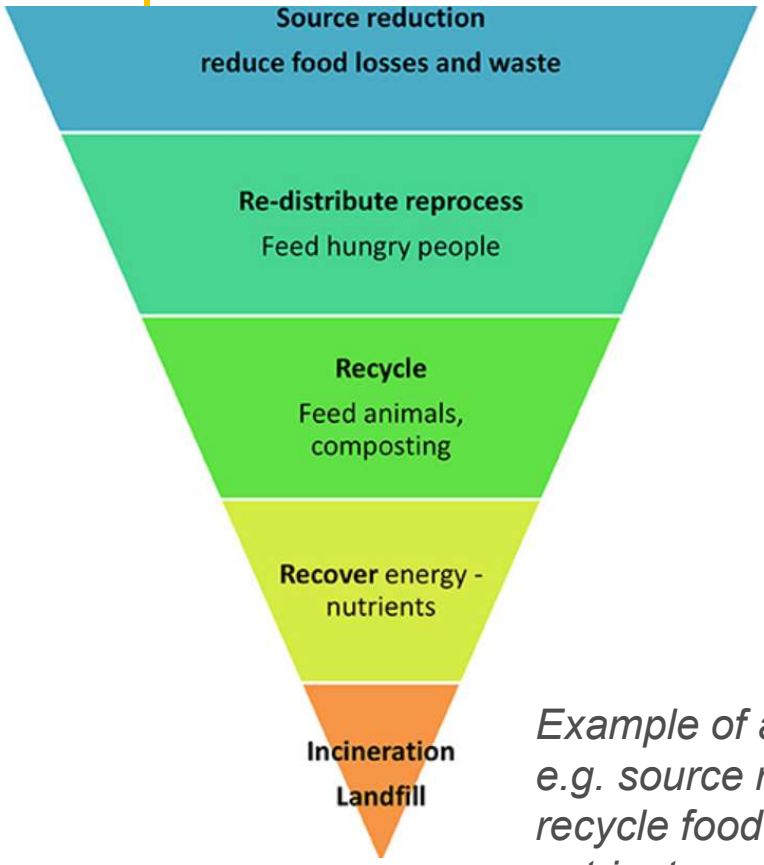
Accelerating together sustainable food needs by embracing next generation (non-animal) food safety testing methods.

Sandra Coecke et al.,
European Commission Joint Research Centre, Ispra, Italy
Horizontal Team Leader F2F Methods and Models for One Health

FoodSafety4EU pre-forum workshop

December 15, 2021

Accelerating together sustainable food needs



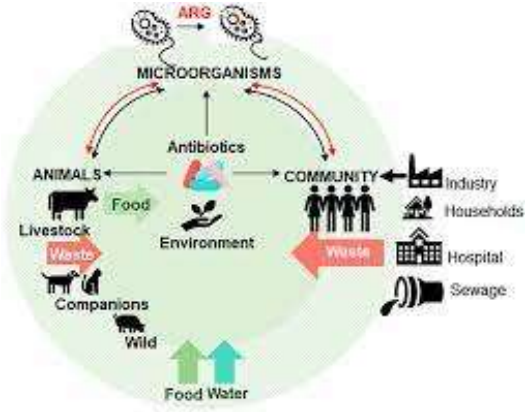
- United Nations sustainable development goals: eradication of hunger.
- Feed 10 billion persons 2050: CRITICAL are the trade-offs between
  1. food sustainability,
  2. food security,
  3. food safety
- and make better use of food already produced.

Example of a hierarchy of strategies for reducing food losses e.g. source reduction, reusing or reprocessing surplus foods, recycle food as feed for animals, recover the energy as biofuels, nutrients as compost, or raw materials for industry, while as last resorts one may consider recovering the energy by incineration or dumping as garbage in landfills.
https://www.frontiersin.org/articles/10.3389/fsufs.2020.00016/full

European Commission

Accelerating together sustainable food needs

In this regard our FUTURE trade-offs need to be informed by the PAST lessons LEARNED from the use of antimicrobials to e.g. intensify food production and contain microorganism and from the outbreak of bovine spongiform encephalopathy (BSE) in terms of circular food production



antibiotics

MDPI

Review

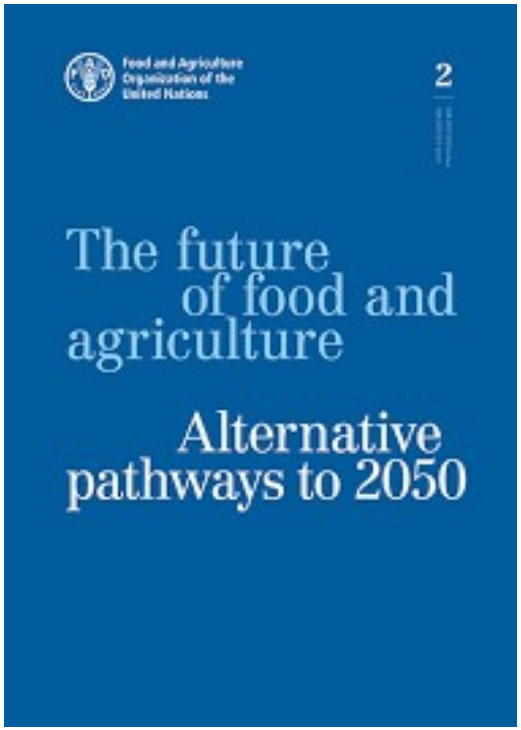
Antibiotics in Food Chain: The Consequences for Antibiotic Resistance

Shashi B. Kumar, Shanvanth R. Arnipalli and Ouliana Ziouzenkova *

Department of Human Sciences, The Ohio State University, Columbus, OH 43210, USA; kumar.864@osu.edu (S.B.K.); arnipalli.1@buckeyemail.osu.edu (S.R.A.)
* Correspondence: ziouzenkova.1@osu.edu

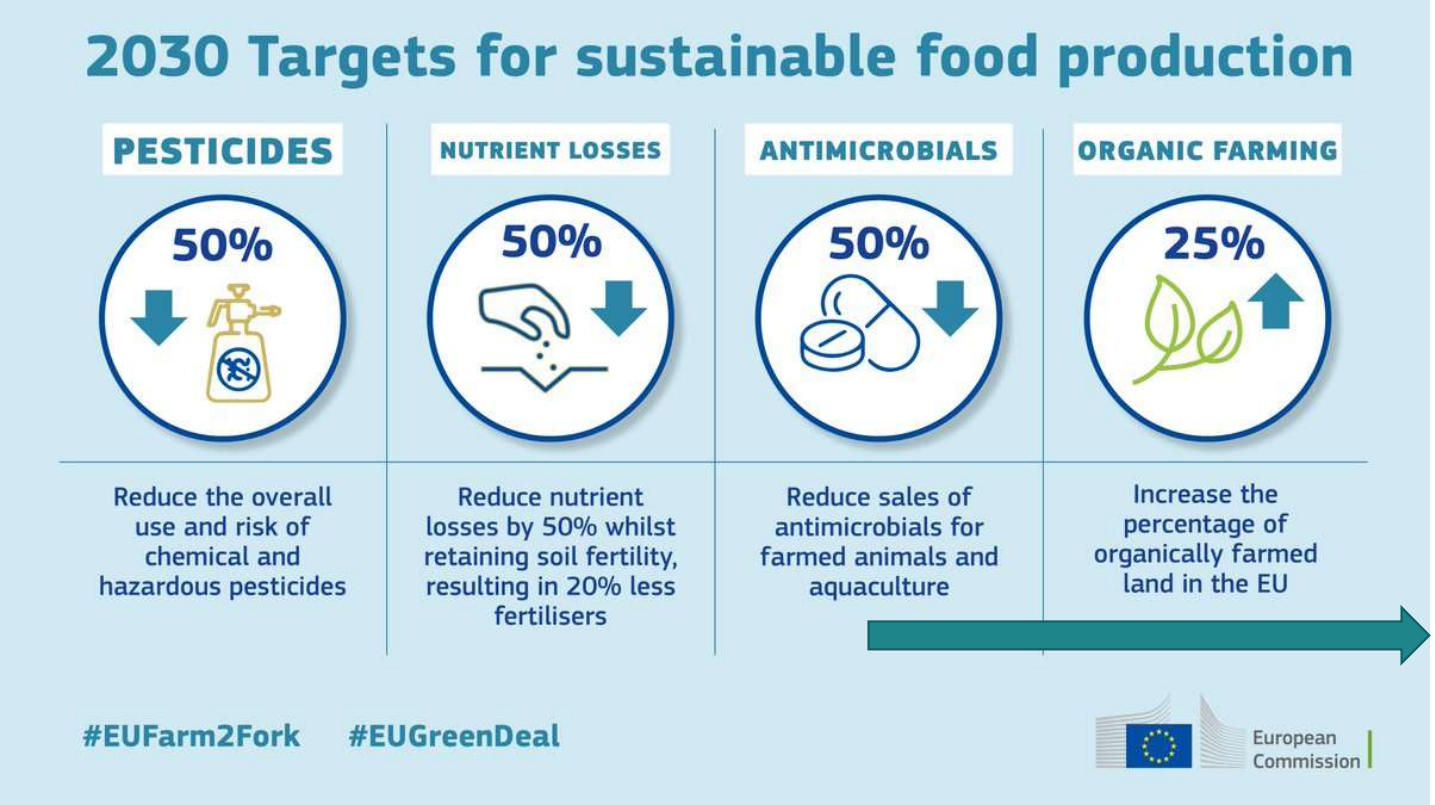
Received: 19 August 2020; Accepted: 8 October 2020; Published: 13 October 2020

check for updates



European Commission

Embracing next generation (non-animal) food safety testing models and methods for one health



Circular food production systems will contribute to future sustainable food but:
A sustainable future requires control of pathogens by other means since it is critical to avoid that cycles of nutrients become cycles of pathogens and/or hazards -> new generation of antimicrobials e.g. essential oils

Solutions to sustainability and food security should integrate feed and food safety considerations from the start:

NEW Approach Methods (NAMs) and Models

European Commission

European Commission

Directorate-General for Health and Food Safety (DG SANTE)

Food Safety

Safety

Animals

Plants

European Commission

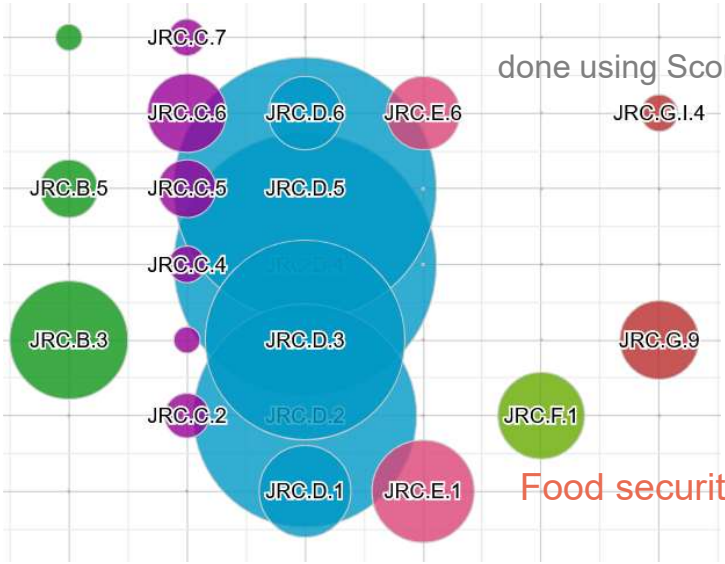
Accelerating together

JRC.F – Food Health and Reference Materials
JRC.B – Growth and Innovation
JRC.C – Energy, Transport and Climate
JRC.D – Sustainable Resources
JRC.E – Space, Security and Migration
JRC.I – Competences
JRC.H – Knowledge Management
JRC.G – Nuclear Safety and Security

done using ScoMap

Food safety

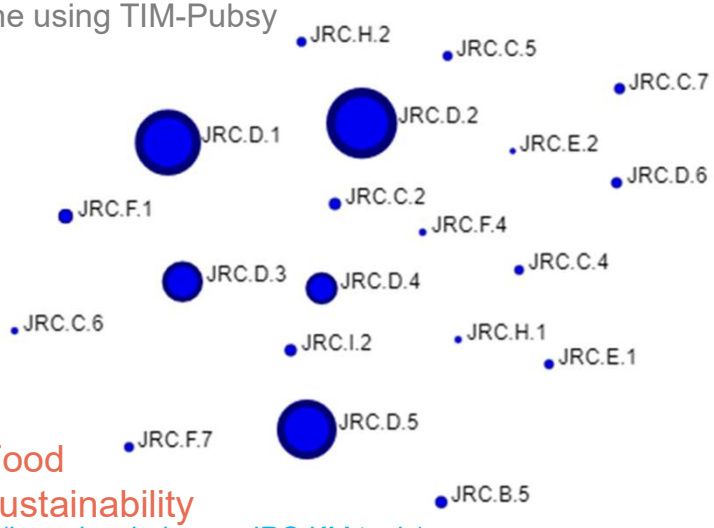
done using ScoMap



Food security

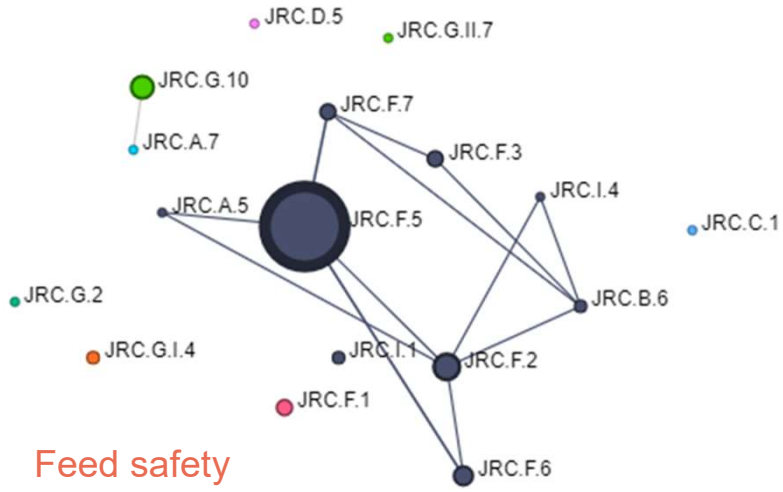
JRC sites

done using TIM-Pubsy



Food sustainability

done using TIM-Pubsy



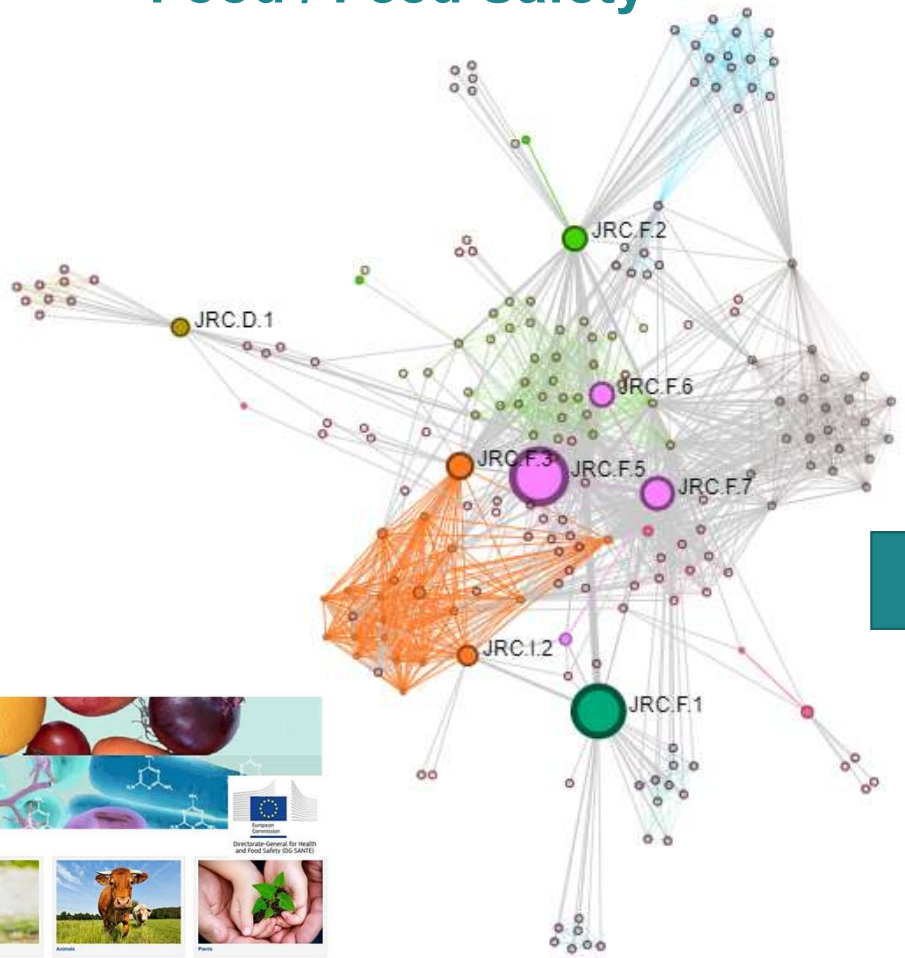
Feed safety

Source: F7 Amalia.MUNOZ-PINEIRO (based on in-house JRC KM tools)

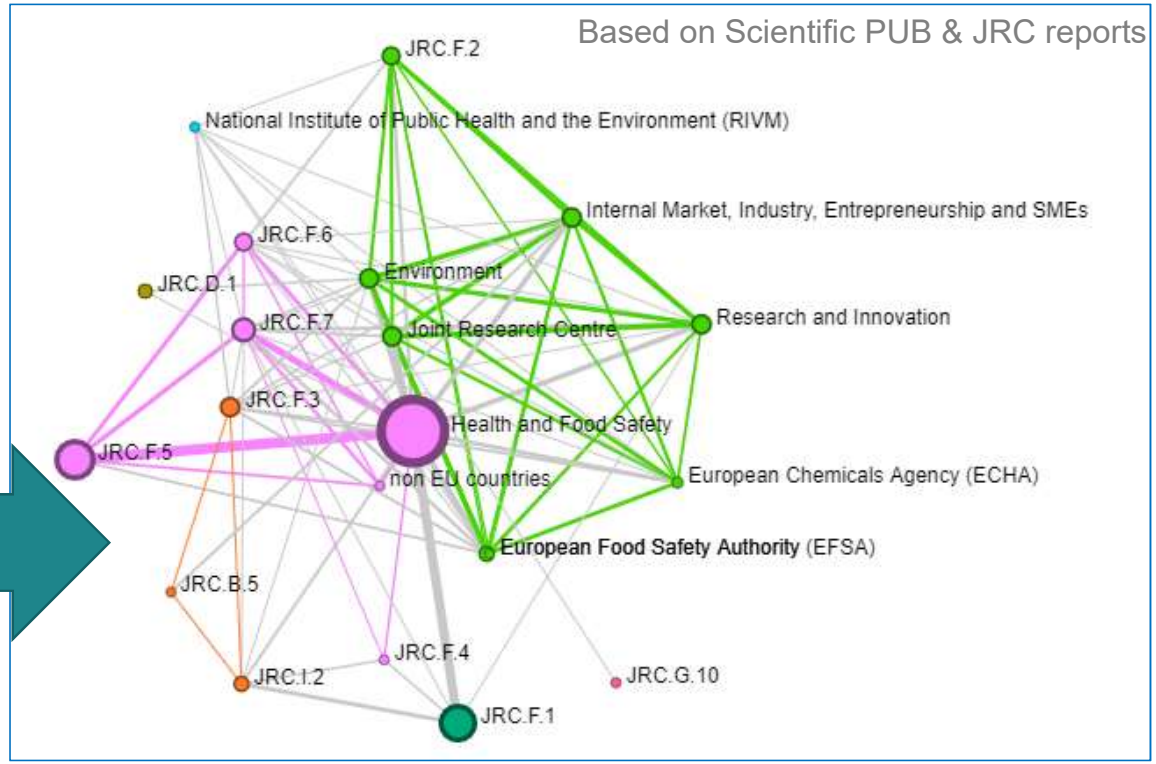
Accelerating together feed and food safety needs

Overall view of network of collaborators of ECJRC units working on

Food / Feed Safety



Zooming in and filtering most collaborations on the topic



European Commission

Source: F7 Amalia.MUNOZ-PINEIRO (based on in-house JRC KM tools)

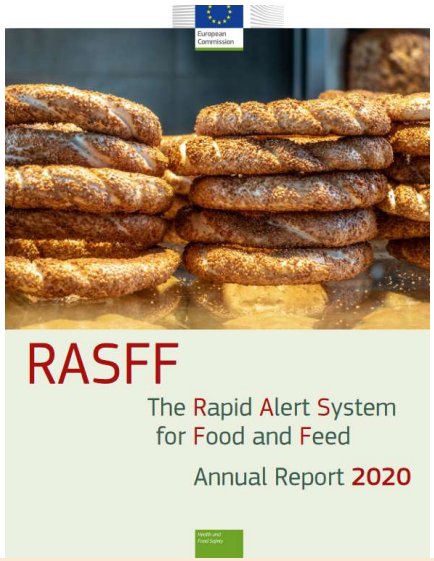
Sustainable Food Needs / Food Safety

Relevant EU Policies; EU General Food Law and related risk-based food safety regulatory frameworks; The EU Green Deal; Farm to Fork strategy; Biodiversity strategy; Strategy for sustainable Chemicals; Common agricultural policy (CAP); EU consumer policy; EU environment policy; EU global food security

revealed that the key drivers with impact in Food Safety are:

1. Climate change,
2. Changes in food and farming systems;
3. Rapid technological advancements and emerging technologies;
4. Assessment of new technologies;
5. The current COVID-19 pandemic
6. Integration and improving hazard and risk assessment methodologies -> NAMs

NAMs are essential in the processes of risk assessment and risk evaluation, especially the processes surrounding the new generation of genetically modified foods and new anti-microbials and new types of feed and food exponentially introduced in the food supply chain.



In Europe, the Regulation (EU) 2019/1381, published on the 6th September 2019, aims to improve the transparency and sustainability of the EU risk assessment in the food chain by amending the General Food Law Regulation (EC 178/2002) and a number of other regulations related to the food sector.
This Regulation is introduced as a response to the Fitness Check of the General Food Law Regulation as well as a response to public concerns expressed by a European Citizens' Initiative on glyphosate and pesticides.

European Commission

FOOD SAFETY TESTING NAMs NEEDS

human cell/tissues

1. Feed Additives
2. Flavouring substances
3. Food additives
4. Food contact materials
5. Food enzymes
6. GMO
7. Health Claims
8. Infant/Follow-on formulae
9. Novel foods
10. Pesticides

Human relevant in vitro mechanistic methods

Reliability (reproducibility)

TEST SYSTEM(S) & TECHNOLOGIES (MF etc.) + MEASURE ENDPOINTS / BIOMARKERS + DATA INTERPRETATION

Relevance: scientific basis

Relevance: Applied use for a specific purpose

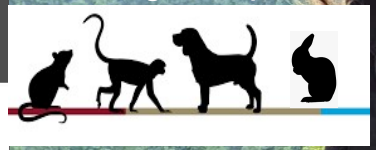
European Commission

The pharmaceutical, cosmetics and chemical industries are working on NAMs development but still lots of work to do: an old and recent example

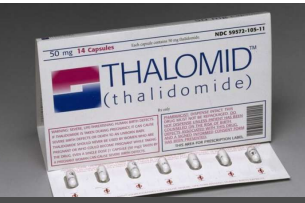
toxicological decision-making & toxicity testing needs continued innovation

Montelukast Thalidomide

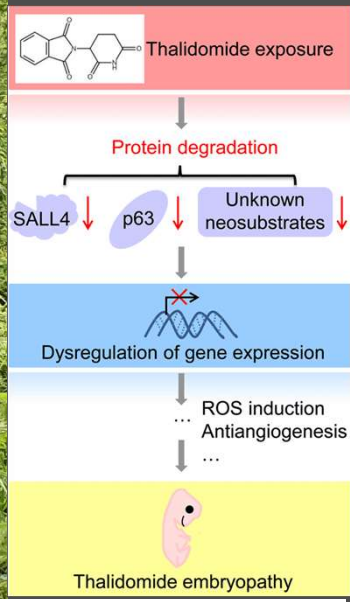
Toxicological species



Sandra & Silvia
adverse drug reaction survivors
30 May 2021 near Uscio, Italy



Thalidomide (immunomodulator) Teratogenicity



Pharmacology

Review

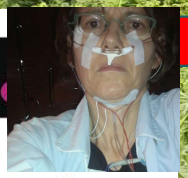
Pharmacology 2014;94:60–70
DOI: 10.1159/000366164

Received: June 20, 2014
Accepted after revision: July 27, 2014
Published online: September 2, 2014

Montelukast-Induced Adverse Drug Reactions: A Review of Case Reports in the Literature

Gioacchino Calapai[b] Marco Casciaro[a] Marco Miroddi[b] Fabrizio Calapai[b]
Michele Navarra[c] Sebastiano Gangemi[a,d]

[a]School and Division of Allergology and Clinical Immunology, at [b]Department of Clinical and Experimental Medicine, and [c]Department of Drug Sciences and Health Products, University of Messina, and [d]Institute of Clinical Physiology (IFC), Consiglio Nazionale delle Ricerche (CNR), Messina Unit, Messina, Italy



PRP Pharmacology Research & Perspectives

ORIGINAL ARTICLE

Adverse drug reactions of montelukast in children and adults

Meindina G. Haarman[1], Florence van Hunsel[2] & Tjalling W. de Vries[3]

[1]Department of Pediatric Cardiology, Center for Congenital Heart Diseases, Beatrix Children's Hospital, University Medical Center Groningen, The Netherlands
[2]Netherlands Pharmacovigilance Center Lareb, Den Bosch, The Netherlands
[3]Department of Pediatrics, Medical Center Leeuwarden, Leeuwarden, The Netherlands

ASPET THE JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS

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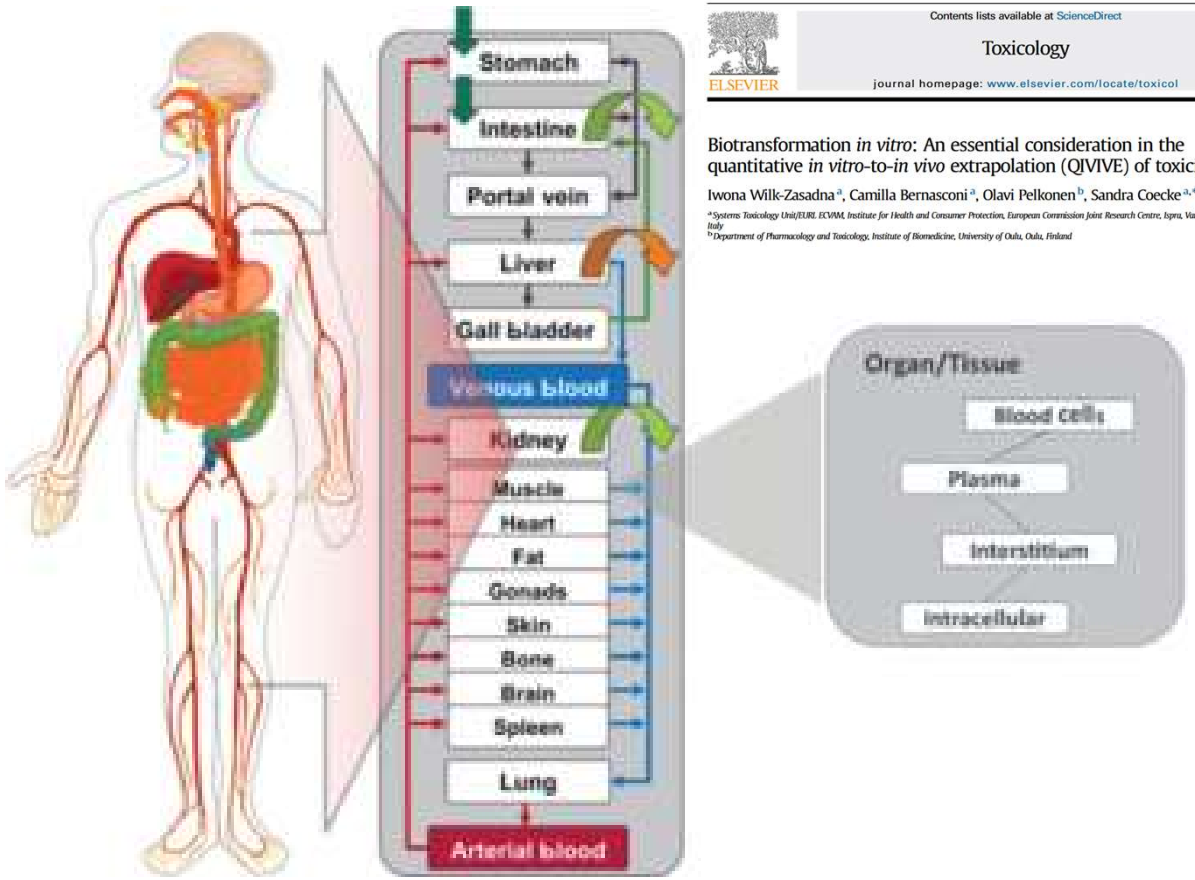
Research Article | ABSORPTION, DISTRIBUTION, METABOLISM, AND EXCRETION

Metabolism of Thalidomide in Liver Microsomes of Mice, Rabbits, and Humans

Jun Lu, Nuala Helsby, Brian D. Palmer, Malcolm Tingle, Bruce C. Baguley, Philip Kestell, and Lai-Ming Ching
Journal of Pharmacology and Experimental Therapeutics August 2004, 310 (2) 571-577; DOI: https://doi.org/10.1124/jpet.104.067793

S. COECKE diagnosis: Montelukast 10 mg, 2009-2015, immunomodulator, anti-leukotriene (asthma) adverse effect with multi-organ and multi-system failure

Integration and improving hazard and risk assessment methodologies -> NAMs



Toxicology 332 (2015) 8–19

Contents lists available at ScienceDirect

Toxicology

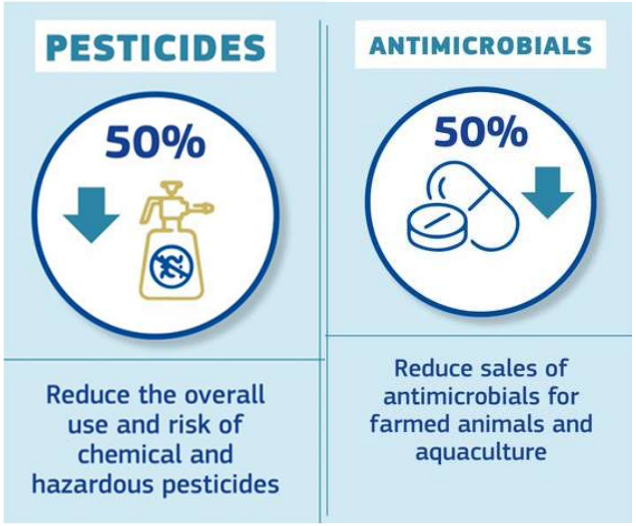
journal homepage: www.elsevier.com/locate/toxicol

Biotransformation *in vitro*: An essential consideration in the quantitative *in vitro*-to-*in vivo* extrapolation (QIVIVE) of toxicity data

Iwona Wilk-Zasadna[a], Camilla Bernasconi[a], Olavi Pelkonen[b], Sandra Coecke[a,*]

[a] Systems Toxicology Unit/EURL ECVAM, Institute for Health and Consumer Protection, European Commission Joint Research Centre, Ispra, Varese I-21027, Italy

[b] Department of Pharmacology and Toxicology, Institute of Biomedicine, University of Oulu, Oulu, Finland



Dynamics: What chemicals e.g. pesticides, microplastics, pathogens do to the human body

Kinetics: What the human body does to chemicals, microplastics, pathogens

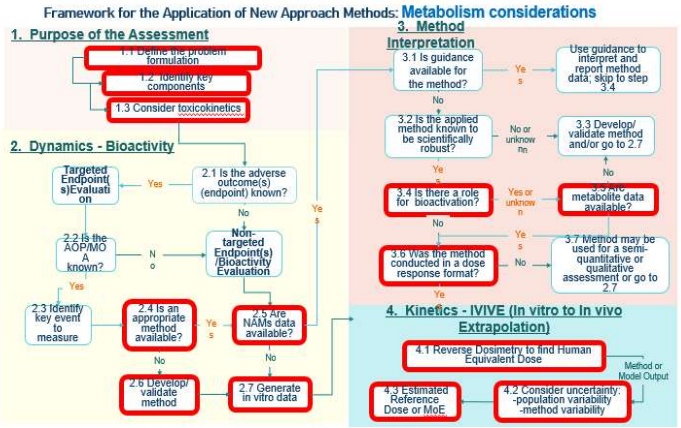
https://www.jpharmsci.org/article/S0022-3549(15)30247-1/fulltext

European Commission

Need for FS NAMs Framework

A Future Framework for Application of *In Vitro* Metabolism and QIVIVE Models to Inform Chemical Risk Assessment

Esther Haugabrooks, Sandra Coecke, Xiaoqing Chang, Kelly Magurany, Sue Marty, Rebecca Clewell



SCIENTIFIC REPORT

EFSA Journal

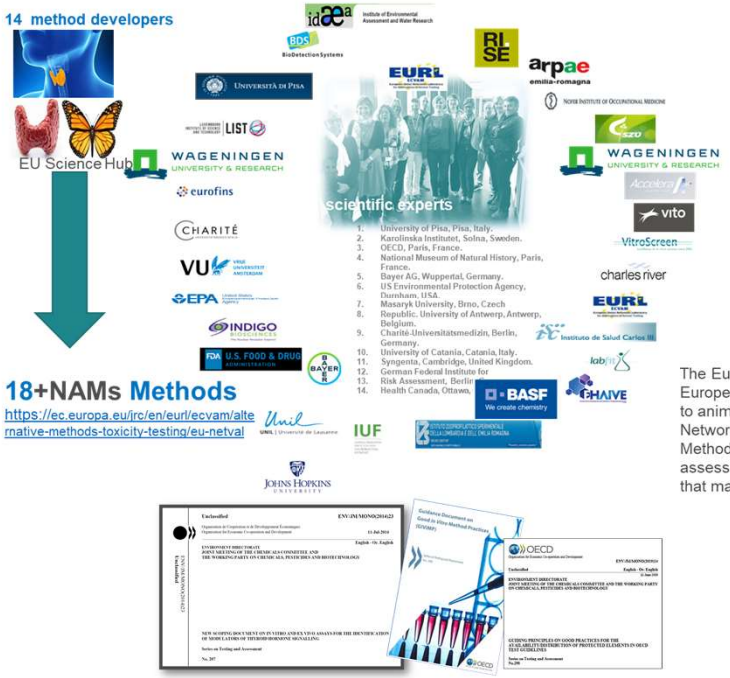
APPROVED: 20 March 2020

doi: 10.2903/j.efsa.2020.6088

Cumulative dietary risk characterisation of pesticides that have chronic effects on the thyroid

European Food Safety Authority (EFSA),
Peter S Craig, Bruno Dujardin, Andy Hart, Antonio F Hernandez-Jerez, Susanne Hougaard Bennekou, Carsten Kneuer, Bernadette Ossendorp, Ragnor Pedersen, Gerrit Wolterink and Luc Mohimont

EU and global Experimental Capacity building



GLP

15 EU-NETVAL labs Thyroid 35 TOTAL

https://ec.europa.eu/jrc/en/eurl/ecvam/alternative-methods-toxicity-testing/eu-netval

European member states, organisations experts, invest in method validation

The European Commission Joint Research Centre's European Union Reference Laboratory for alternatives to animal testing in collaboration with European Union Network of Laboratories for the Validation of Alternative Methods (total 35) has launched a validation study to assess 17-mechanistic methods to detect chemicals that may interact with the thyroid hormone system.

TECHNICAL REPORT

efsa European Food Safety Authority Supporting Publications

APPROVED: 24 April 2020

doi:10.2903/sp.efsa.2020.EN-1836

Outcome of the public consultation on draft scientific report on the cumulative dietary risk characterisation of pesticides that have chronic effects on the thyroid

European Food Safety Authority (EFSA)

SCIENTIFIC REPORT

EFSA Journal

ADOPTED: 26 June 2019

doi: 10.2903/j.efsa.2019.5800

Establishment of cumulative assessment groups of pesticides for their effects on the nervous system

European Food Safety Authority (EFSA),
Federica Crivellente, Andy Hart, Antonio F Hernandez-Jerez, Susanne Hougaard Bennekou, Ragnor Pedersen, Andrea Terron, Gerrit Wolterink and Luc Mohimont

Abstract

Cumulative assessment groups of pesticides have been established for five effects on the nervous system: brain and/or erythrocyte acetylcholinesterase inhibition, functional alterations of the motor, sensory and autonomic divisions, and histological neuropathological changes in neural tissue. Sources of uncertainties resulting from the methodological approach and from the limitations in available data and scientific knowledge have been identified and considered. This report supports the publication of a scientific report on cumulative risk assessment to pesticides affecting the nervous system, in which all uncertainties identified for either the exposure assessment or the establishment of the cumulative assessment groups are incorporated into a consolidated risk characterisation.

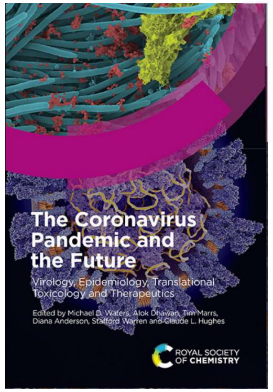
European Commission

NAM

***Methods** are key components in any framework for the application of animal free new approach methods*

Assessing SARS-CoV-2

Or any other food and feed related pathogens and their effect on animal or human health

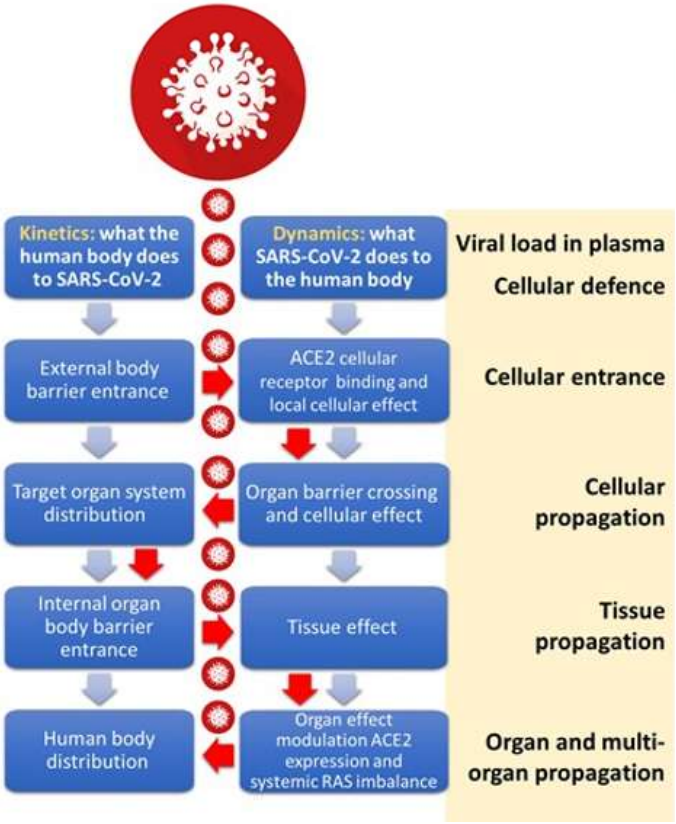


THE CORONAVIRUS PANDEMIC AND THE FUTURE

Knowledge from human relevant cell, tissue and mathematics-based methods as key tools for understanding COVID-19

BY SANDRA COECKE, AMALIA MUNOZ, VITO D'ALESSANDRO, FRANCESCA DE BERNARDI, PIETRO ROMEO, FELIPE TORRES, GEORGINA HARRIS AND SURAT PARVATAM | 20 MAY 2021

Diagnostic tools, preventive and curative strategies will be possible using knowledge from the new generation of in vitro and in silico methods and related technologies



Open Source on-line Chemistry World Web side : This article publicly available is on the Chemistry World web together with other chapters (you need a registration to have free access just with mail and PW) Link below as Chapter 18
https://www.chemistryworld.com/the-coronavirus-pandemic-and-the-future/knowledge-from-human-relevant-cell-tissue-and-mathematics-based-methods-as-key-tools-for-understanding-covid-19/4013732.article

Besides the web version the chapter will be together with all the other chapters **a reference book on COVID 19 for the global population published by Chemistry world** with **ISBNs for the hard copy book 978-1-83916-306-7 and and e-book, which are 978-1-83916-364-7**
https://books.google.nl/books/about/The_Coronavirus_Pandemic_and_the_Future.html?id=vNINzgEACAAJ&source=kp_book_description&redir_esc=y
AVAILABLE FROM APRIL 2022

European Commission

Essential oils: The case of Alpha-Pinene: antimicrobial activities

αPN rates among the most important monoterpenes of human exposure

EFSA (2011) **EFSA panel on food contact materials, enzymes, flavourings and processing aids (CEF)**.

Consideration of aliphatic and alicyclic and aromatic hydrocarbons evaluated by JECFA (63rd meeting) structurally related to aliphatic and aromatic hydrocarbons evaluated by EFSA in FGE.25Rev2. EFSA J 9(6:2178):69. doi:10.2903/j.efsa.2011.2178

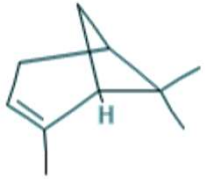
SCIENTIFIC OPINION *Adopted 2015* EFSA Journal

ADOPTED: 1 December 2015 PUBLISHED: 05 January 2016

doi:10.2903/j.efsa.2016.4339

Safety and efficacy of eight compounds belonging to chemical group 31 (aliphatic and aromatic hydrocarbons) when used as flavourings for all animal species and categories

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP)



The FEEDAP Panel concluded that: E-pinene, D-pinene, E-caryophyllene, myrcene, camphene, E-ocimene and δ-3-carene **are safe at the proposed maximum dose level** (5 mg/kg complete feed) for all animal species, except myrcene and β-ocimene when 4 mg/kg would apply for cats. For valencene, the calculated safe use level is 1.5 mg/kg complete feed for cattle, salmonids and non-food producing animals, and 1.0 mg/kg complete feed for pigs and poultry. No safety concern would arise for the consumer from the use of these compounds up to the highest safe levels in feeds. The Panel is unable to conclude on user safety in the absence of specific data.

WHO FOOD ADDITIVES SERIES: 54

Safety evaluation of certain food additives

Common Name: **alpha-PINENE**

Synonyms: 2-Pinene; Cyclic Dexadiene

Chemical Name: Bicyclo[3.1.1]Hept-2-ene, 2,6,6-Trimethyl-

Date: August 2008 Revision: April 2017

CAS Number: 80-56-8

RTK Substance Number: 0052

DOT Number: UN 2368

EMERGENCY RESPONDERS >>>> SEE BACK PAGE

Hazard Summary

Hazard Rating	NJDOH	NFPA
HEALTH	-	1
FLAMMABILITY	-	3
REACTIVITY	-	0

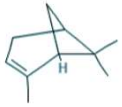
FLAMMABLE
POISONOUS GASES ARE PRODUCED IN FIRE
CONTAINERS MAY EXPLODE IN FIRE

Hazard Rating Key: 0=minimal; 1=slight; 2=moderate; 3=serious; 4=severe

Reasons for Citation

- **alpha-Pinene** is on the Right to Know Hazardous Substance List because it is cited by ACGIH, DOT and NFPA.
- This chemical is on the Special Health Hazard Substance List.

The case of Alpha-Pinene *cont.*



Industrial Crops & Products 124 (2018) 643–652

Differences in essential oil yield, composition, and bioactivity of three juniper species from Eastern Europe

T. Radoukova[a], V.D. Zheljazkov[b,*], I. Semerdjieva[c], I. Dincheva[d], A. Stoyanova[e], M. Kačániová[f,g], T. Marković[h], D. Radanović[h], T. Astatkie[i], I. Salamon[j]

https://www.sciencedirect.com/science/article/pii/S0926669018307064

Toxicology and Applied Pharmacology 418 (2021) 115496

Toxicokinetic evaluation of the common indoor air pollutant, α-pinene, and its potential reactive metabolite, α-pinene oxide, following inhalation exposure in rodents

Suramya Waidyanatha[a,*], Michael Hackett[b], Sherry R. Black[c], Mathew D. Stout[a], Timothy R. Fennell[c], Melanie R. Silinski[c], Scott L. Watson[c], Joseph Licause[c], Veronica G. Robinson[a], Barney Sparrow[b], Reshan A. Fernando[c], Stephen Cooper[c], Cynthia V. Rider[a]

https://www.sciencedirect.com/science/article/abs/pii/S0041008X21001034

IMAP Group Assessment Report, Australia , 2020

This group assessment contains chemicals related to alpha-pinene. Three of the chemicals in this group are: alpha-pinene(unspecified isomer) (CAS No. 80-56-8), the (1S,5S)- or (-)-alpha-pinene (CAS No. 785-26-4) isomer and the (1R,5R)- or (+)-alpha-pinene isomer (CAS No. 7785-70-8). They are closely structurally-related and are expected to have similar . The chemicals are naturally-occurring and the racemic mixture of both enantiomers does not occur in nature. In thisassessment, 'alpha-pinene', refers to the unspecified isomer, unless stated otherwise.This assessment also includes the chemical 'oil of turpentine, alpha-pinene fraction' (CAS No. 65996-96-5). This chemical is the distillation fraction of turpentine oil containing >80 % alpha-pinene . While this fraction is expected to also contain small amountsof the other terpene hydrocarbons in turpentine (beta-pinene, delta-3-carene, camphene, terpinolene, carene and limonene), its toxicological profile is expected to be closely related to that of alpha-pinene (CAS No. 80-56-8)

Phytotherapy Research

Volume 28, Issue 9
September 2014
Pages 1284-1287

Research Article

Daily Inhalation of α-Pinene in Mice: Effects on Behavior and Organ Accumulation

Tadaaki Satou, Hikaru Kasuya, Kazumi Maeda, Kazuo Koike

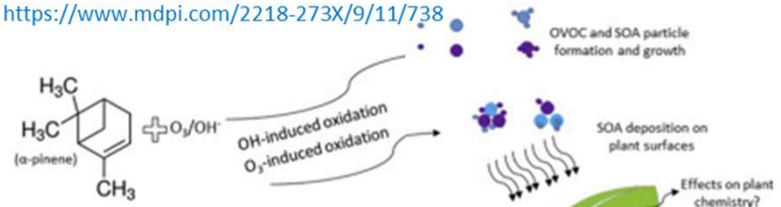
First published: 26 December 2013 | https://doi.org/10.1002/ptr.5105 | Citations: 28

Environmental Pollution
Volume 263, Part B, August 2020, 114437

Deposition of α-pinene oxidation products on plant surfaces affects plant VOC emission and herbivore feeding and oviposition ☆

Archives of Toxicology **91**, 677–687 (2017)

https://www.mdpi.com/2218-273X/9/11/738



Human metabolism of α-pinene ar metabolite kinetics after oral administration

Lukas Schmidt & Thomas Göen

biomolecules

Therapeutic Potential of α- and β-Pinene: A miracle Gift of Nature

Biomolecules. 2019 Nov; 9(11): 738.
10.3390/biom9110738

Comparative Biochemistry and Physiology Part C: Pharmacology, Toxicology and Endocrinology
Volume 124, Issue 3, November 1999, Pages 239-246

Induction of xenobiotic metabolising enzymes in the common brushtail possum, *Trichosurus vulpecula*, by *Eucalyptus* terpenes

Georgia J Pass, Stuart McLean, Ieva Stupans

MOLECULAR ECOLOGY

Volume 29, Issue 9
May 2020
Pages 1674-1683

ORIGINAL ARTICLE

Strategies in herbivory by mammals revisited: The role of liver metabolism in a juniper specialist (*Neotoma stephensi*) and a generalist (*Neotoma albigula*)

Teri J. Orr, Smiljka Kitanovic, Katharina M. Schramm, Michele M. Skopec, P. Ross Wilderman, James R. Halpert, M. Denise Dearing

Alpha-pirene: Human health tier II assessment

https://www.industrialchemicals.gov.au/sites/default/files/Alpha-pinene_Human%20health%20tier%20II%20assessment.pdf

The cytochrome P450 CYP6DE1 catalyzes the conversion of α-pinene into the mountain pine beetle aggregation pheromone *trans*-verbenol

Christine C. Chiu, Christopher I. Keeling & Joerg Bohlmann

https://www.nature.com/articles/s41598-018-38047-8

Need for FS NAMs methods and foresight

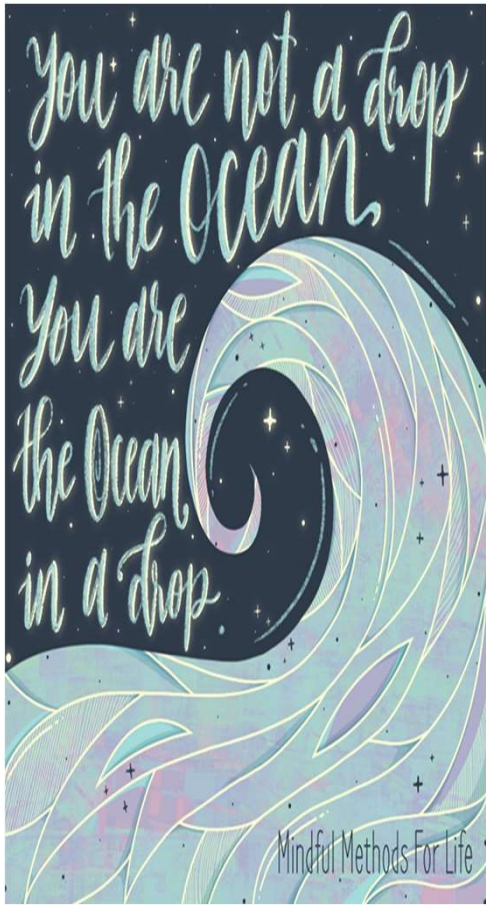
Proving method reproducibility (in-house and between laboratories)

is recommended SCIENTIFIC GOOD PRACTICE prior to using NAMs to generate data and is essential for regulatory use of the data.

#GrowingTogether
#StrongerTogether
#Paradigmshift to
#humanrelevant #qualityscience

Fast-response for emerging hazards Target groups:

National authorities, policy makers and risk managers, research, industry, consumers, society, professional associations, ad hoc young people structured group to guarantee a systemic approach and cross-sectorial approach for global uptake of NAMs in food safety testing



European Commission

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