THE GUT AS A TARGET ORGAN AND BARRIER:

CHALLENGES AND OPPORTUNITIES FOR NAMs IN CHEMICAL RISK ASSESSMENT

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Disclaimer: The views, thoughts and opinions presented are not necessarily those of EFSA

SETTING THE REGULATORY SCENE

FOOD AND CHEMICAL SAFETY IN THE EU

1.2.2002 EN Official Journal of the European Communities L 31/1

I

(Acts whose publication is obligatory)

REGULATION (EC) No 178/2002 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 28 January 2002
laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety

30.6.2009 EN Official Journal of the European Union L 170/1

I

(Acts adopted under the EC Treaty/Euratom Treaty whose publication is obligatory)

DIRECTIVES

DIRECTIVE 2009/48/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 18 June 2009
on the safety of toys
(Text with EEA relevance)

30.12.2006 EN Official Journal of the European Union L 396/1

I

(Acts whose publication is obligatory)

REGULATION (EC) No 1907/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 18 December 2006

concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC

22.12.2009 EN Official Journal of the European Union L 342/59

REGULATION (EC) No 1223/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 30 November 2009
on cosmetic products
(recast)
(Text with EEA relevance)

Overview – different regulations and different data requirements!

→Environmental pollutants – **No Testing**

→Pharmaceuticals, food additives, plant protection products, biocides – **Extensive testing**

→Industrial and consumer chemicals (>30K in the EU) – **Limited testing to extensive testing**

→Cosmetics – **No animal data**

EFSA was established under EU law in 2002 following a series of food crises

TO

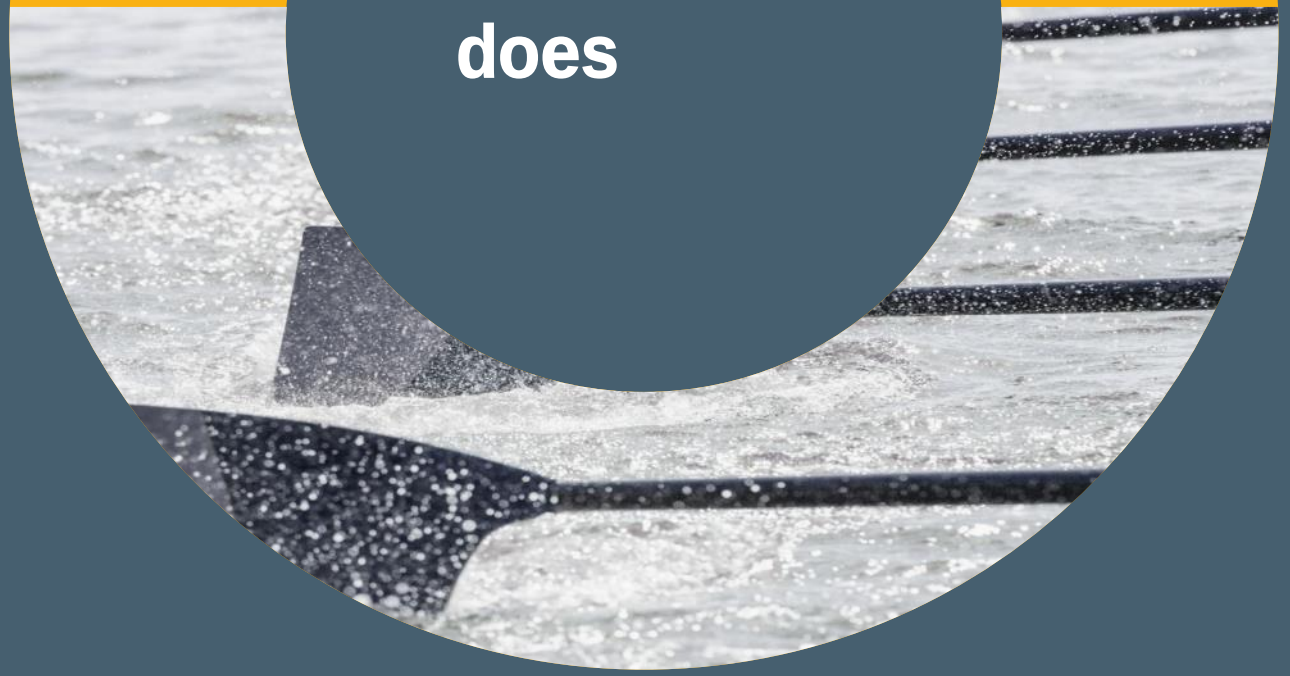
Improve the EU food safety system

Help ensure a high level of consumer protection

Restore and maintain confidence in the EU food supply

Clearly separate risk assessment and risk management functions

What EFSA does



- Provides independent scientific advice and support for EU risk managers and policy makers on food and feed safety
- Provides independent, timely risk communication
- Promotes scientific cooperation

SETTING THE EFSA SCENE (I)

Regulated products

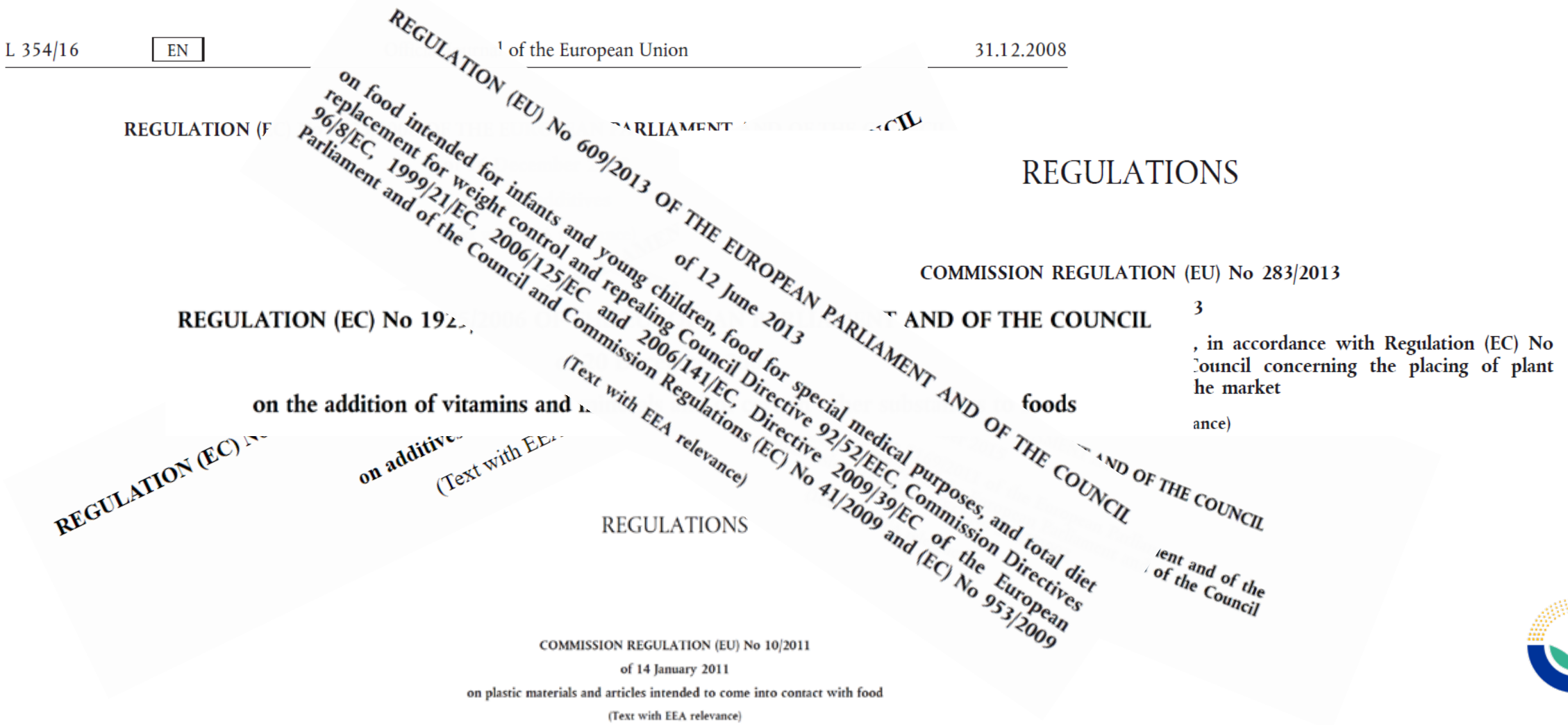
Contaminants

Applicants

No commercial producer

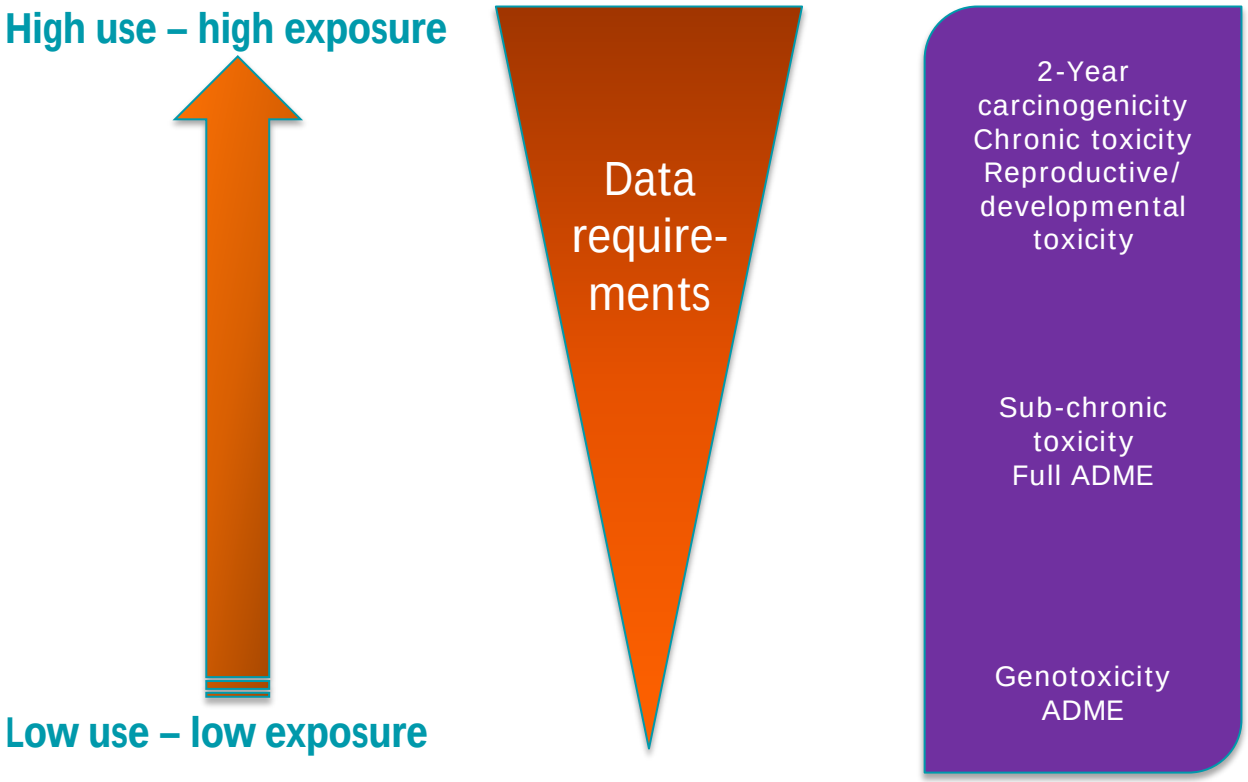
New chemicals or already on market

SETTING THE EFSA SCENE (II)



SETTING THE EFSA SCENE (III)

DATA: WHAT DO WE GET?



MAIN SOURCES AND TYPES OF DATA RECEIVED BY EFSA

In vivo biological studies	• ADME studies • Following OECD TG and GLP criteria • Traditional TK parameters (Tmax, t1/2, AUC, analytical data, etc...)
In vivo toxicological studies	• Sub-chronic, chronic, repro-dev studies • Following OECD TG and GLP criteria • Traditional Tox parameters (biochemistry, histopathology, weight, food consumption, etc...)
In vitro studies	• Mainly for genotoxicity and metabolism • Following OECD TG and GLP criteria • Traditional parameters (biochemistry, markers for mutagenesis and chromosomal aberrations, etc..)

Traditional chemical risk assessment relies mainly on animal bioassays

NEW CHALLENGES AND THREATS

Environmental risks

- multiple stressors and bees

Evaluation of the safety of new products

- novel foods
- nanomaterials (e.g. nano-pesticides)

Development of new assessment methods

- NAMs (in vitro, in chemico, in silico)
- '-omics', less animal testing

Chemical mixtures/ combined toxicity of substances in food

Antimicrobial resistance

Hazards linked to globalisation

- plant pests, animal diseases, vector-borne diseases

TRANSITION TO NGRA

SCIENCE-POLICY INTERFACE

The Commission will:

- foster multidisciplinary research and digital innovations for **advanced tools, methods and models, and data analysis capacities**[102] to also move away from animal testing;

EC policy

Safety testing and chemical risk assessmeneed to innovate in order to reduce dependency on animal testing but also to improve quality, efficiency and speed of chemical hazard and risk assessments.

EFSA strategy 2027

STRATEGIC OBJECTIVE 2

Ensure preparedness for future risk analysis needs

KEY ACTIONS

- Develop and integrate new approach methodologies (NAMs) and omics for regulatory risk assessment

NAMs landscape

European Partnership for the Assessment of Risks from Chemicals
Horizon Europe

EURL ECVAM
European Union Reference Laboratory for Alternatives to Animal Testing

APCRA

OECD

ASPIS Consortium (RISK-HUNT3R, ONTOX and PrecisionTOX)

efsa
European Food Safety Authority

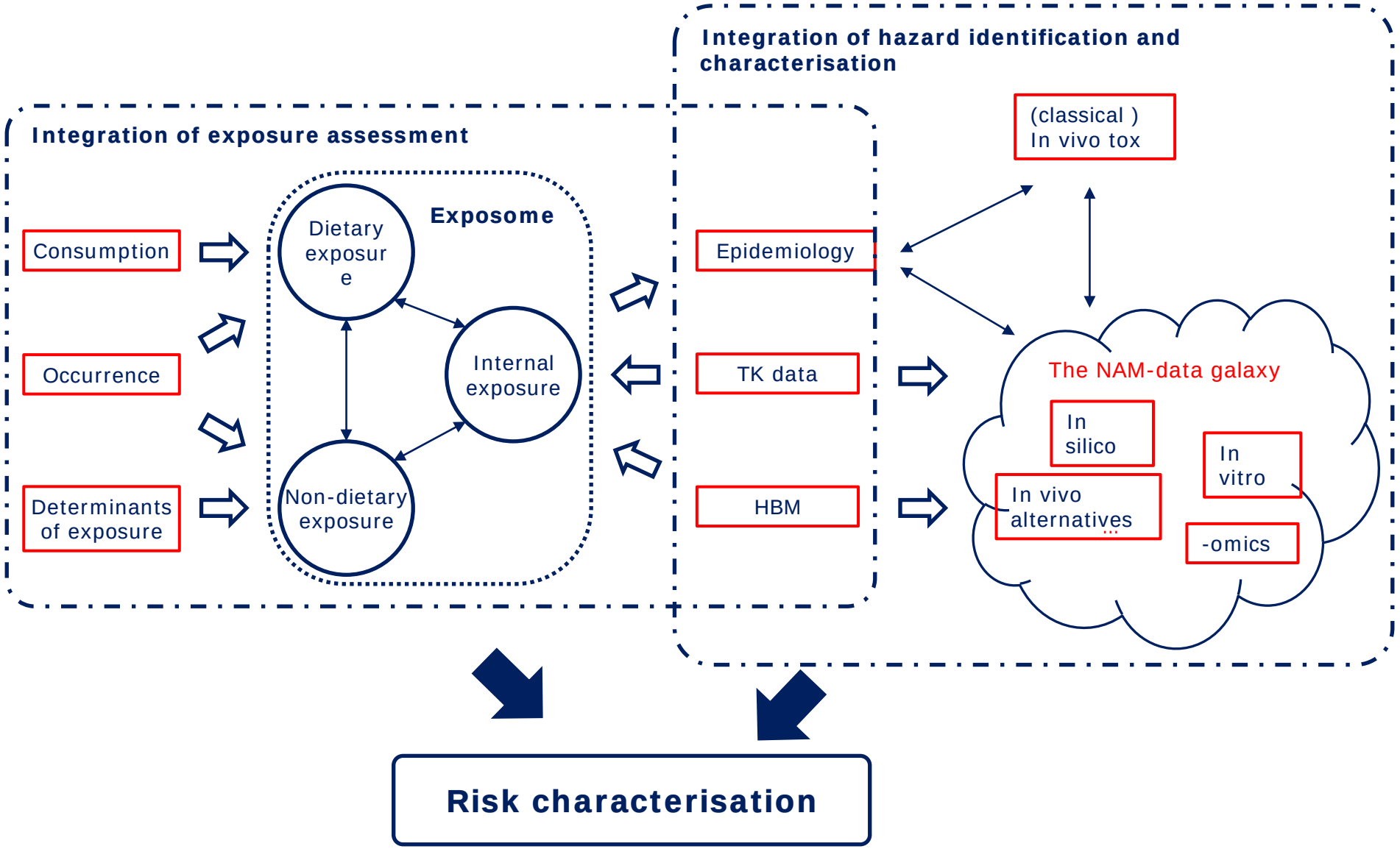
ECHA

Global Coalition for Regulatory Science Research

ILMERAC

EUTOXRISK

3R, NAMS AND EFSA: OUR VISION – SHORT TO MEDIUM TERM



EFSA'S JOURNEY TO NGRA

Under development

Guidance on the Use of the Read-across Approach in Food Safety Assessment

EFSA Scientific Committee

EFSA Journal

SCIENTIFIC OPINION

ADOPTED: 22 September 2021

doi: 10.2903/j.efsa.2021.6877

Opinion on the impact of non-monotonic dose responses on EFSA's human health risk assessments

EFSA Scientific Committee,

SCIENTIFIC OPINION

ADOPTED: 21 April 2021

doi: 10.2903/j.efsa.2021.6599

Development of Integrated Approaches to Testing and Assessment (IATA) case studies on developmental neurotoxicity (DNT) risk assessment

EFSA Panel on Plant Protection Products and their Residues (EFSA PPR Panel).

EFSA Journal

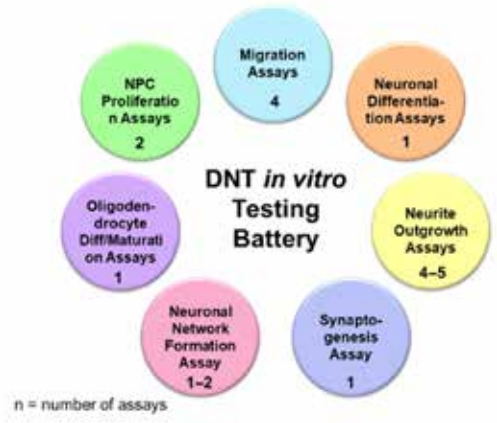
GUIDANCE

ADOPTED: 30 June 2021

doi: 10.2903/j.efsa.2021.6768

Guidance on risk assessment of nanomaterials to be applied in the food and feed chain: human and animal health

EFSA Scientific Committee.



EFSA Journal

GUIDANCE

ADOPTED: 17 November 2021

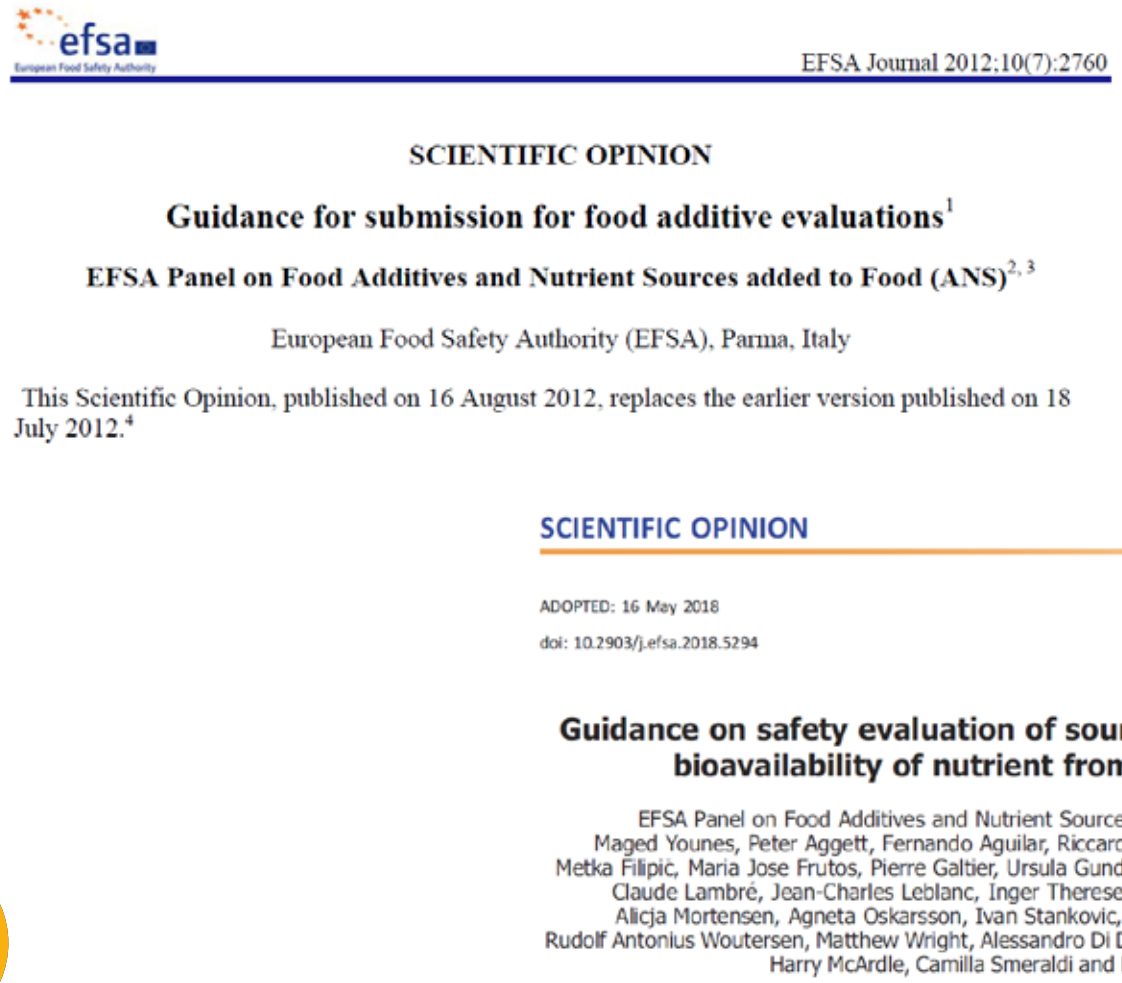
doi: 10.2903/j.efsa.2021.7033

Guidance Document on Scientific criteria for grouping chemicals into assessment groups for human risk assessment of combined exposure to multiple chemicals

EFSA Scientific Committee.

UNDERSTANDING ABSORPTION/PHARMACO-KINETICS: WHY?

3R IN TIERED APPROACHES IN EFSA GUIDANCE



efsa
European Food Safety Authority

EFSA Journal 2012;10(7):2760

SCIENTIFIC OPINION

Guidance for submission for food additive evaluations[1]

EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS)[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

This Scientific Opinion, published on 16 August 2012, replaces the earlier version published on 18 July 2012.[4]

SCIENTIFIC OPINION

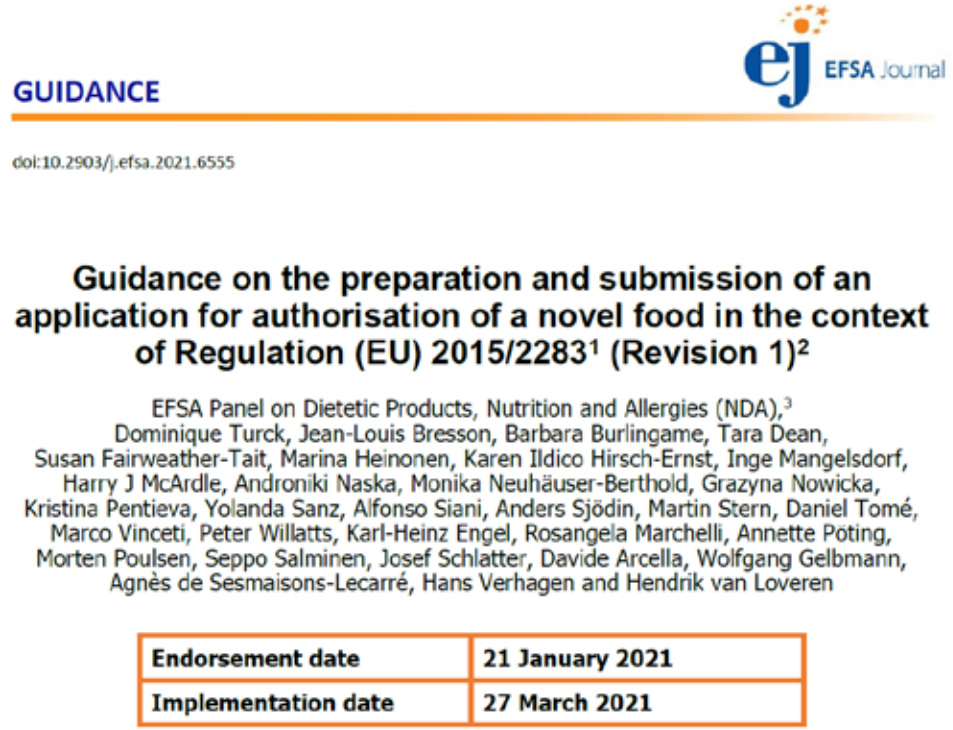
EFSA

ADOPTED: 16 May 2018

doi: 10.2903/j.efsa.2018.5294

Guidance on safety evaluation of sources of nutrients and bioavailability of nutrient from the sources

EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS),
Maged Younes, Peter Aggett, Fernando Aguilar, Riccardo Crebelli, Birgit Dusemund, Metka Filipič, Maria Jose Frutos, Pierre Galtier, Ursula Gundert-Remy, Gunter Georg Kuhnle, Claude Lambré, Jean-Charles Leblanc, Inger Therese Lillegaard, Peter Moldeus, Alicja Mortensen, Agneta Oskarsson, Ivan Stankovic, Ine Waalkens-Berendsen, Rudolf Antonius Woutersen, Matthew Wright, Alessandro Di Domenico, Susan Fairweather-Tait, Harry McArdle, Camilla Smeraldi and David Gott



GUIDANCE

EFSA Journal

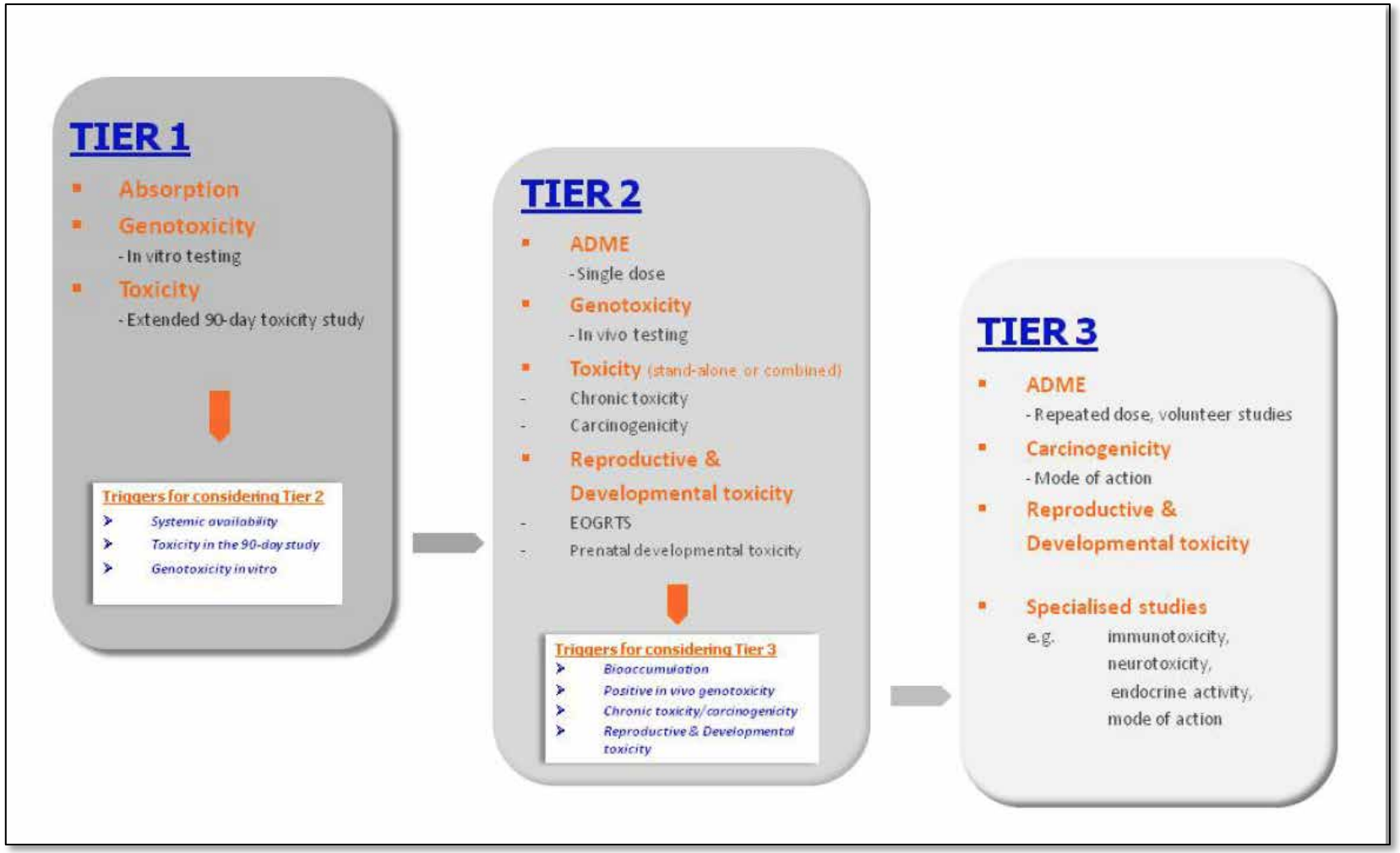
doi:10.2903/j.efsa.2021.6555

Guidance on the preparation and submission of an application for authorisation of a novel food in the context of Regulation (EU) 2015/2283[1] (Revision 1)[2]

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA),[3]
Dominique Turck, Jean-Louis Bresson, Barbara Burlingame, Tara Dean, Susan Fairweather-Tait, Marina Heinonen, Karen Ildico Hirsch-Ernst, Inge Mangelsdorf, Harry J McArdle, Androniki Naska, Monika Neuhäuser-Berthold, Grazyna Nowicka, Kristina Pentieva, Yolanda Sanz, Alfonso Siani, Anders Sjödin, Martin Stern, Daniel Tomé, Marco Vinceti, Peter Willatts, Karl-Heinz Engel, Rosangela Marchelli, Annette Poting, Morten Poulsen, Seppo Salminen, Josef Schlatter, Davide Arcella, Wolfgang Gelbmann, Agnès de Sesmaisons-Lecarré, Hans Verhagen and Hendrik van Loveren

Endorsement date	**21 January 2021**
Implementation date	**27 March 2021**

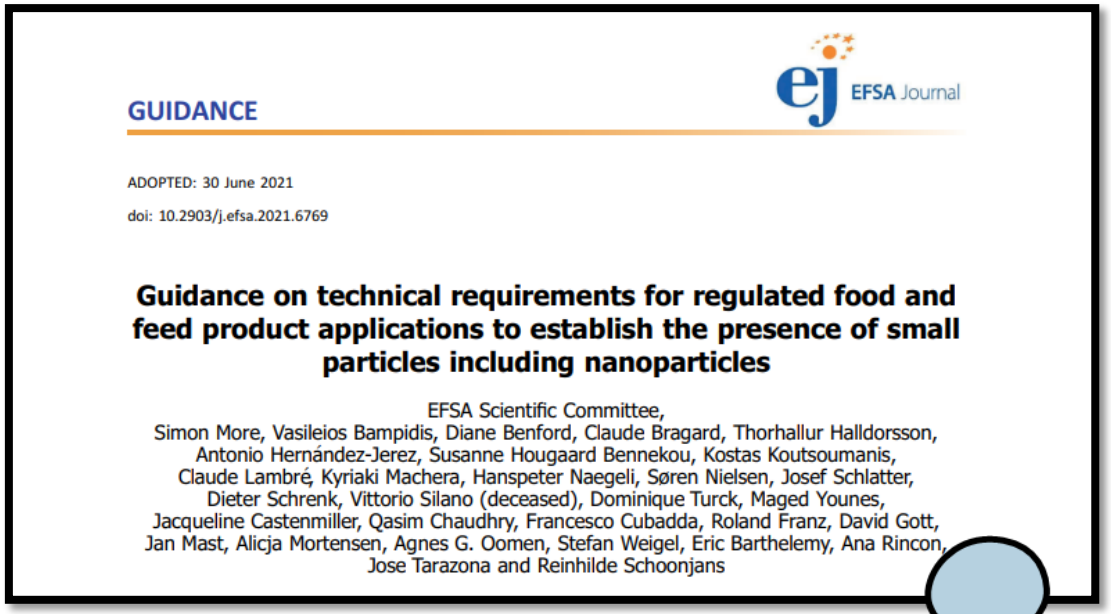
ABSORPTION AS A DECISION POINT FOR HIGHER TIERED STUDIES



'Demonstration of negligible absorption may provide a scientific justification for not undertaking higher tiered toxicological studies.'

NANO GUIDANCE OVERVIEW

Guidance on Particle - Technical Requirements



GUIDANCE

EFSA Journal

ADOPTED: 30 June 2021

doi: 10.2903/j.efsa.2021.6769

Guidance on technical requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles

EFSA Scientific Committee,
Simon More, Vasileios Bampidis, Diane Benford, Claude Bragard, Thorhallur Halldorsson, Antonio Hernández-Jerez, Susanne Hougaard Bennekou, Kostas Koutsoumanis, Claude Lambré, Kyriaki Machera, Hanspeter Naegeli, Søren Nielsen, Josef Schlatter, Dieter Schrenk, Vittorio Silano (deceased), Dominique Turck, Maged Younes, Jacqueline Castenmiller, Qasim Chaudhry, Francesco Cubadda, Roland Franz, David Gott, Jan Mast, Alicja Mortensen, Agnes G. Oomen, Stefan Weigel, Eric Barthelemy, Ana Rincon, Jose Tarazona and Reinhilde Schoonjans

Guidance on Nano - Risk Assessment

GUIDANCE

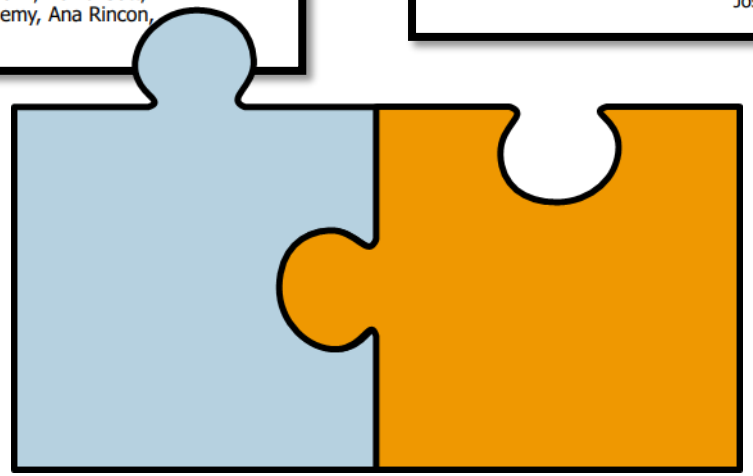
EFSA Journal

ADOPTED: 30 June 2021

doi: 10.2903/j.efsa.2021.6768

Guidance on risk assessment of nanomaterials to be applied in the food and feed chain: human and animal health

EFSA Scientific Committee,
Simon More, Vasileios Bampidis, Diane Benford, Claude Bragard, Thorhallur Halldorsson, Antonio Hernández-Jerez, Susanne Hougaard Bennekou, Kostas Koutsoumanis, Claude Lambré, Kyriaki Machera, Hanspeter Naegeli, Søren Nielsen, Josef Schlatter, Dieter Schrenk, Vittorio Silano (deceased), Dominique Turck, Maged Younes, Jacqueline Castenmiller, Qasim Chaudhry, Francesco Cubadda, Roland Franz, David Gott, Jan Mast, Alicja Mortensen, Agnes G. Oomen, Stefan Weigel, Eric Barthelemy, Ana Rincon, José Tarazona and Reinhilde Schoonjans



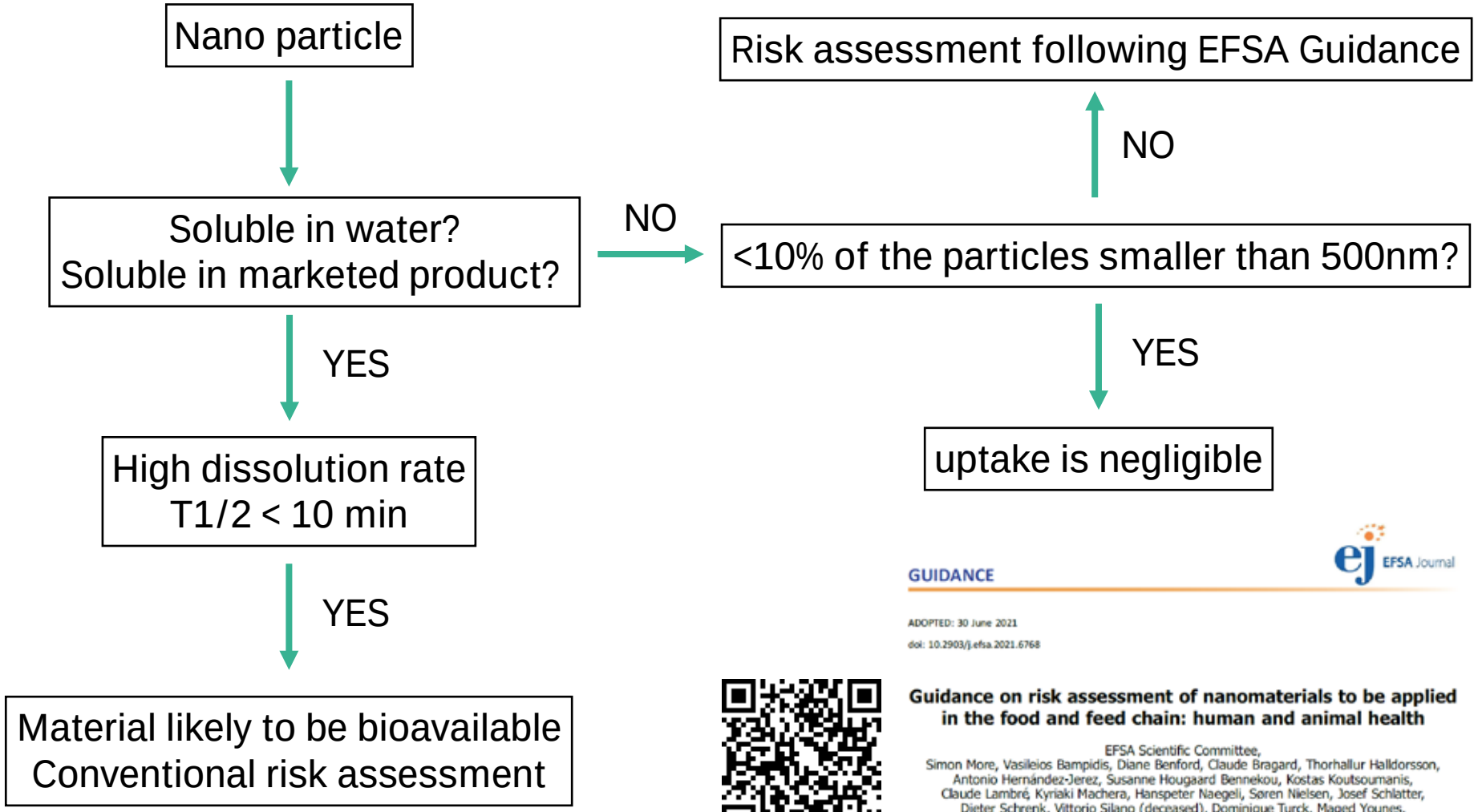
APPRAISAL ROUTES PROPOSED

- S.2 Solubility
- S.2 Dissolution rate
- S.3 Screening particle size
- S.3 Quantification particle size
- S.4 Coverage by existing studies

Cost & Complexity

‘Exit routes’ of information requirements complementing the conventional risk assessment designed to ‘exclude’ the needs of nano-specific assessment according to Guidance on Nano - RA

SCHEMATIC FLOW



GUIDANCE

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ASSESSING ABSORPTION: MOVING AWAY FROM IN VIVO

EXTERNAL SCIENTIFIC REPORT

APPROVED: 2 May 2022

doi:10.2903/sp.efsa.2022.EN-7341

Development of a Roadmap for Action on

New Approach Methodologies in Risk Assessment

Sylvia E. Escher[1], Falko Partosch[1], Sebastian Konzok[1], Paul Jennings[2], Mirjam Luijten[3], Anne Kienhuis[3], Victoria de Leeuw[3], Rosmarie Reuss[4], Katrina-Magdalena Lindemann[4], Susanne Hougaard Bennekou[5]

[1] Fraunhofer ITEM, [2] Vrije Universiteit Amsterdam, [3] National Institute for Public Health and the Environment, [4] Eura AG, [5] The National Food Institute Denmark

Use of New Approach Methodologies for the hazard assessment of nanofibers

Nanocellulose oral exposure: gastrointestinal digestion, nanofibers uptake and local effects

NANOCELLUP

Francesco Cubadda

Dept. Food Safety, Nutrition and Veterinary Public Health

Istituto Superiore di Sanità - *National Institute of Health*

Rome, Italy

Stakeholder workshop on small particles and nanoparticles in food | 31 March – 1 April 2022

New EFSA projects	ADME4NGRA
	NAMS4NANO

Thank you!

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