Therefore national level studies with several MSs are essential.

Our proposed approach is fourfold:



1. *We intend to assess the validity of the set criteria and control options and make proposals of ways to improve their efficacy. The studied criteria, e.g. microbe criteria or contaminant maximum levels, may concern either raw materials or products. Are the criteria set for the most important sources for the hazards and what is their effect on the exposure? Do the criteria produce desired public health outcomes? How can we verify the fulfillment of these goals?*

2. *We will develop data analytical tools for timely updating of assessments with accumulating evidence from open access data (if available). We will estimate, compare and rank the population risks or similar metrics towards assessment of burden of diseases due to food. Thus it is possible to identify the most important microbiological and chemical foodborne hazards. The study will also include expanding risks on the food safety and public health, most of all antimicrobial resistance.*

3. *For improvement of public health, not only legal criteria but also the behaviour of consumers is important. We will therefore investigate the effects of food risk perceptions and dietary advice to find out if consumers are aware of the recommendations and if they follow them or alternative information. Health, social and economic impacts will also be studied.*

4. *Use of results of new laboratory technologies and older methods (e.g. whole genome sequencing vs. culturing) need correspondence adjustment. Thus, results from previous and current years can be interpreted and trends noticed.*

Impacts

Lowering occurrence levels is costly. This research would provide **information how to focus efforts for maximum effect**, thus giving **better outcome for same cost**.

Evira
Finnish Food Safety Authority

Who will benefit?

1. **Decision makers** → information for improving acceptance criteria
2. **Public health sector** → improved public health, decreased health related costs
3. **Food production sector** → better value for food safety related costs/ decreased costs

Why public funding?

Large, multidisciplinary studies are often outside bounds of national budgets and fall between traditional funding sources.

Independence of risk assessment limits possible sources of non-public funding.

Public benefits from risk ranking and identifying criteria with little / great effect on public health

→ decreased human suffering
→ decreased control and public health costs.

What is needed?

1. **Funding** to gather and process data as well as fund researchers.
   - 5 M€ (including indirect costs) would allow Finland to gather and analyse data for studying all four areas. Additional funding for partners from other MSs will depend on number of partners.
2. **Multidisciplinary approach** at national level
   - Finland has a multidisciplinary collaboration group interested in the project idea
   - Approach includes: From exposure to burden of disease; Costs; Consumer behaviour; Development of a data-based model for criteria and health effect evaluation.
3. **Data** on occurrence and food consumption for specific set of hazard-food combinations, preferably open data. Results for correspondence adjustment.
4. **Extended collaboration** and/or interaction with additional partners for deeper and wider view of the problem
   - Risk ranking collaboration of Finnish Food Safety Authority Evira's Risk Assessment Research Unit with Swedish National Food Agency (RAA project) to be continued
   - Pilot project in Finland beginning
   - Other partners from other MSs with additional expertise?

Contacts at RARA

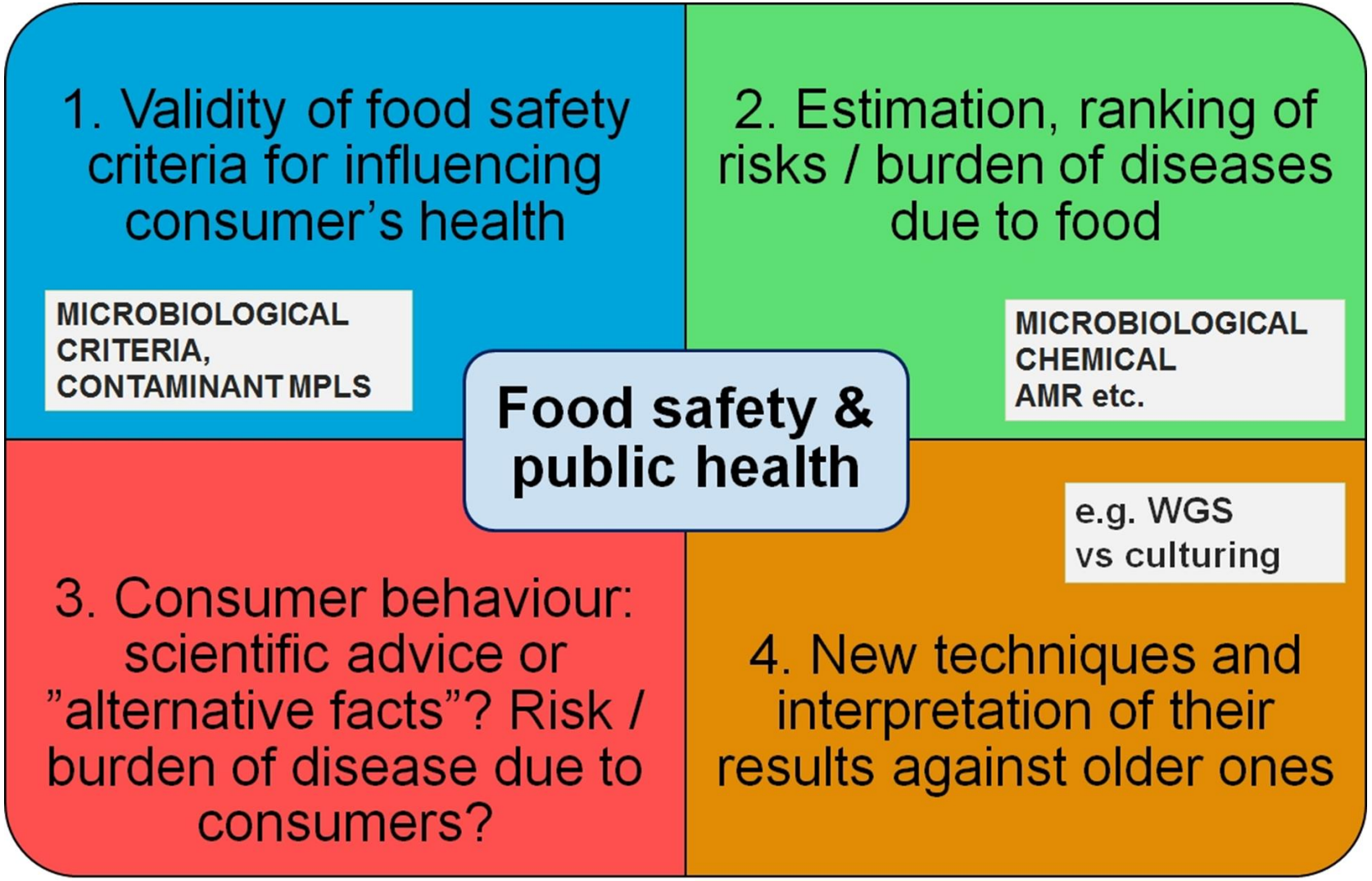
Pirkko Tuominen, Professor, Head of Risk Assessment Research Unit
(pirkko.tuominen@evira.fi)

Johanna Suomi, Assoc.Prof, PhD, Senior researcher
(johanna.suomi@evira.fi)

Kirsi-Maarit Siekkinen, EFSA Focal Point Finland
(kirsi-maarit.siekkinen@evira.fi)

Effects of acceptance criteria on exposure and public health

Johanna Suomi & Pirkko Tuominen
Risk Assessment Research Unit
Finnish Food Safety Authority Evira, Finland


1. Validity of food safety criteria for influencing consumer's health
MICROBIOLOGICAL CRITERIA, CONTAMINANT MPLS
2. Estimation, ranking of risks / burden of diseases due to food
MICROBIOLOGICAL CHEMICAL AMR etc.
Food safety & public health
3. Consumer behaviour: scientific advice or "alternative facts"? Risk / burden of disease due to consumers?
4. New techniques and interpretation of their results against older ones
e.g. WGS vs culturing

WHY?

Better value for same cost

- Assessing effects of food safety criteria(* on public health → focusing efforts on high effect measures
  - Decreased public health costs and control costs
  - National studies … EU-averages may dismiss nationally important problems
- Results benefit (1) decision makers, (2) public health sector and (3) food producers
- … but not feasible without public funding ☹

(* food safety criteria = contaminant MPLs, microbial criteria etc.

HOW?

- Public funding for
  - Researchers
  - Gathering & processing data
  - 5 M€ (incl indirect costs) for FI, collection and analysis of reasonably large data

- Other necessary ingredients are
  - Multidisciplinary study (FI group ready + SE, partners from other MSs?)
  - Open data (occurrence & consumption) on hazard-food combos

European Food Safety Authority

Risk Assessment Research Assembly feb '18

Harmonization and improvement of a decision-support tool for microbial risk assessment

Arícia Possas, Fernando Pérez-Rodríguez

GOBIERNO DE ESPAÑA MINISTERIO DE SANIDAD, SERVICIOS SOCIALES E IGUALDAD aecosan agencia española de consumo, seguridad alimentaria y nutrición

ceiA3 campus de excelencia internacional agroalimentario

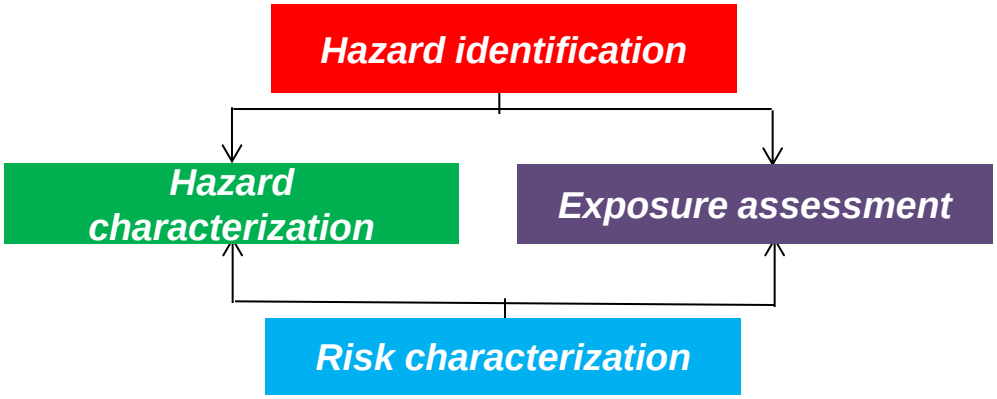
UNIVERSIDAD DE CÓRDOBA

IRTA RECERCA I TECNOLOGIA AGROALIMENTÀRIES

Background

Risk Assessment

"Framework for systemic and objective evaluation of all available information pertaining to a foodborne hazard."



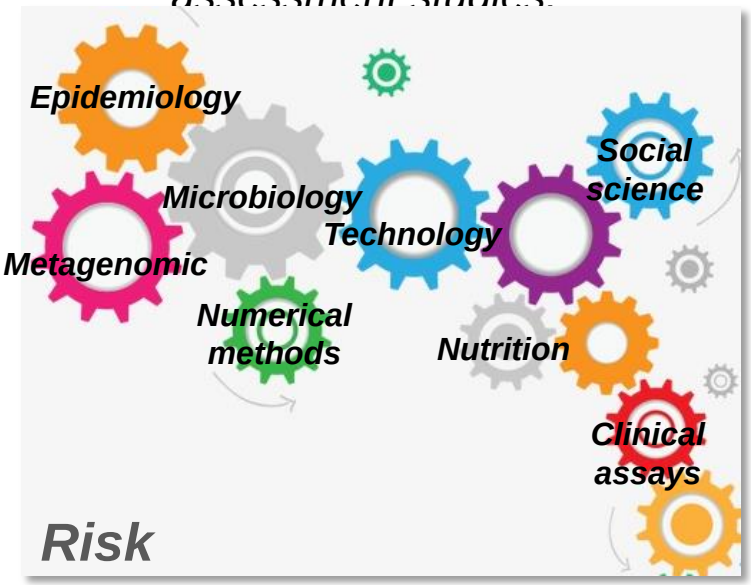
Who is involved:

The employment of a common structure is crucial to compare hazards, risks, management measures, etc. between autonomous regions and ideally between countries, and over time.

Limitations and challenges in Microbial Risk Assessment

- Integration of data from different fields

Complexity derived from the multidisciplinary approach required to accomplish risk assessment studies.

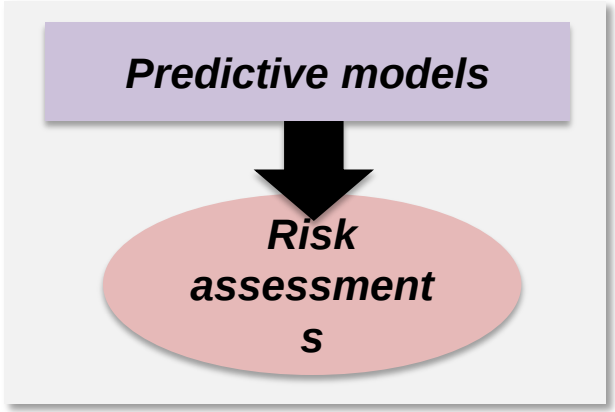


- Use of predictive models in risk assessmen

Models are difficult to implement or not available;

Lack of standardization in terminologies and annotations in model development;

Complexity of mathematical methods.



- There are not available guides or protocols to develop Quantitative Microbial Risk Assessments

- Lack of training and instructional resources to build skills for quantitative risk assessment

Proposal

1) *Development of an ontology to standardize terminology and creation of a common vocabulary in microbial risk assessment and predictive microbiology, e.g.: OFSMR;*

2) *Creation of Data Bases and repositories for predictive models to be integrated into risk assessments;*

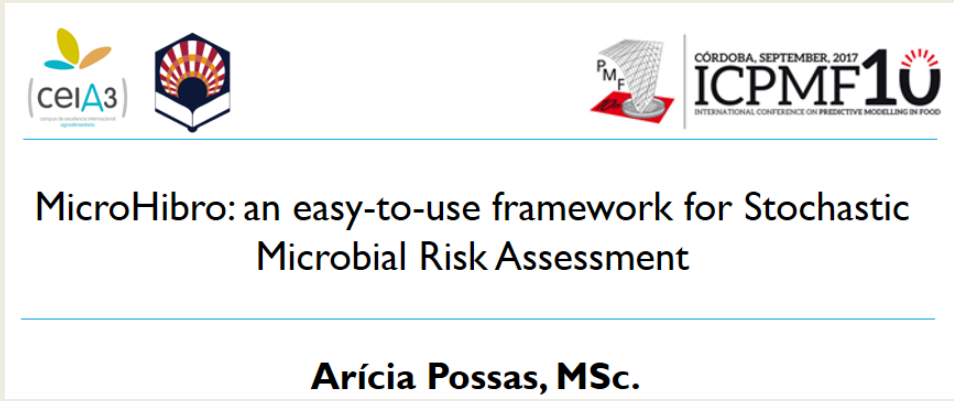
3) *Development of a common structure for predictive model application and quantitative microbial risk assessment;*

4) *Development of an EU-wide Platform for scientific cooperation, data and model exchange and educational resources in the field of microbial risk assessment.*

The initiatives so far

Designing a food matrix ontology supporting predictive microbiology databases

Salvador CUBERO GONZÁLEZ[1], **Fernando PÉREZ-RODRÍGUEZ[1]**, Elena CARRASCO JIMENEZ[1], Antonio VALERO[1], Matthias FILTER[2]



July 6, 2017 Software Open Access

Listeria monocytogenes risk assessment model for three ready-to-eat food categories in the EU

Pérez-Rodríguez, Fernando; Carrasco, Elena; Bover-Cid, Sara; Jofré, Anna; Valero, Antonio

https://zenodo.org/record/822350#.WnH71K6nHIV

Foreseen impact and benefits

- Ontologies would facilitate an effective mathematical model exchange and application among predictive microbiology practitioners and developers (i.e. import/export systems in predictive software);

- Model and data exchange will be significantly improved, enhancing accuracy, reliability, and optimization of the microbial risk modelling process;

- A community/taskforce promoting interdisciplinary collaboration and synergies in the field;

- **A decision support tool for Microbial Risk Assessment and Risk prioritization intended to different actors along the Food Chain:**

"*e.g.…assessors and/or managers of competent authorities (and industry) would be responsible for entering official and confidential data into the software to obtain reliable and comparable risk estimates*"

Infravec2

Research infrastructures for the control of insect vector-borne diseases

Dr Eva Veronesi

Infravec2 Stakeholder Networking Coordinator

University of Zürich, Switzerland

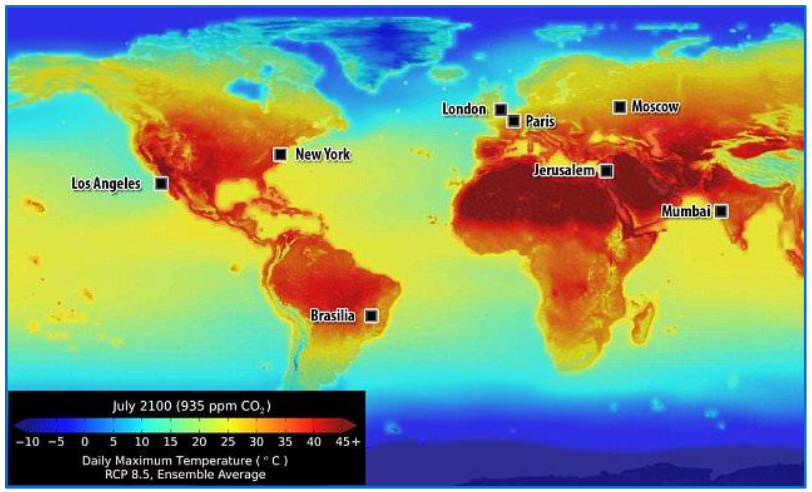
European Commission Horizon 2020 Research Infrastructure Program (INFRAIA)

Project N° 731060, project period 2017-2021

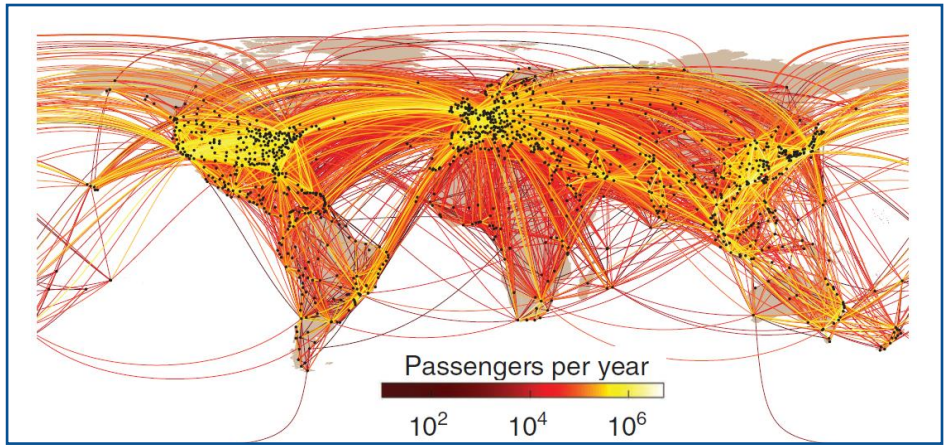
Coordination: Institut Pasteur, Paris. Coordinator: Ken Vernick

Email: infravec2@pasteur.fr, Web**: www.infravec2.eu**

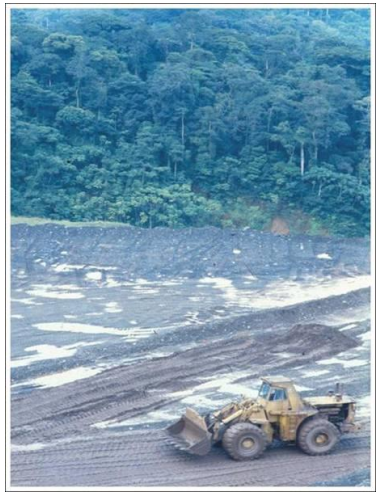
Why do we need Infravec2? Insect-borne disease is now a global public health risk



Source: NASA, USA, 2015.



Source: Grady, 2012, Nat Comm 3:864.



www.Infravec2.eu

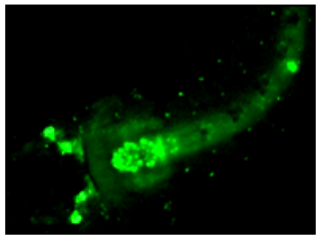
This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 731060

Infravec2 project overview

- Infravec2 provides access to unique vector infrastructures and technologies at **NO COST** to vector researchers (paid by EU)
- Infravec2 **Networking Activities** integrate and strengthen the vector research community
- All vector researchers **worldwide are eligible**
  - 80% of budget reserved for researchers in EU and 16 EU-associated countries

Products

Services



Facilities

www.Infravec2.eu

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 731060

What do we need to make our idea happen?

- Funding to **organize regular meetings and workshops with key stakeholders** (persons/groups) in the field of animal welfare and vector-borne diseases to improve standards, benchmarks and goals.

- Funding for development of a digital web environment to improve communication and data sharing.

- Complementary funding will support the **creation of an expert working group** to develop harmonized EU operating procedures to reduce risks to the food supply from vector borne disease.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 731060

Why this idea needs to be funded from public sources?

- **Animal health and food chain safety** is a public health issue. Most of the research is supported by government.

- **Research on animal food safety** should produce maximum impact for human health.

- Under the **“OneHealth”** concept, animal diseases have direct effects for human health (zoonosis, welfare, etc..).

This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 731060

What will be improved by our idea, impact and who will benefit

- Increasing the **biosafety level** of the environment and animal health by conducting research experiments under standardized operating procedures that are harmonized on a European scale;
- More **coordination** among research groups;
- **Standardization and traceability** of scientific data generated;
- **Reducing costs** by reproducibility of data across European laboratories.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 731060

Thank you!!

Email: infravec2@pasteur.fr
Web: www.infravec2.eu

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 731060

Developing methods for potency estimation for individual members of groups of toxins

Food Standards Agency, UK

What is the aim and the goal?

- to develop an innovative method(s) for estimating relative potency (or toxicological equivalency factors) for structurally-related chemicals with limited toxicological data.
- refinement of the risk assessment approaches for groups of related substances in food, in a manner that is protective for consumers without imposing undue restrictions on food businesses.

Why do we want to do it?

- Currently risk assessment for such chemicals is dependent either
- on the few members of the chemical class for which data are available, hence underestimating the combined risk, or
- by making a conservative assumption that all members of a class are equally toxic, which has the potential to overestimate the risk.
- Therefore there is a need to include more members of a class, taking into account their individual potency, in order to take a more proportionate approach to risk assessment and to development of regulations for these chemicals in food

What do we envisage?

- Developing a paradigm for estimating the relative potency based on studies on one group of chemicals that can occur in food, which could be verified using a different group of chemicals.
- Relevant groups of chemicals could include toxins produced by plants (e.g. pyrrolizidine alkaloids) or fungi (various classes of mycotoxin), or environmental contaminants that are persistent in the environment and hence widely present in the food chain (e.g. polybrominated diphenyl ethers, which were previously used as flame retardants).
- Limited potential for purification or synthesis of individual members of these classes means that conventional toxicity testing is not feasible.
- In silico and/or in vitro approaches are likely to be needed, which should take into account quantitative aspects of toxicokinetics and toxicodynamics
- Recommendations for applying the approach to other classes of chemicals

What are we looking for?

- The good news we have some money to invest in this project
- The bad news we know what we want but not how to do it!
- What do we need?

  Ideas on how to do the project

  Proposals to prove the concept

For Further information please contact:
David Gott: david.gott@food.gov.uk
Claire Potter: claire.potter@food.gov.uk

Food Standards Agency
food.gov.uk

Food Standards Agency
food.gov.uk

07/02/2018

Dr Patrick Miller

Developing methods for potency estimation for individual members of groups of toxins

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Food Standards Agency
food.gov.uk

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Food Standards Agency
food.gov.uk

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Food Standards Agency
food.gov.uk

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For more information please contact:
Dr David Gott: david.gott@food.gov.uk
Claire Potter: claire.potter@food.gov.uk

Food Standards Agency
food.gov.uk

Translational strategy to predict food allergenic potential

Raymond Pieters[1,2], Joost Smit[1], Stefan Vaessen[2], Jean Paul Ten Klooster[2], Marianne Bol Schoenmakers[1]

[1]Institute for Risk Assessment Sciences (IRAS), Faculty of Veterinary Medicine, Utrecht University
[2]Research group Innovative Testing in Life Sciences & Chemistry, University of Applied Research Utrecht (UASU), Utrecht
The Netherlands

Universiteit Utrecht

CFA
UTRECHT CENTER FOR FOOD ALLERGY

UNIVERSITY OF APPLIED SCIENCES UTRECHT

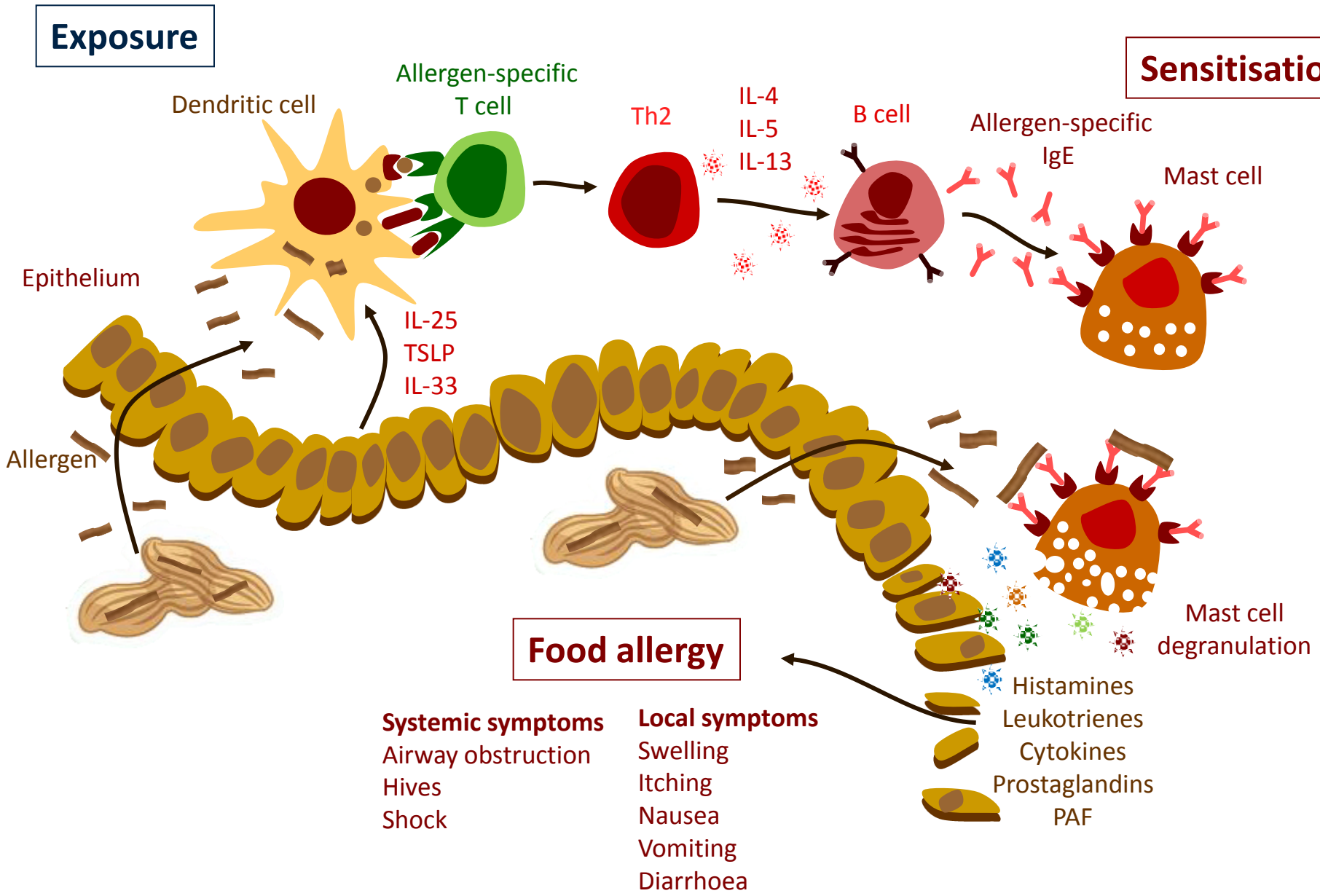
Translational strategy to predict food allergenic potential

new proteins appear in human food chain

possible health risk, i.e. food allergy

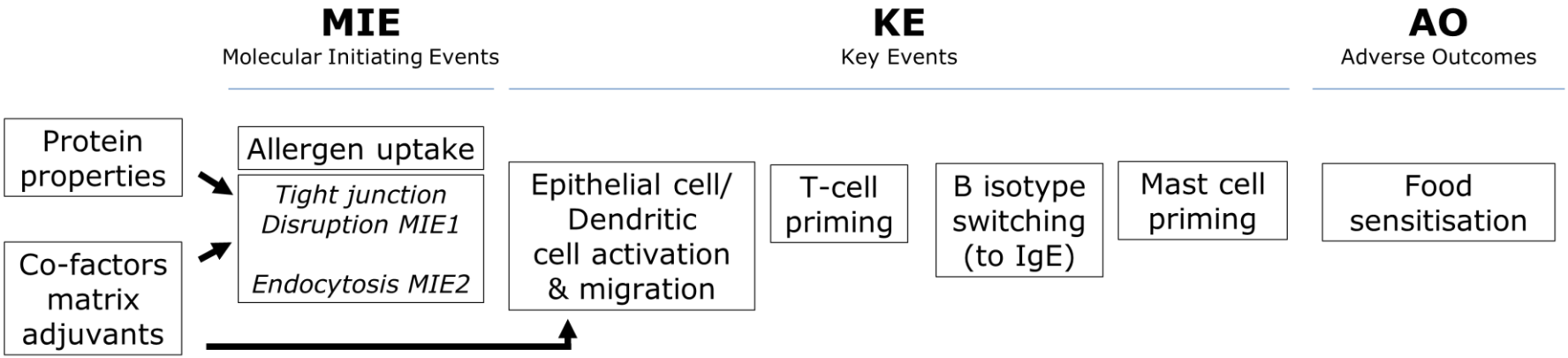
-to feed the growing world population
(e.g. insects)
-genetically modified proteins
(e.g. to protect crops from diseases)
-modified proteins that have specific application
(e.g. to change texture or functionality)

Translational strategy to predict food allergenic potential



Translational strategy to predict food allergenic potential

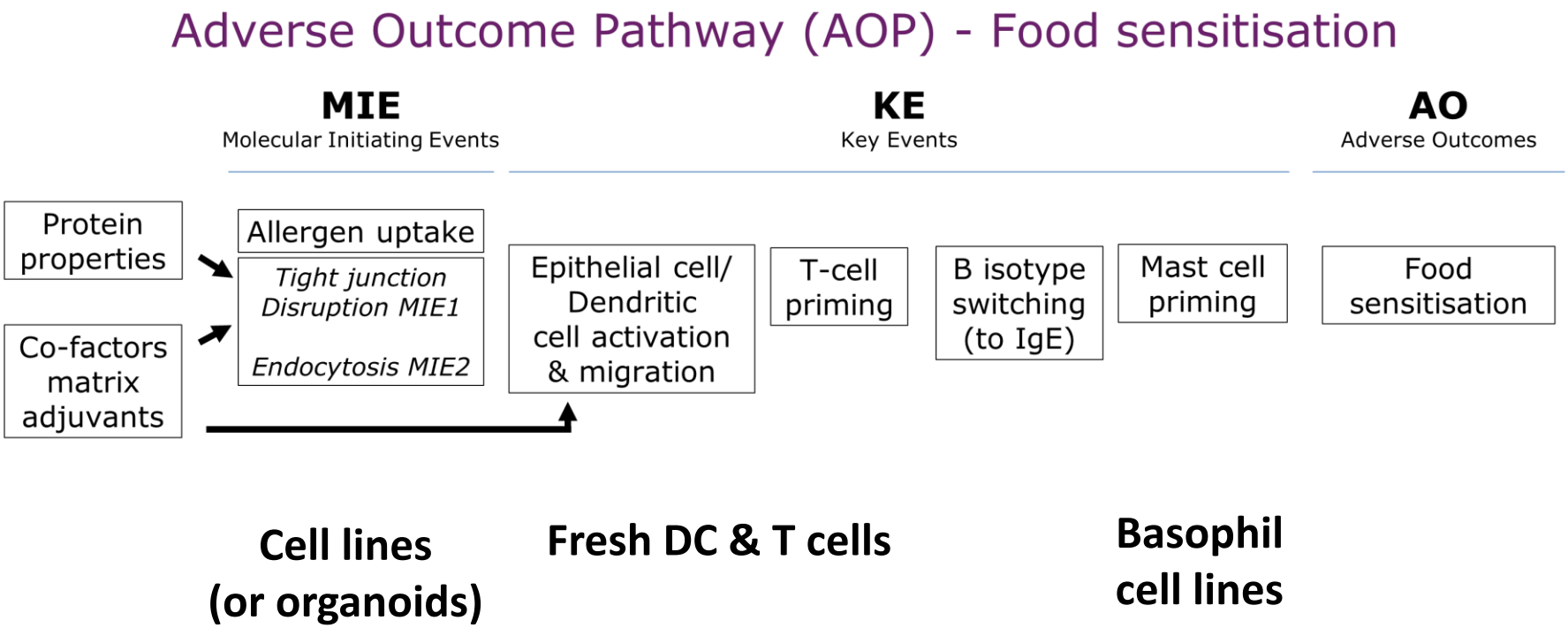
Adverse Outcome Pathway (AOP) - Food sensitisation



Aim: develop and validate a predictive 3R compliant translational strategy to predict food sensitizing potential.

Adapted from: Van Bilsen et al., Clin Transl Allergy (2017) 7:13
Publication from EU-COST IMPARAS consortium

Translational strategy to predict food allergenic potential



Translational strategy to predict food allergenic potential

Why do we need public funding?

Available test methods need further development and validation to obtain regulatory acceptance. For this company-independent public funding is highly needed.

What is needed?

Well-characterized individual food proteins ((non-)allergenic, (un)modified).
Collaboration between independent knowledge institutes for further optimization and interlaboratory validation.

Development of an allergenicity risk assessment strategy to support a safe introduction of new and sustainable food

Kitty CM Verhoeckx, PhD

TNO, Zeist, The Netherlands, e-mail: kitty.verhoeckx@tno.nl

TNO innovation for life

OBJECTIVE

To enable the safe introduction of novel and more sustainable protein sources while protecting humans from food allergy towards them by better predicting their potential allergenicity.

ISSUE & STATE OF THE ART

- The food industry must serve 9 billion people sustainably by 2050 while facing a shortage of protein sources.
- Consumers will encounter numerous novel foods in the coming years, ensuring a significant increase in food allergy through exposure.
- Food allergy is currently affecting ±50 million Europeans and costing the health care system €55 billion annually.
- Assessment focusses on the impact of a protein on individuals with pre-existing allergies (cross-reactivity), but only addresses sensitisation (initiate new allergy) superficially.
- Assessment of food allergy risks is not yet fully developed: Interplay between different factors, such as protein characteristics, mechanisms of sensitization and individual risk factors remains unclear.
- Consistency and methods used for risk assessments are often not scientifically sound, validated and harmonized.

COST ACTION IMPARAS

"**Imp**roved **A**llergenicity **R**isk **A**ssessment **S**trategy" (FA1402, www.imparas.eu).
ImpARAS is a H2020-sponsored European intersectoral network of scientists from 30 countries. Members have identified gaps, new ideas and plans for an improved allergenicity assessment strategy. Taking these forward now requires a multidisciplinary European-funded project to undertake the necessary research, develop and foster acceptance of the new strategy.

WHY PUBLIC FUNDING

This idea focusses on the development of an improved allergenicity risk assessment strategy based on

- the premise that newly introduced food protein products must not increase the burden of allergies on society and
- an urgent need to expedite the introduction of sustainable, nutritious and safe foods to the market.

These issues clearly fall in the realm of public interest, and pre-competitive rather than commercial. The topic is closely related to and could be seen as a follow-up of the COST Action FA 1402 and the GMO EFSA panel meeting in 2015. This proposal also complements the EU projects iFAAM and Europrevall, which focused on the research gaps related to the management of allergy and allergens in relation to existing known allergenic foods. The topic is also in line with the strategic research agenda of JPI.

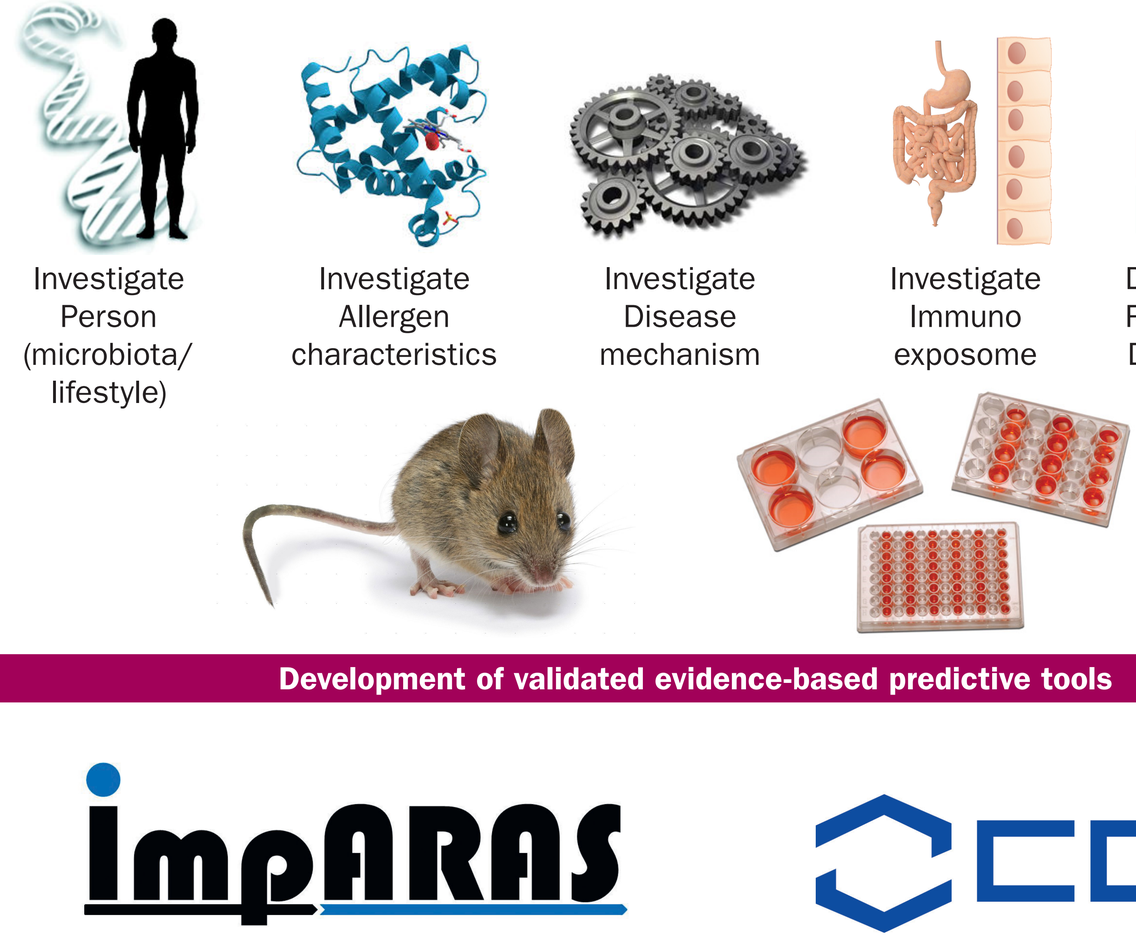
NEEDED AND APPROACH

The GMO EFSA panel and COST Action ImpARAS stress that a transparent, evidence-based, validated, allergenicity risk assessment based on novel methodologies is a necessity.
To accomplish these we need:

- A multi-disciplinary approach to understand the basic mechanisms and risk factors leading to food allergy, to identify those at risk of developing food allergy, and thereby predict which foods could be allergenic.
- Development of evidence-based approaches and tools to assess the risk of sensitization to proteins.
- A network covering core aspects of food allergy, immunology, protein chemistry, bioinformatics and risk modelling.

Who benefits	Impact
Scientific Community	– Build European networks of leading institutes on food allergy, food safety and food processing. – Develop a transparent, evidence based and validated approach for allergenicity risk assessment of novel food proteins. – Unravel new mechanisms for food allergy and what makes a protein an allergen.
Food industry	– Expedite the introduction of sustainable, nutritious and safe foods to the market. – Reduced call-backs related to allergenicity. – Reduce costs for Industry by early prediction of allergenicity during development of novel foods with innovative, quick, reliable, and food industry-tailored tools for allergenic risk assessment.
Public	– Safe nutritious foods with very low allergenicity risk – Education on lifestyle factors for healthy living – Increase the assurance that allergenic risks posed by novel foods are effectively managed. – Ensure that newly introduced food protein products do not increase the burden of allergies on society
Health care	– Cost savings (e.g., lower medical costs) through better management of food allergy burden
Risk assessors	– New clear and scientifically sound approaches for food allergy risk assessment
Regulators	– Support to EU novel food regulation

Multi-disciplinary approach for an Improved Allergenicity Risk Assessment Strategy



Investigate Person (microbiota/ lifestyle) | Investigate Allergen characteristics | Investigate Disease mechanism | Investigate Immuno exposome | Defining target for Risk management Descision making

Development of validated evidence-based predictive tools

ImpARAS

cost

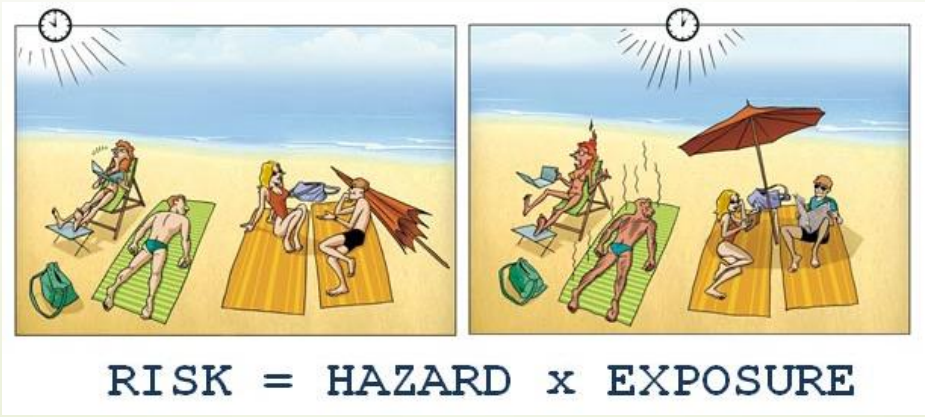
The influence of food components – an underestimated parameter in chemical risk assessment?

Tomaž Langerholc, Antonio Marques and Salomon Sand

Risk Assessment Research Assembly (RARA) Utrecht, 7 February 2018

Chemical risk assessment

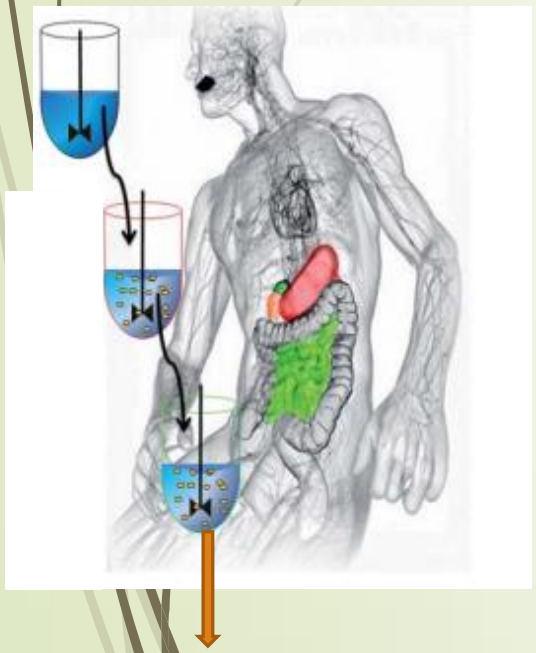
- Dietary exposure assessment is performed by combining food consumption data and data on concentrations of chemicals in foods.
- This approach is rather conservative and it does not take into account that bioavailability of contaminants can depend on food carrier as well as the combination of foods ingested during a meal.
- Food components can significantly affect physiological conditions during digestion, inhibit proteolytic enzymes and hinder release of food trapped contaminants, (de)stabilize chemical forms of contaminants by complexation, prevent absorption.



http://toxedfoundation.org/hazard-vs-risk/

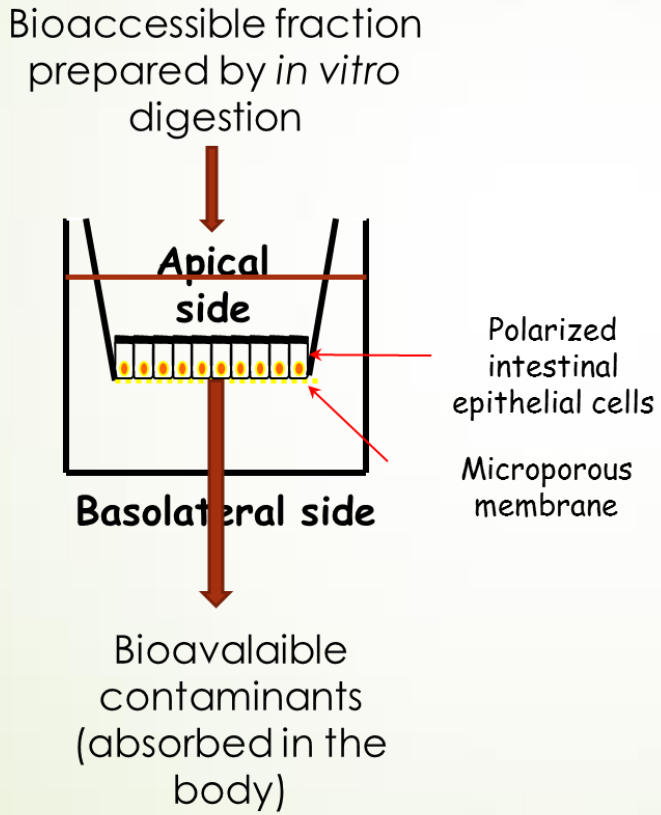
Do we have data in support?

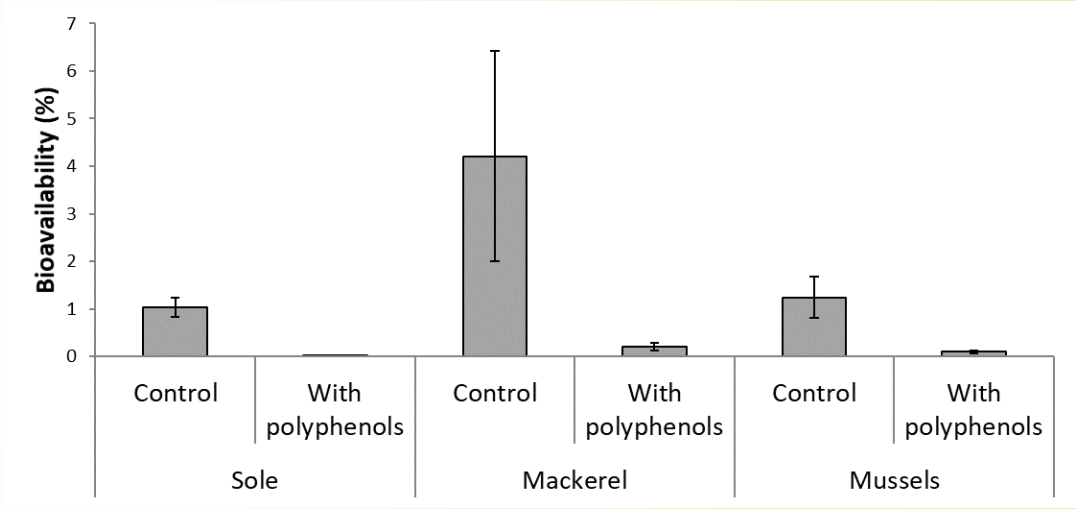
Artificial *in vitro* digestion



Bioaccessible fraction

Minekus (2014)





Bioavailability (bioaccessibility and absorption) of mercury from seafoods without (control) and in the presence of polyphenols. Bar errors represent standard deviation.

What needs to be done?

- **A more detailed and systematic study should be performed to better understand the effect of food components on bioavailability.**
- The effects of typical nutrients, i.e. carbohydrates, fats, proteins, polyphenols and dietary fibers should be tested with selected food contaminants to find potential effects on bioavailability. Ratios between the components?
- Food combinations vary substantially both geographically and culturally. Extraction of data on food combinations from existing dietary surveys? Integration into the risk assessment platform? Adaptation of the methodology?

Foreseen impact

- Better estimation of human dietary exposure
- More targeted consumer risk assessments of contaminants
- Management of health concerns related to a long term consumption of contaminated foods
- Advice on cunsumers, mitigation strategies
- Tailored functional foods

- However,
  - financing of research on this issue is needed to expand current knowledge

Thank you for your attention.

Acknowledgements: EU-FORA fellowship (EFSA)

Contact: tomaz.langerholc@um.si

Maribor, Slovenia

Uppsala, Sweden

Advanced methods for integrating evidence for dose-response and antimicrobial resistance modelling

R. Bruyndonckx, S. Jaspers, C. Ensoy, S. Vercruysse, C. Faes and M. Aerts

UHASSELT

I-BioStat

KU LEUVEN

Interuniversity Institute for Biostatistics and statistical Bioinformatics

Data science for enhanced risk assessment

- Benchmark Dose(BMD) models

Compound	Endpoint	Study	
• Additive • Contaminant • Pesticide	• Bodyweight • Risk of cancer • Survival rate • Omics data	• Animal experiments • Epidemiology • In vitro	**Data integration meets EFSA/EPA recommendation**[1]

- Source attribution models for AMR

Animal data	Human data	Trade info	
• Food animals • Pets	• AMR prev. • Food & AM Consumption	• Food import • Food export	**Data integration meets One Health approach of WHO**

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1: www.efsa.europa.eu/en/events/event/171025-0

New approaches for BMD modelling

Classic approach

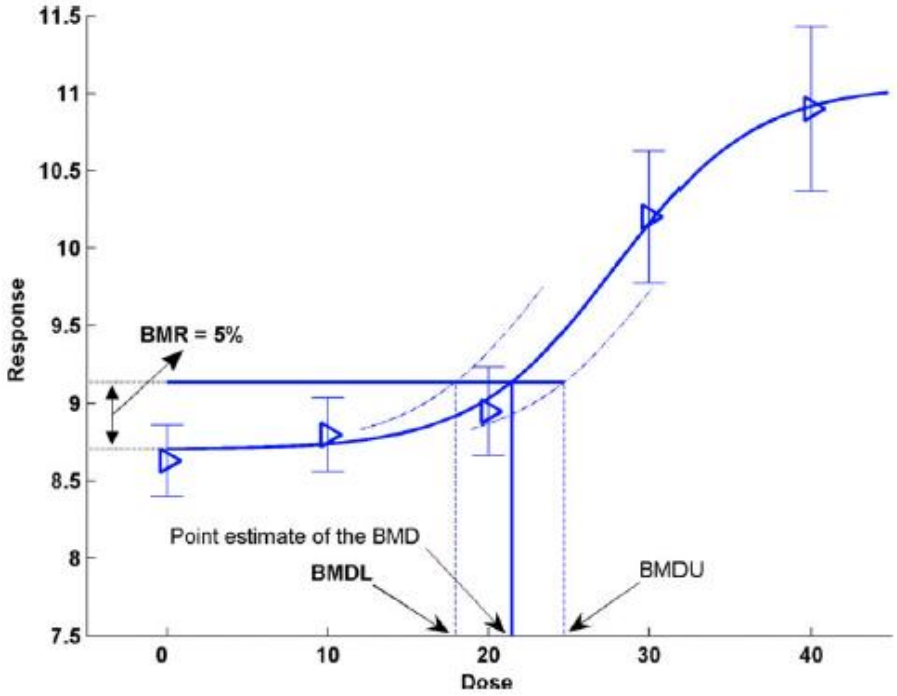


Fig retrieved from: EFSA Scientific committee. EFSA Journal 2017;15(1):4658, 41 pp. doi:10.2903/j.efsa. 2017.4658

Step-wise innovation

Composite endpoints & Meta-analytic methods

Bayesian approach

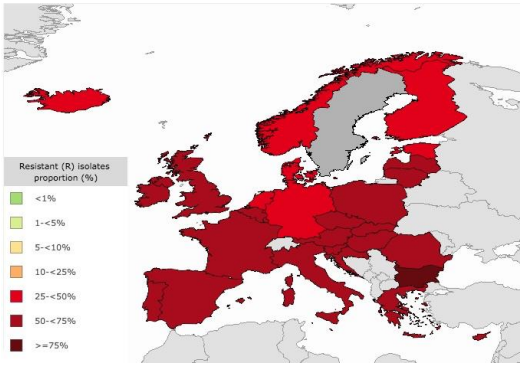
Heterogeneity Unified inference paradigm

Mechanistic, empirical, hybrid models & adverse outcome pathways

Big data (in vitro/omics)

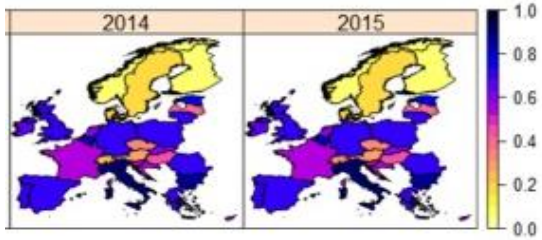
New approaches for AMR modelling

Classic approach



Human AMR (Ampicilline)

https://ecdc.europa.eu/en/antimicrobial-resistance



Animal AMR (Ampicilline)

Jaspers et al., EFSA supporting publication 2016:EN-1084.54pp.

Proposed innovation

$$logit(\pi) = \beta_0 + \sum \beta_k x_k + \sum \alpha_k M_k + \sum \gamma_k x_k {}^* M_k + \delta y$$

π Probability that human isolate is resistant to antibiotics

x_k Proportion of kth food-type resistant isolate

M_k Consumption quantity of the kth food type

y Antibiotic use in humans (daily dose/package)

Logistic regression

Multi-level models

Spatio-temporal models

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Impact & beneficiaries

Scientific community

- Innovative research
- Methodological advancements
- High-impact publications
- Increased international collaboration
- Data science for food sciences

Public health/ Risk assessment agencies & policy makers

- Updated guidance for BMD estimation
- Better insights in AMR sources
- Better use of available data
- Enhanced monitoring tools and alert systems

General public

- Safer food
- Healthier animals
- Increased awareness of AMR sources
- Better (tailored) strategies to fight AMR resistance

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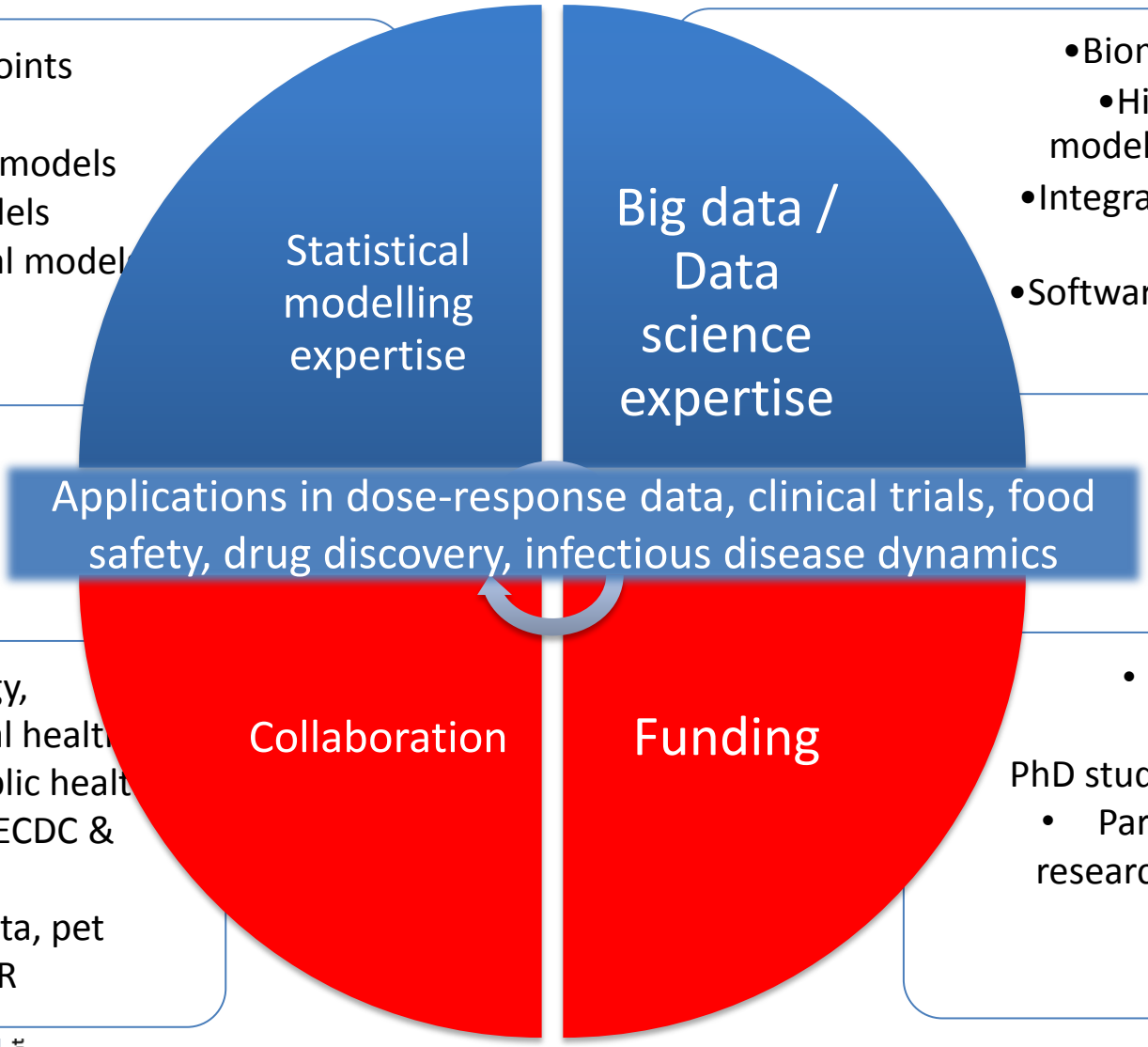
Available and missing resources/expertise

- Composite endpoints
- Meta-analyses
- Spatio-temporal models
- Mechanistic models
- Bio-mathematical model
- Missing data



- Biomarker research
- High dimensional modelling techniques
- Integrative omics data analysis
- Software development

- Experts in biology, toxicology, animal healt
- Universities, public healt institutes (EFSA, ECDC & national level)
- Consumption data, pet ownership & AMR

- Joint funding applications

PhD student (50K/year)

- Part-time postdoc researcher (30K/year)

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Greetings from CenStat / I-BioStat Belgium

Why work with us?

- 70 FTE
- Multidisciplinary backgrounds
- Pioneering statistical work
- Broad application areas
- Research, training & consultancy
- Academic, industrial, governmental partners
- Prestigious funding
- International network

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Research Idea for RARA: “Development of a web-based intake model for chemical contaminants and nutrients”

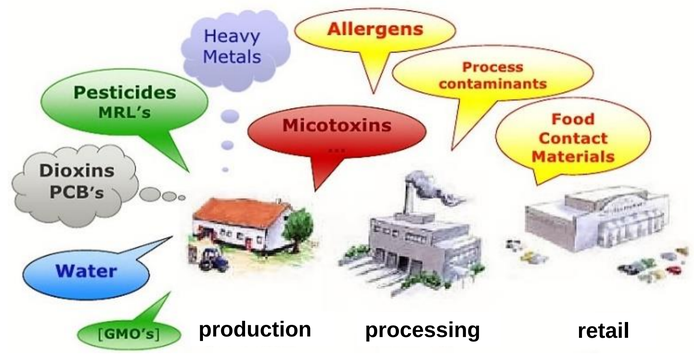
Georgios Stavroulakis[1], Demetris Kafouris[1], Lefkios Paikousis[2], Maro Christodoulidou[1], Stelios Yiannopoulos[1]

[1]Risk Assessment Unit, State General Laboratory (SGL), Ministry of Health, Cyprus

[2]IMPROVAST Ltd

The Research Idea

- A dietary risk assessment model for chemical contaminants and food additives. The model will function both in a probabilistic and deterministic way. Probabilistic methodology is considered to lead to more accurate risk assessment, as compared to the deterministic method. The model will be configured in order to be compatible with the EFSA FoodEx2. Additionally, through the deterministic part of the model, it will be possible to conduct nutrient intake assessment, using the same food consumption data and either of the following data: (a) Food nutrient data and (b) Food Composition Data. Regarding the latter option, the model can be linked to a Food Composition Database of a country in order to estimate the micronutrients and macronutrients intake of a given population group or the general population of that country. This model is intended to be used by risk assessors.
- An “extension” will be made in the sense of a “personalized” nutrient intake model. Specifically, an EU citizen, by choosing the Food Composition Database of the country of interest and matching it with his/her own food consumption instances of a particular day, will be able to assess his/her nutrients intake and compare it with established Dietary Reference Values (DRVs). The whole procedure will be rather simple.



Impact/benefit on food safety and public health

What will be improved:

- Harmonization. The model will be developed according to EFSA requirements, and compatible with FoodEx2.
- Comparability of intake assessments at European level.
- Accurate intake assessment for chemicals and nutrients, because it will be based on the FoodEx2 coding.
- A web application, attractive and user-friendly.
- A quick, automated and reliable calculation of nutrient intake.
- Transparency.

Who will benefit:

A great impact/benefit on food safety and public health both at national and European level.

- National Food Safety Authorities. It will help the development of better risk-based monitoring plans.
- Support to EFSA’s Risk Assessments.
- Regulators will have more accurate results on risk of several contaminants in order to proceed to legislative actions.
- Industry can estimate the possible risk of their own products and will have the opportunity to improve their production,
- Consumers will have both direct and indirect benefit.

Expertise/partners needed

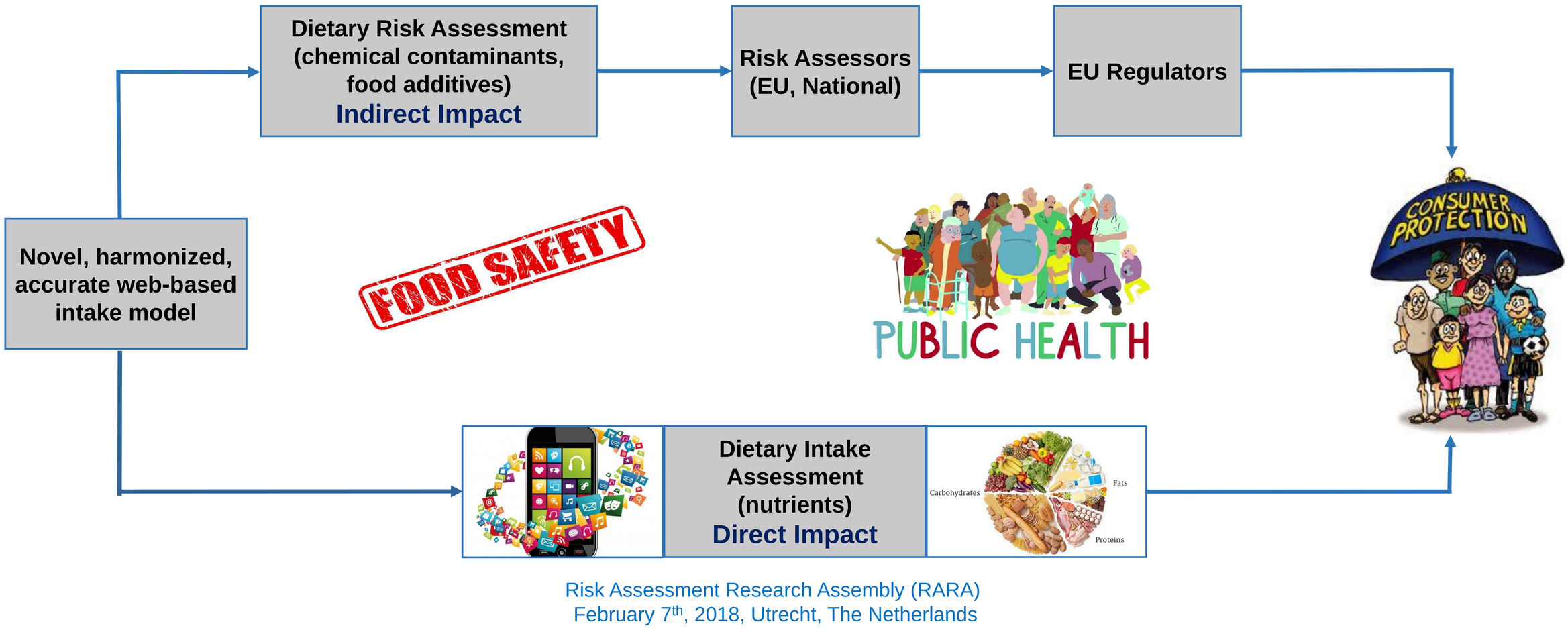
A multidisciplinary team of experts will be needed to execute the tasks of this research idea. Collaborations and trainings will be necessary for this project.

- **Web developers, Software engineers:** The models will be based on a web application. Experts in this area will contribute to appropriate software developments
- **Risk Assessment expertise:** Establish collaboration with other National Food Safety Authorities, with high expertise in RA methodologies, especially in probabilistic method.
- **Dieticians and Nutritionists:** These experts will be involved with the development of Food Consumption and Food Composition Databases, compatible with the dietary intake models. Collaboration with the private sector and academia.
- **Statistical expertise:** The models will be based on specialized statistical models, so a collaboration with the private sector and academia in this field will be of high importance.

Why public funding?

High impact on food safety and public health at European level. EU citizens will have both direct and indirect benefit.

Public Money for Public Benefit



Research Idea for RARA: "Development of a web-based intake model for chemical contaminants and nutrients"

Dr. Georgios Stavroulakis

Dr. Demetris Kafouris

Mrs. Maro Christodoulidou

Dr. Stelios Yiannopoulos

Risk Assessment Unit

State General Laboratory (SGL)

Ministry of Health, Cyprus

Mr. Lefkios Paikousis

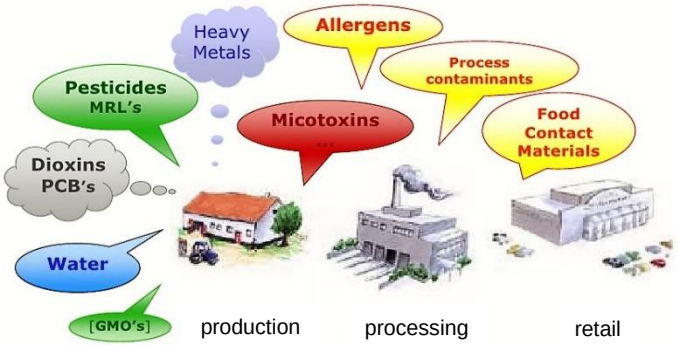
IMPROVAST Ltd

Risk Assessment Research Assembly (RARA)
Utrecht, 7 February 2018

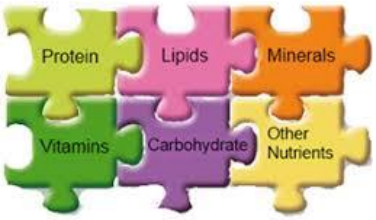
Brief description of the Research Idea

A tool for:

- **Dietary Risk Assessment of**
  - ✓ **Chemical Contaminants**
  - ✓ **Food Additives**
  - ❖ **Deterministic and Probabilistic function**
  - ❖ **Embed EFSA FoodEx2**



- **Dietary Intake Assessment of nutrients**
  - ✓ **Support the use of Food Composition Data**
  - ✓ **"Personalized" tool directly used by consumers, based on individual dietary patterns**
  - ❖ **Deterministic function.**



- **Estimating consumer exposure at European level**

Impact/benefit on food safety and public health

- **What will be improved:**
  - **Harmonization (Model according to EFSA requirements, FoodEx2, etc.)**
  - **Comparability of intake assessments at European level**
  - **Accuracy (FoodEx2 coding)**
  - **Transparency**

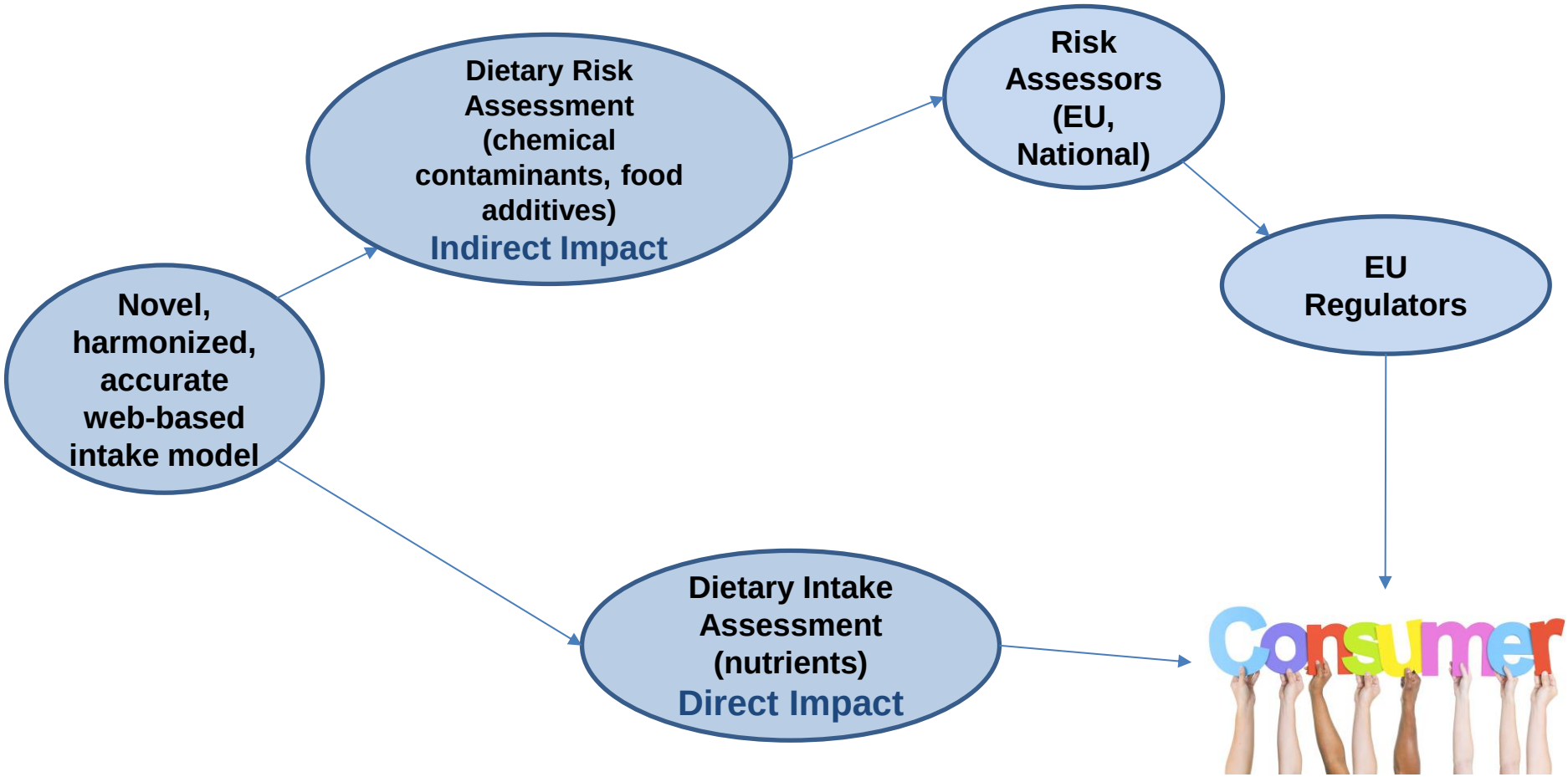
- **Who will benefit:**
  - **National Food Safety Authorities (Risk-based**
  - **EFSA**
  - **Regulators (Legislative actions)**
  - **Industry (Improved products)**
  - **Consumers (Direct and indirect benefit).**

Expertise/partners needed

- **I.T., Web developers, Software engineers: Software developments. Mobile and Web application**
- **Risk Assessment expertise: Establish collaboration with other Food Safety Authorities, with high expertise in RA methodologies, especially in probabilistic method**
- **Dieticians, Nutritionists and experts in Food Composition Databases: Collaborate with the private sector and academia**
- **Statistical expertise: Collaborate with the private sector and academia.**

Why public funding?

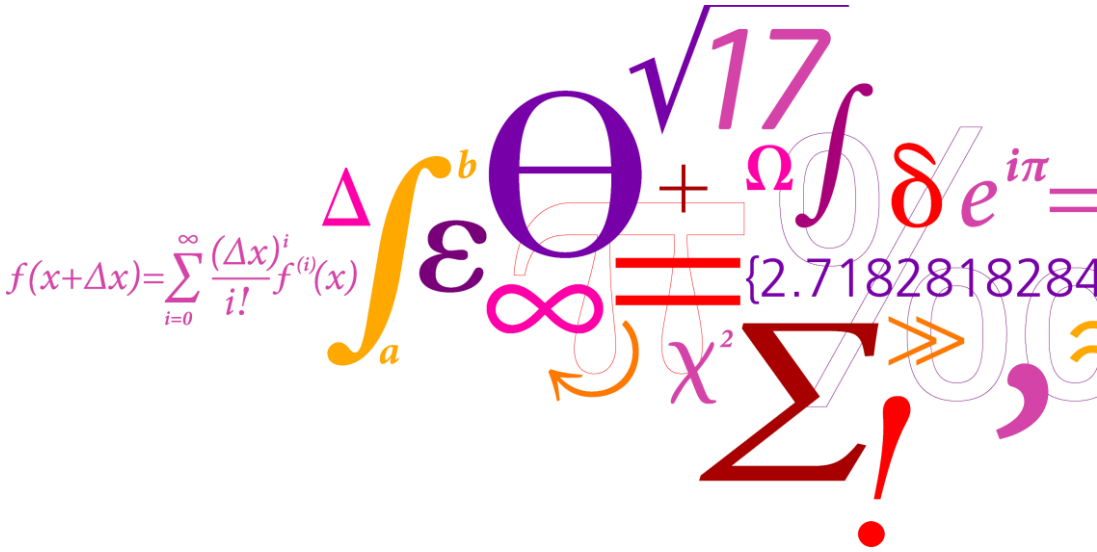
- Because the consumers will have both direct and indirect benefit



The Cocktail Effect Calculator

Julie Boberg

Senior Scientist, PhD
Division of Diet, Disease Prevention and Toxicology
Technical University of Denmark



DTU Food
National Food Institute

What is the Cocktail effect calculator?

A tool/database for **pragmatic mixture risk assessment**

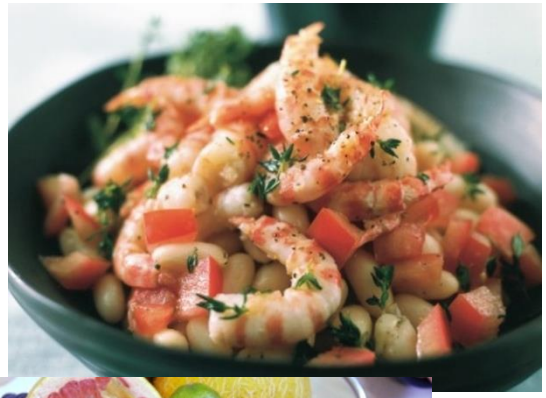
- Chemical exposures from food and environment
- Toxicity data collected to set human "safe dose" for various endpoints
- Grouping based on similar effects and/or mode of action

Ideas:

Using the Cocktail effect calculator

We call for collaboration on specific applications:

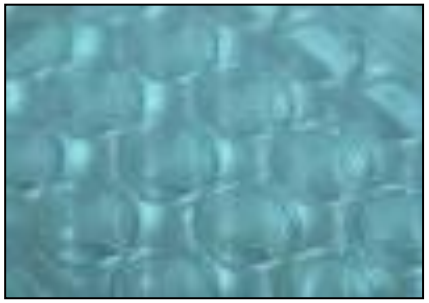
- performing cumulative risk assessment
- determining critical food groups or chemicals
- determining the impact of altering food habits and intake patterns



Expanding the Cocktail effect calculator

- Lack of information limits the number of chemicals in Calculator

- Perspective: including risk assessment based on "alternative" data
  - In vitro/biomonitoring – In vitro in vivo extrapolations
  - Relative potency factors



- Exposure and toxicity data
- Case study proposals

HEALTH RISK ASSESSMENT OF COMBINED EXPOSURE TO CHEMICALS

PESTICIDES AND PLANT GROWTH REGULATORS STUDIES

Mykola Prodanchuk, Serhii Kolesnyk et al

L.I. Medved's Research Center of Preventive Toxicology, Food and Chemical Safety, Ministry of Health of Ukraine

Outline

- Research idea: what to do and expected results
- Foreseen impact and beneficiaries
- Reasons for public funding
- What we have and what we need

Research idea: what to do and expected results

1. Planning and design

Different methodologies to select chemicals and tests

- ✓Assessment of difference in lists

Substances to be included in further experiments

- ✓List of substances

Testing methods to be included (ED and DART)

- ✓List of tests/testing guidlines to be used and suggestions for their possible modification to ensure fit-for -purpose

2. Data acquisition

1. Existent data

- ✓refined study plan taking into account existent data

2. ***In vivo*** studies (TK, subchronic, DART, chronic)

- ✓data on toxicokinetic interactions
- ✓data on toxicity of mixtures

3. *In vitro* (OECD GD 150, gene reporter assays)

- ✓mechanistic data on the same mixtures, as tested *in vivo*

4. ***In silico*** (QSAR and molecular docking models)

- ✓ Set of predictions from different in silico models for tested chemicals

3. Data analysis and interpretation

Analysis of presence/absence of toxicological interaction in *in vivo* tests

Integration of *in vivo* data and results of alternative methods

Assessment of predictive value of alternative methods used

✓ Refined testing strategy for mixtures

4 Sharing and dissemination of information

- Creation of databank for results of studies

- Publication of all information in peer reviewed open access journals

Main reasons to sustain this study through public funding

- To ensure transparency and independency of study
- To enable further dissemination of results
- Methodology/approaches elaborated to be used by public authorities

Beneficiaries of realization of idea

Public	Research institutions and risk assessment bodies	Risk managers
• better protection of public health	• improved understanding of mixture toxicity and methodology for its assessment	• improved background for decision making

Resources to make idea happen?
What we have

- Facilities and equipment
  - ✓GLP compliance
  - ✓Own SPF vivarium
  - ✓ISO 17025 testing laboratory
- Expertise
  - ✓More than 50 years of experience in risk assessment
  - ✓Highly trained and experienced staff
  - ✓Continuing training
- Collaboration
  - ✓WHO, FAO,OSCE in research projects, standards, capacity building etc

SNAS SLOVAK NATIONAL ACCREDITATION SERVICE
Karloveská 63, 840 00 Bratislava 4, Slovak Republic

STATEMENT
OF GLP COMPLIANCE

No. G-042

Slovak National Accreditation Service certifies

conformity with GLP according to the Law No. 67/2010 Coll, the OECD Principles of GLP and Directive 2004/10/EC, of the European Parliament and of the Council, in the test facility:

L.I. Medved's Research Center of Preventive Toxicology, Food and Chemical Safety, Ministry of Health, Ukraine
Center for preventive and regulatory toxicology
Heroiv oboroni 6, 03023 Kiev, Ukraine
ID number: 01897914

Area of expertise: Toxicology studies, toxicokinetics studies, mutagenicity studies, physical-chemical studies, field studies.

The above mentioned test facility is included in the Slovak National GLP Compliance Programme and is inspected by Slovak National Accreditation Service on a regular basis.

Prof. Mykola Prodanchuk MD - director, is the statutory body of the test facility, who manages and represents it and acts on its behalf.

This statement is granted on 09.03.2015 and is valid until 09.03.2020.

Bratislava, 09.03.2015

Martin Šenčák
Director

SNAS

Toxicological studies from α to Ω

Modern equipment

Resources to make idea happen?
What we need

- Funding for long term *in vivo* studies
- Some equipment (e.g. luminiscenese spectrophotometer, MALDI-TOF, Orbitrap LC/GC-MS)
- Access to more in silico models
- Trainings on specific topics
- Collaboration with EuroMix, EDC-MixRisk and other projects partners

THANK YOUR FOR ATTENTION!

Human biomonitoring for the assessment of dietary exposure to contaminants and micronutrient intake

Francesco CUBADDA, Alberto MANTOVANI, Marco SILANO

Unit of Human Nutrition and Health, Department of Food Safety, Nutrition and Veterinary Public Health
Istituto Superiore di Sanità - Italian National Institute of Health, Rome, Italy

Introduction

Intake assessment is a key step in dietary risk assessment and forms the basis for risk characterization, which establishes whether exposure to harmful chemicals is safe compared to the health based guidance values (HBGVs) or whether intake of nutrients is in the optimal range for human health defined by the dietary reference values (DRVs), i.e. that preventing deficiency and excess (**Figure 1**).

The assessment of nutrient Intake or exposure to contaminants and other harmful chemicals in the food chain can be performed *via* **Dietary-based methods**, by combining food consumption data with concentration data of nutrients or substances, or *via* **Human biomonitoring (HBM)**:

Intake/exposure assessment

- **Dietary-based methods**
  E.g. total diet studies, duplicate diet studies
- **Human biomonitoring (HBM)**
  Systematic standardized measurement of the concentration of a substance or its metabolites in human fluids/tissues (e.g. blood, urine, milk, hair, nails)

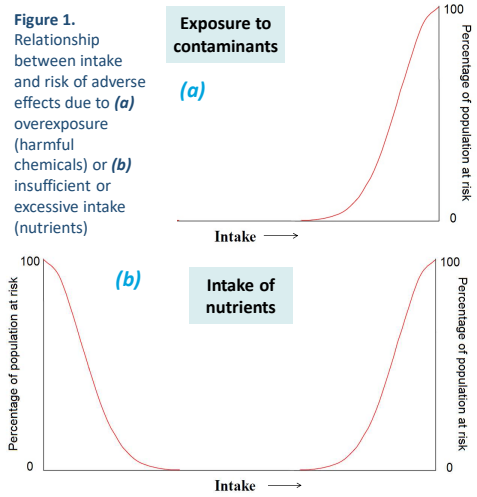


Figure 1. Relationship between intake and risk of adverse effects due to ***(a)*** overexposure (harmful chemicals) or ***(b)*** insufficient or excessive intake (nutrients)

Dietary-based methods are difficult and/or costly to be implemented in many cases. On the other hand, **HBM** provides complementary information and is essential to improve the use of epidemiological studies in food safety and nutrition, i.e., the use of human data in risk assessment.

For **nutrients**, appropriate biomarkers of intake and status are used to identify specific risks of inadequate supply of, e.g., key trace elements and vitamins, especially in vulnerable groups, and assess the nutritional status of a population and the association with health and wellbeing outcomes with a view to pursuing health promotion and disease prevention.

For **contaminants and regulated products** HBM gives an indication of the **aggregated (i.e. dietary plus non-dietary) exposure** of a population. If estimates of dietary exposure are available (e.g. by means of total diet studies), HBM may enable to assess the **relative magnitude of the different exposure pathways**. In many cases, e.g. for some trace elements, the diet is the major source of exposure and HBM directly assesses the intake through food and water. The integrated HBM of toxic substances and nutrients may pinpoint subgroups more vulnerable because of their nutritional status (e.g., iodine status) and support risk-benefit assessment for certain foods (e.g., seafood).

Foreseen impact on food safety and public health

The **identification, validation and application of appropriate biomarkers in food safety studies** are developing fields where much remains to be done.

HBM, integrated with a variety of dietary-based approaches and mechanism-driven toxicological data, can yield **robust and novel evidence for risk and risk/benefit assessment**.

Developing novel biomarkers of exposure would have a significant impact by underpinning the different phases of risk assessment (e.g. linking evidence on external exposure, internal exposure, ADME and critical effects on target organs) and **substantially reducing associated uncertainties** (**Figure 2**).

Example

Exposure to pesticides: HBM as the way forward

Possibility to evaluate cumulative exposures (e.g. through common metabolites) and peak exposures

- Different target groups: consumers, operators, workers, residents, bystanders
- Hundreds of substances
- The internal dose may be the result of exposure via different routes (oral, dermal, inhalation)
- Biomarkers can be identified on the basis of ADME and other toxicological studies in regulatory data sets

Figure 2. Improving exposure assessment and reducing uncertainties

Reducing uncertainties in risk assessment → **Benefits for consumers, industry, regulators**

Exposure assessment is a key part of all **epidemiological studies** and misclassification of exposure weakens the ability of a study to determine **whether an association exists with adverse health effects**. At present, this limits integration of epidemiological findings into regulatory risk assessment.

A cross-cutting interdisciplinary effort relying on public funding

Setting of priorities for the development of new specific and sensitive biomarkers

Biomarkers of exposure ⟷ (integrated with) **Biomarkers of effect**

The research idea requires a **considerable effort** from the European research community and critically relies on **cross-cutting interdisciplinary research**.

It is very unlikely to be addressed appropriately if not sustained through **public funding**.

feb '18 Risk Assessment Research Assembly

Utrecht, 7 February 2018

Human biomonitoring for the assessment of dietary exposure to contaminants and micronutrient intake

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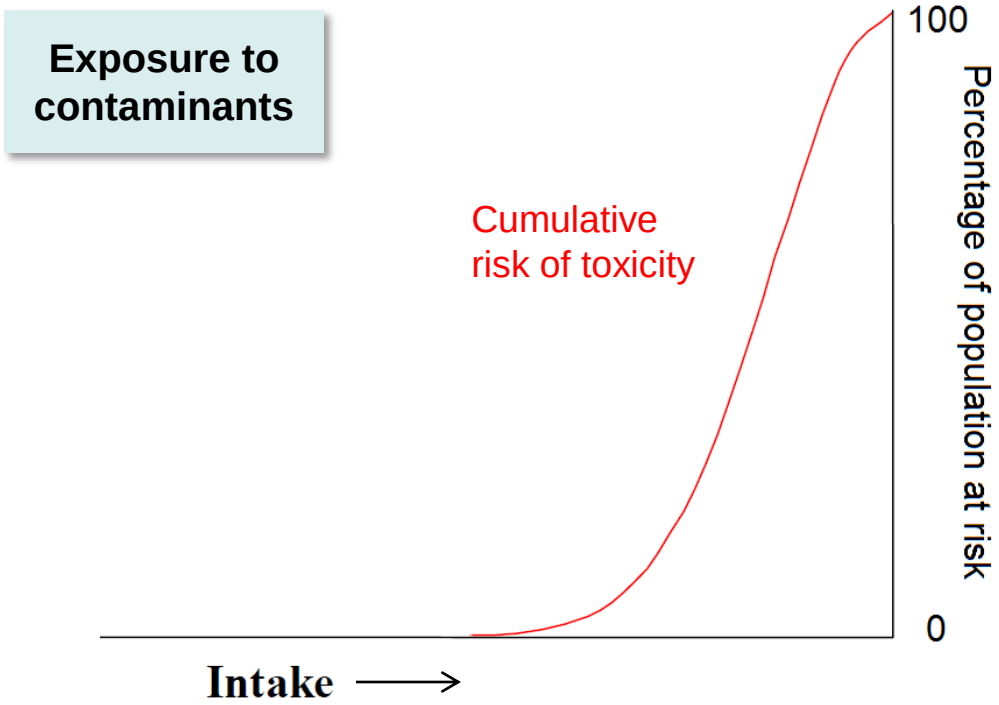
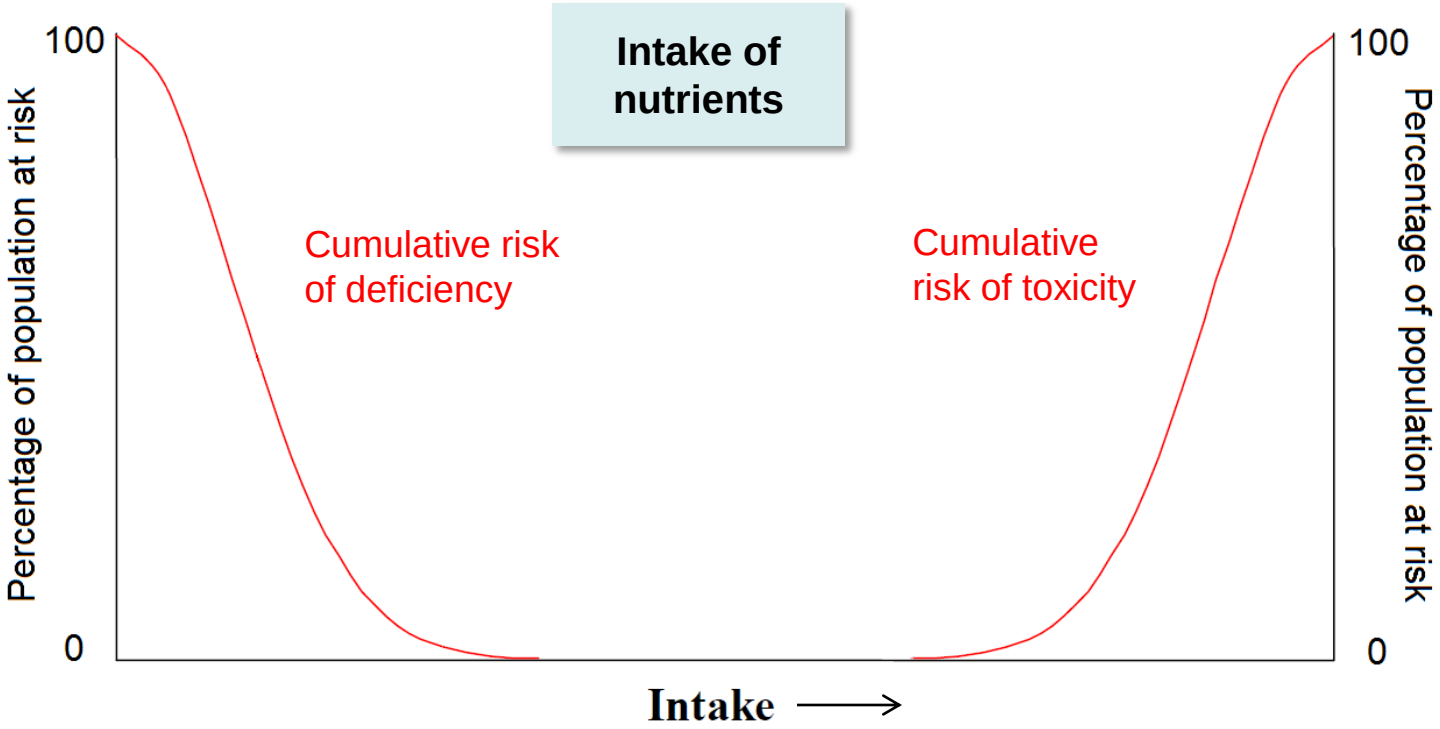
7 February 2018

Dietary exposure to contaminants and health risk



Intake of nutrients and health risk



The issue the research idea is addressing

Do we get enough or too much?

❑ **Intake/exposure assessment**

Dietary-based methods
E.g. total diet studies, duplic

Difficult and/or costly in many cases

Human biomonitoring (HBM)
Systematic standardized measurement of the concentration of a substance or its metabolites in human fluids/tissues (e.g. blood, urin milk ir, nails)

Essential to improve epidemiological studies: use of human data in risk assessment

Nutrients
Biomarkers of intake and status

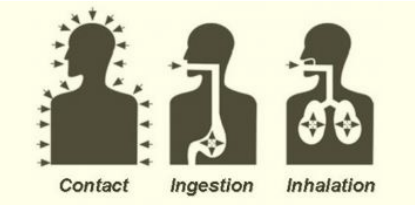
Is there an inadequate intake (deficiency) or excess intake?

Dietary
Regulated p
Biomarker

Is the aggregated exposure of health concern?

Human biomonitoring in food safety and nutrition

- For contaminants and regulated products HBM gives an indication of the **aggregated (i.e. dietary plus non-dietary) exposure** of a population



- If estimates of dietary exposure are available (e.g. by means of total diet studies), HBM may enable to assess the **relative magnitude of the different exposure pathways**

- In many cases, e.g. for some trace elements, the diet is the major source of exposure and **HBM directly assesses the intake through food and water**

Methylmercury

- The **integrated HBM of toxic substances and nutrients** may pinpoint **subgroups more vulnerable because of their nutritional status** (e.g., iodine status) and support **risk-benefit assessment** for certain foods (e.g., seafood)

Prioritizing substances for a HBM approach

- The **identification, validation and application of appropriate biomarkers in food safety studies** are developing fields where much remains to be done
- HBM, integrated with a variety of dietary-based approaches and mechanism-driven toxicological data, can yield **robust and novel evidence for risk and risk/benefit assessment**

Prioritization of substances for a HBM approach

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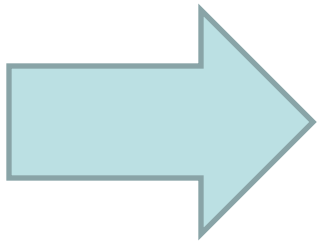
Improving exposure assessment and reducing uncertainties

- **Developing novel biomarkers of exposure** would have a significant impact by underpinning the different phases of risk assessment (e.g. linking evidence on external exposure, internal exposure, ADME and critical effects on target organs) and **substantially reducing associated uncertainties**
- Exposure assessment is a key part of all **epidemiological studies** and misclassification of exposure weakens the ability of a study to determine **whether an association exists with adverse health effects**
- At present, this **limits integration of epidemiological findings into regulatory risk assessment**

Reducing uncertainties in risk assessment



Benefits for consumers, industry, regulators

Needs to make this idea happen

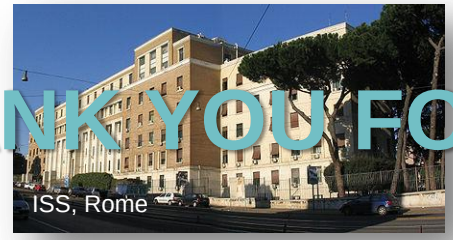
A cross-cutting interdisciplinary effort relying on public funding

Setting of priorities for the development of new specific and sensitive biomarkers

integrated with

Biomarkers of exposure <----------> **Biomarkers of effect**

- The research idea requires a **considerable effort** from the European research community and critically relies on **cross-cutting interdisciplinary research**
- It is very unlikely to be addressed appropriately if not sustained through **public funding**


ISS, Rome

THANK YOU FOR YOUR ATTENTION !

HARMONIZATION OF THE ENVIRONMENTAL RISK ASSESSMENT AND RISK MANAGEMENT OF PESTICIDE USE

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"The impact of chemicals on the ecosystem (release of chemicals into the environment)" is one of the 28 food safety risk assessment areas of priority for research identified by Member States and EFSA as part of the EU Risk Assessment Agenda (EU RAA)

In agricultural systems, the main aim is to achieve high crop yields under sustainable management systems, so the control of pests, weeds and diseases becomes fundamental. This requires the use of plant protection products (PPPs), which must be used in a proper, safe and effective way (Regulation 1107/2009 EC and Directive 2009/128/EC).

WHAT IS SOUGHT IN AGRICULTURAL SYSTEMS?

ACHIEVE HIGH & SAFE YIELDS (CROPS)

UNDER SUSTAINABLE MANAGEMENT SYSTEMS

But maintaining
"BIODIVERSITY RESERVOIR"

Necessary to control pests, weeds and diseases
PLANT PROTECTION PRODUCTS

Pollutants can enter into the system and affect:

Soils | Waters | Air | Fauna | Flora

General description

The European Union (EU) has currently one of the most developed pesticide control systems in the world. EU Regulation 1107/2009 lays down rules for the authorization of PPPs for marketing, use and control within the European Union.

The purpose of this regulation is to ensure a high level of protection of human and animal health, and the environment, as well as the improvement of the functioning of the European internal market. It recognizes the need to have safe PPPs available on the market to guarantee the competitiveness of EU agriculture.

This regulation establishes the need to perform the environmental risk assessment of pesticides, to demonstrate that the use of the PPPs complies with the criteria set in the Regulation and that the substances are not persistent, bioaccumulative, or meet the criteria of potential long-range transport in the environment.

In the risk assessment process, the FOCUS (FOrum for the Co-ordination of pesticide fate models and their USe) models are used.
These models consider different scenarios at European level to calculate exposure concentrations.
It would be necessary to develop a set of new scenarios that cover the specific conditions of other areas, such as the Mediterranean conditions.
The inherent diversity of landscapes, soils, vegetation, fauna, water fluxes,… and the overwhelming range of processes, interactions and controls that create the pattern of landforms at a particular area and determine the ecosystem biodiversity, influences the environmental risk assessment.

Assessment of the fate and behavior of pesticides in the environment

REGULATION 1107/2009 EC of placing of plant protection products on the market

Assessment: A tiered modeling approach

Models and Scenarios (FOCUS)

- Soil
- Ground water
- Surface water → **Sediments**

Scales: In-field / Edge off-field

Establish different "Risk Mitigation Measures" (RMM)

* To reduce the impact of use of pesticides
* To ensure an acceptable risk to non-target species

Directive 2009/128/EC of sustainable use of pesticides

Establish the framework to reduce the impact of use of pesticides

The implementation of MM to protect aquatic systems and vulnerable areas plays a main role

Assess how the RMM established at field level under Regulation 1107/2009 are acting at landscape/catchment level

The aquatic environment is especially sensitive to PPPs. It is necessary to pay particular attention to avoid pollution of surface and ground waters by taking appropriate measures, such as the establishment of buffer and safeguard zones or planting hedges along surface waters to reduce exposure of water bodies to spray drift, drain flow and run-off.

The dimensions of buffer zones should depend in particular on soil characteristics and pesticide properties, as well as agricultural characteristics of the areas concerned.

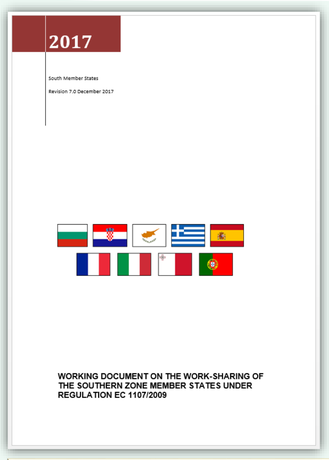
Use of PPPs in areas for the abstraction of drinking water, or on along transport routes, or on sealed or very permeable surfaces can lead to higher risks of pollution.

Connectivity concept is essential

To understand the transfer process of surface water, sediments and pollutants throughout catchments

For the success of the implemented measures for the sustainable management of pesticides at different scales (field, landscape and catchment levels)

In prioritising pesticide management activities, connectivity concept should be taken into account. Connectivity approach can be used across Europe to determine pressures and limiting factors to pesticide assessment and the capacity we may have to forecast future environmental/ecotoxicological conditions in order to define the impact of pesticides on the ecosystem. Mapping pesticide risk, vulnerability and environmental recovery would be very helpful for risk characterization, categorization and prediction.



4.3 National data requirements
Despite the fact that data requirements for PPPs are described in detail in the Regulation (EC) 284/2013, there are environmental conditions and agricultural practices that are specific to each MS. It is therefore necessary in order to ensure a high level of protection that each MS sets and makes publicly available the national data requirements and the conditions under which the relevant data should be submitted.
(Appendix IV: National data requirements for dossiers of PPPs)

4.4 Mitigation measures accepted by each MS of the southern zone
To minimise the risk for humans and the environment from the use of PPPs there are available different options. Risk mitigation measures are left to the individual member state (MS).
(Appendix V: List of mitigation options accepted in the countries belonging to the southern zone)

Progress in the harmonization of risk assessment and risk management and lines of future work among SMS in order to reach a harmonized approach for zonal evaluations

Proposals and aims to establish the basis to agree the possible refinements that MMSS can apply for the risk assessment

Foreseen impact/benefit

The impact/benefit of this risk assessment research approach focus on the harmonization of the criteria, procedures and conditions for the authorization of PPPs and the use of as much information as possible taking into consideration new scientific and technical knowledge in the interest of predictability, efficiency and consistency of the environmental risk assessment carried out. Careful attention shall be given to climatic, agronomic and environmental conditions.
The research will focus on the development of scenarios of typical Mediterranean crops, citrus and olive, and subtropical crops, banana.

Need to be sustained through public funding
The impact of the research is of general interest, having a social, economic and environmental impact at EU level. Productivity is only one dimension of sustainability and it is necessary to ensure a stable supply of food and feed, dealing in harmony with the essential natural resources on which agriculture depends. Crop pests are a major constraint to agricultural production in many parts of the world, with new challenges related to global change (climate, land use, biological invasions, plagues and emerging diseases, etc.), food security, conservation of natural resources and biodiversity.
Food security: pillar of the economic policy of a country → The use of PPPs in a proper, safe and effective way becomes fundamental.
In the evaluation process different gaps have been identified in the environmental risk assessment, whose approach can help **safeguard public health.**

To make this idea happen

key aspect: the funding, to support the hiring/granting of the necessary technical personnel, the purchase of equipment/material, and the cost of the training courses and work meetings. Our group has the facilities and expertise to help this research from the initial idea to development and result.

Collaboration with other partners is very interesting and helpful to cover different expertise areas, such as software and modelling. Furthermore, **collaboration with environmental risk assessors from other Member States** is advisable and thus considered.

Evaluation of microbiological risks of food handlers and food contact surface in the Czech catering facilities

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[2]Veterinary Research Institute, Brno Czech Republic

The monitoring and improving the safety of prepared foods catering facilities are key measures to protect consumers from foodborne diseases!

The focus of this study was to assess the hygienic standards of 11 foodservice facilities located in the Czech Republic by a microbiological monitoring of food contact surfaces (n = 290), and food handlers (n = 152) from April 2016 to September 2017.

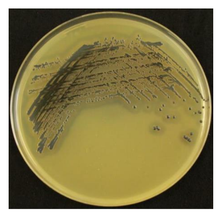
We used swabbing for testing of microbiological contamination on the area in gastronomy and glove-juice tests for hands of the food handlers.

The samples were analysed for the presence of the following bacteria: *Escherichia coli, Bacillus cereus, Staphylococcus aureus, Salmonella* spp., *Campylobacter* spp., and *Listeria monocytogenes* .

Bacillus cereus

The presence of *Bacillus cereus* was confirmed in 38.7% of the samples.

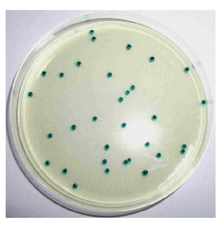
- food contact surface 28.7%
- handlers 10.0%.



Staphylococcus aureus

The presence of *S. aureus* was confirmed in 17.6% of the samples.

- food contact surface 11.1%
- handlers 6.5%.

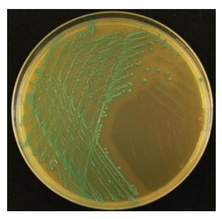


Escherichia coli

The presence of *Escherichia coli* was confirmed in 12.2% of the samples.

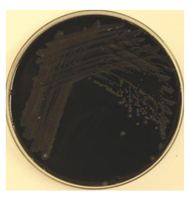
- food contact surface 8.4%
- handlers 3.8%.

The presence of verotoxigenic *E. coli* was not confirmed in samples.

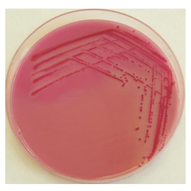


Listeria monocytogenes

L. monocytogenes was confirmed in 1 examined sample (0.2%).



Campylobacter spp.



Salmonella spp.

The microbial analysis examined showed an absence of *Salmonella* spp. a *Campylobacter* spp.

OUR OTHER RESEARCH:

- ✓ **Foodborne disease agents in meals.**
- ✓ **The presence of toxigenic strains in catering facilities (especially *Bacillus cereus* and *Staphylococcus aureus*).**
- ✓ **Microbiological risk assessment of food in various catering facilities.**

References available from the author.

Foto: Š. Bursová