International Association for Food Protection WEBINAR

Food Toxicology Webinar-
Introduction to Toxicology Part II: New Methodologies: Application in Food Safety and International Trade

Organized by: IAFP's International Food Protection Issues PDG

Moderator: Steven Hermansky, DABT

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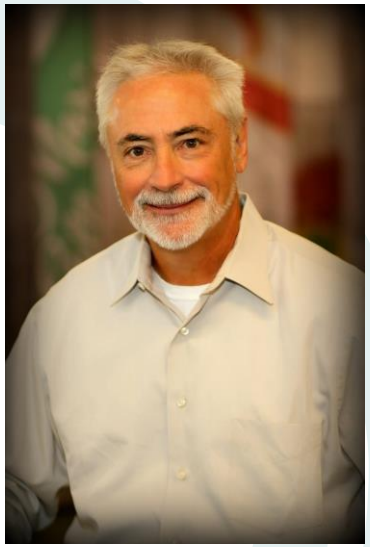
- This webinar is being recorded and will be available for access by IAFP members at www.foodprotection.org within one week.

Introductions:

Marianne Solomotis Ph.D. FDA
Deputy Director, and Director of Research, Office of Applied Research and Safety Assessment, Center for Food Safety and Applied Nutrition, FDA
As such, she oversees the research in the office, including microbiology and toxicology.

After completing her Ph.D. at the University of the Witwatersrand, South Africa, she was invited to do a Post-Doctoral Fellowship at the University of Maryland School of Medicine, Center for Vaccine Development, Baltimore, MD. She started working at the FDA/CFSAN as a research microbiologist and then changed positions serving as a Risk Assessment Team Lead and/or Project Manager on risk assessments of specific pathogen and/or commodity of concern until she moved on to her current role.

Today's moderator:



Steven J. Hermansky, Pharm.D., Ph.D., DABT
Senior Science Advisor, Toxicology

Steven J. Hermansky joined FDA in April 2022 to work in the area of chemical food safety and to evaluate and move to New Alternative Methods in their continuing effort to reduce, refine and even replace animal use in toxicology.

Dr. Hermansky left Conagra Brands in April 2022 where he directed & oversaw the corporation's toxicology & product safety risk assessment programs as well as headed the Food Protection, Regulatory Affairs and Analytical and Applied Sciences departments. In this role, Dr. Hermansky led teams of scientists in the Safety Sciences including microbiology, toxicology and analytical chemistry as well as the global regulatory affairs and food safety corporate audit functions. Prior to joining Conagra in 2007, he worked in the pharmaceutical industry as a toxicologist with responsibilities in drug safety clinical trials and adverse event tracking, trending and reporting.

He started his career as a toxicologist conducting contract laboratory animal studies with Union Carbide. Steve has a Doctor of Pharmacy degree as well as Master of Science and Doctor of Philosophy degrees in toxicology from the University of Nebraska. He is a Diplomate of the American Board of Toxicology and has published over 40 textbook chapters, peer reviewed publications and scientific abstracts. He is an adjunct professor at the University of Nebraska College of Public Health and has served on the Advisory or Editorial Boards of several organizations.

José Vicente Tarazona Lafarga

Prof. Dr. Jose V. Tarazona

Head of the Risk Assessment Unit and Research Professor on Environmental Health Risk Assessment Science at the Spanish National Environmental Health Centre (Instituto de Salud Carlos III) in Madrid, Spain. Doctor in Veterinary Medicine, holds a PhD in Toxicology by the University Complutense of Madrid, and has devoted his professional career to chemical risk assessment, covering human health and the environment; focusing on the developing of new scientific methodologies and approaches; as well as on their regulatory applications. Between 1982 and 2009, developed his professional activity at the National Institute for Agricultural and Food Research and Technology (INIA) holding positions of responsibility, including Director of the Department of the Environment. Between 2009 and September 2022, developed his professional activity as scientific staff in European Union Agencies, first as Chairman of the Risk Assessment Committee at the European Chemicals Agency (ECHA) in Finland and later as Head of the Pesticides Unit and Senior Scientist at the Scientific Committee and Emerging Risks Unit at the European Food Safety Authority (EFSA) in Italy. Current main research interests are related to the development of innovative frameworks for addressing the impacts on human and ecosystem health of pesticides and other environmental pollutants. Is involved in the EU projects PARC and URBANOME, and co-chair of the Working Group on New Approach Methodologies (NAMs) of the International Network on Methods for Risk Assessment of Chemical Substances in Food (ILMERAC).

Fitzpatrick, Suzanne

Suzanne Fitzpatrick, PhD, DABT, ERT
Center for Food Safety & Applied Nutrition
US Food and Drug Administration

New Approach Methodologies for Use in FDA Food Safety Assessments

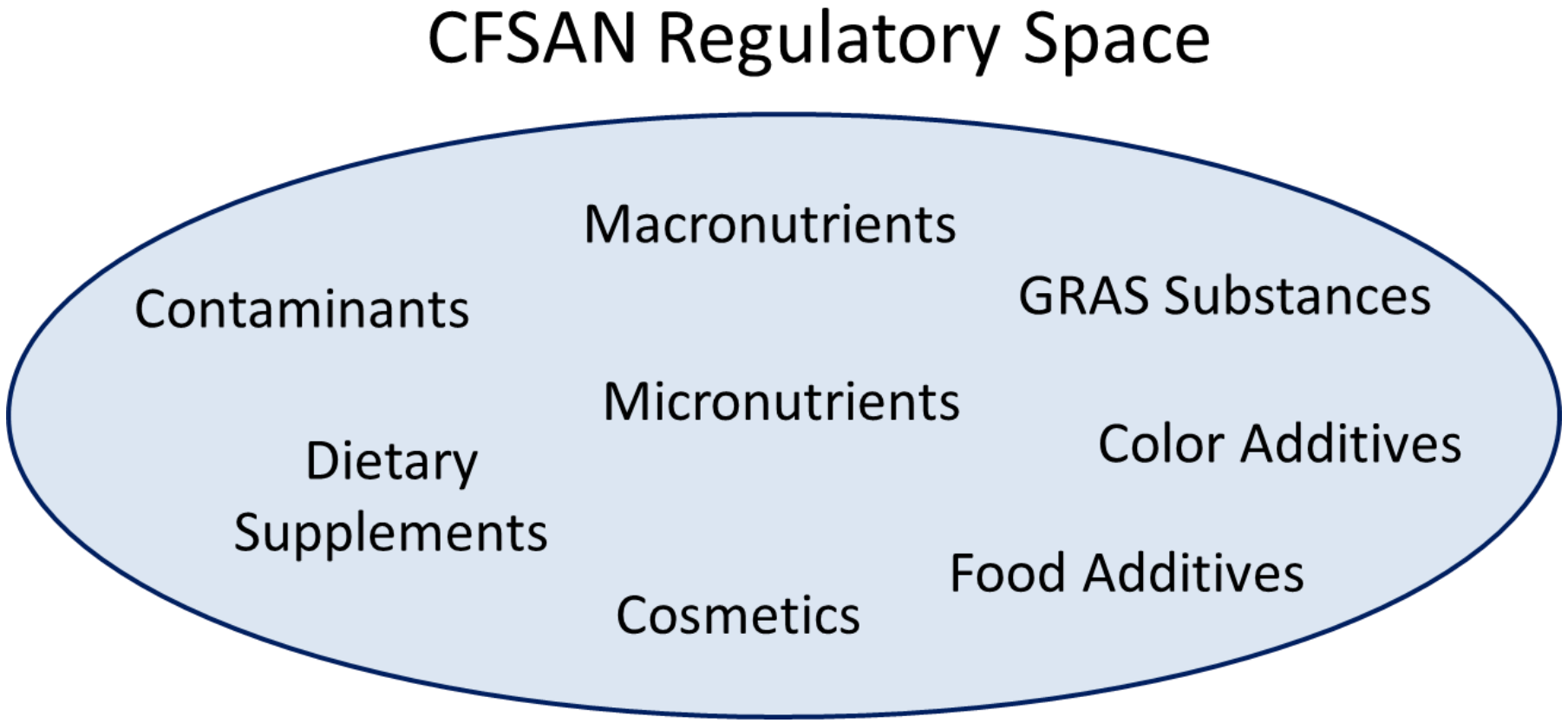
Suzanne Fitzpatrick, PhD, DABT, ERT
Center for Food Safety & Applied Nutrition
US Food and Drug Administration
IAFP Public Meeting
May 16, 2023

Advancing new alternative methodologies at FDA

- FDA recognizes that new technologies may help bring FDA-regulated products to market faster, with improved efficacy, or prevent products with increased toxicological risk from reaching the market.
- FDA supports the development of new regulatory tools that can help improve predictivity and potentially replace, reduce, and/or refine animal testing.
- FDA recognizes that each of its product centers are unique and encourages development of Center-specific Qualification Programs that can then share knowledge across the agency.

Report available on the FDA webpage

What CFSAN regulates- For most of these products CFSAN lacks pre-approval authorities



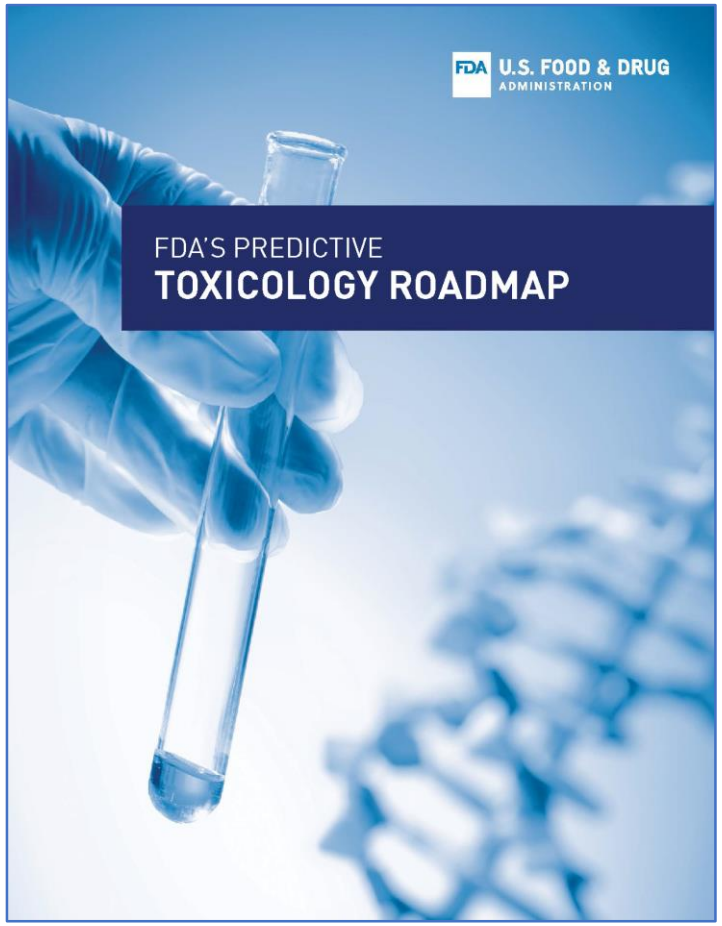
CFSAN Vision: Advancing Toxicology

Transition to 21st century technologies to enhance chemical risk management

CURRENT APPROACH	FUTURE DIRECTION
• Heavy reliance on animal studies • Evaluation of multiple apical endpoints • Based on traditional toxicity tests	• Less reliance on animal studies • Tailored data generation • Based on toxicity pathways

FDA Predictive Toxicology Roadmap Announced December 6, 2017

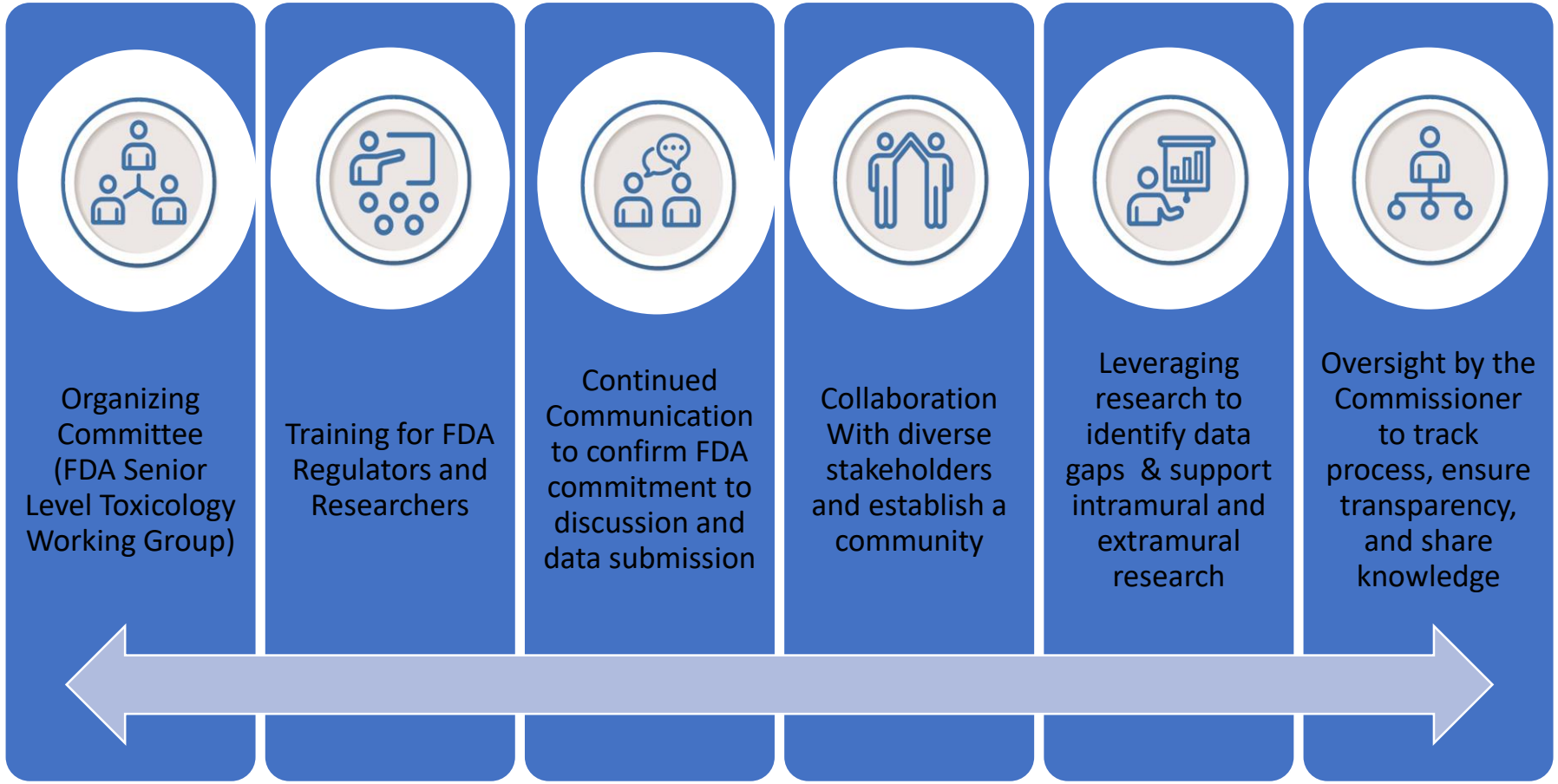
- https://blogs.fda.gov/fdavoice/index.php/2017/12/fda-launches-predictive-toxicology-roadmap-to-enable-advances-in-toxicity-testing/



The FDA Predictive Toxicology Roadmap -A Six-Part Framework for New or Enhanced FDA Engagement in the Science of Toxicology

- The key goal of the roadmap is to invigorate and strengthen FDA's long commitment to promoting the development and use of new technologies to better predict human, animal, and environmental
- CFSAN has incorporated the principles of the FDA Predictive Toxicology Roadmap into its program on New Approach Methodologies for Food Safety Assessments.

FDA's Roadmap: Framework for Incorporating Emerging Predictive Toxicology Methods in Regulatory Reviews



CFSAN Senior Level Toxicology Working Group

CFSAN's Office of the Center Director has created a NAMS working group to leverage CFSAN resources to advance the integration of emerging predictive toxicology methods into regulatory food safety and risk assessments.

The NAMS WG includes senior and junior scientists from both CFSAN regulatory and research programs and has liaisons from ORA and NCTR.

Charter of the CFSAN NAMS Working Group

Goal : To develop criteria for developing confidence in NAMs for use in human food safety assessments and regulatory decisions and to test these criteria using case studies

- Identify which NAMs are currently being used in the food industry, academia and other government agencies (nationally and internationally).
- Develop a plan to evaluate NAM's for applicability to human food safety evaluation that includes qualification criteria, feasibility, cost, how far the method is in the development stage (early vs commercially available).
- Develop a draft qualification guidance. Consider where a separate guidance is needed for different categories of NAMs (e.g., microphysiological systems vs. *in silico* models vs. biomarkers).
- Conduct stakeholder workshops on Qualification criteria, NAMs status, gaps and use at CFSAN.

Training of CFSAN regulators and researchers

- Continuing ongoing education in new predictive toxicology methods is essential priority for both CFSAN regulators and researchers
- CFSAN has establish a Center-wide education calendar of courses, events and publications as a resource for all its scientists
- CFSAN incorporates the principles of “Training by Doing”- Includes Junior Scientists in the planning and implementation of all NAMS activities.

Collaborations with Stakeholders

- CFSAN encourages collaborations across sectors and disciplines nationally and internationally.
- CFSAN supports the importance of collaborations in identifying the needs, maintaining momentum, and establishing a food safety community to support delivery of new predictive toxicology methods.

Potential Partnerships Avenues to Work with CFSAN on NAMS

- Public-private partnerships (PPP)
  - FDA invited to participate
  - Increased access to resources and expertise
- Memorandum of understanding (MOU)
  - Relationship between federal agencies
  - Share information and resources
- Research collaboration agreement (RCA)
  - Share resources, methods, technology during research project
  - Both parties get something out of the agreement

INTERNATIONAL LIAISON GROUP ON METHODS FOR RISK ASSESSMENT OF CHEMICALS IN FOOD (ILMERAC)

Created through partnership with CFSAN/FDA and EFSA.

Facilitating and coordinating research and regulatory efforts on NAMs through an international framework will provide the best path to harmonized outcomes.

ILMERAC created a working group on New Approach Methods.

ILMRERC NAMS WG is new but already has selected the first list of priority actions for increasing the use of NAMs in food safety assessments.

International Liaison Group for Methods on Risk Assessment of Chemicals in Food (ILMERAC)

Organisation	Contact person
US FDA – Food and Drug Administration	Suzanne Fitzpatrick (co-chair) Goncalo Gamboa Steven Hermansky Jason Aungst Paul South
EFSA – European Food Safety Authority	Jose Tarazona (co-chair) Maria Chiara Astuto Irene Cataneo Jean-Lou Dorne Yann Devos Georges Kass Maria Bastaki
HC - Health Canada	Tara Barton-Maclaren Sonya Billiard John Field David Lefebvre Zoe Gillespie Marc Beal

Organisation	Contact person
RIVM	Esther de Jong Astrid Bulder Anne Kienhuis Ellen Hessel
JRC - Joint Research Centre	Sandra Coecke
BfR - German Federal Institute for Risk Assessment	Philip Marx-Stoelting Majlinda Lahaniatis
NVWA - the Netherlands Food and Consumer Product Safety Authority	Michiel den Braver
CFSA -China National Center for Food Safety Risk Assessment	Haixia Sui
OECD - Organisation for Economic Co-operation and Development	Patience Brown
NZFS - New Zealand Food Safety	Jeane Nicolas
KIT - Korean Institute of Toxicology	Yu WookJoon Lee Seung-Jin

Experts from non-ILMERAC organizations are invited for specific topics.

Priorities of the ILMERAC Work Group on NAMS

First challenge: To cover key data gaps with NAMs, minimizing requests for additional *in vivo* studies. Mixtures were identified as a global problem. The mixtures themselves could be different but hopefully the tools to assess the toxicity of them could be harmonized.

Second challenge: To provide guidance for using non-guideline studies (i.e., peer-reviewed publications), including harmonized reporting, and to explore the "context of use qualification" approach.

Third challenge: (R)evolution of the risk assessment paradigm, facilitating the integration of mechanistic information rather than apical endpoints at the end of a study.. Mechanistic information includes AOPS and IATAs.

Continued Communication

- CFSAN is committed to incorporating data from newly qualified toxicology methods into regulatory assessments
- CFSAN encourages discussions with stakeholders as part of the regulatory submission process.
- CFSAN encourage sponsors to submit a scientifically valid approach for using a new method early in the regulatory process

Food Chemical Toxicology Public Private Partnership

Goal is to provide the food toxicology community with a repository and credible source of science-based information on food toxicology.

The Institute for Food Safety and Health agreed to serve as the designated convener of the FTPPP.

Open to anyone in the food toxicology community

CFSAN has several members

Agenda is being developed

Leveraging Research

CFSAN’s research programs will use regulatory gaps and needs identified by the NAMS WG to direct and support all intramural and extramural research to ensure that the most promising technologies are identified, developed, validated, and integrated into the product pipeline.

CFSAN Research Principles Governing Both In House and Collaborative Research Projects

Recognize that regulators have to be included up front in new method development.

Regulators will identify gaps for additional research.

Regulators will delineate what tools were needed.

New CFSAN toxicology research must answer regulatory questions.

Continued ongoing training for regulators in new methods is required.

Oversight Senior Management at CFSAN and FDA

- CFSAN NAMS Work Group updates its progress directly to CFSAN Senior Management on a monthly basis.
- CFSAN collaborates with other Center/Programs thru its role as Co-Chair of the FDA Alternative Methods Work Group.
- CFSAN works thru its public NAMS website to contiually ensure transparency, to foster opportunities to share ideas and knowledge, showcase technologies, and to highlight collaborations on developing and testing new methods

Collaboration on the Roadmap Principles Across FDA

- Greater FDA cross-center collaboration can help accelerate the use of emerging predictive toxicology methods in various programs and in the regulatory arena.
- One size may not fit all; each of FDA's product centers has different legal authorities for product safety evaluations.
- CFSAN's incorporation of key roadmap principles helps to assure the continued success of it NAMS programs.
- CFSAN will work to assure that its toxicology testing is applied across the breadth of FDA-regulated products.

FDA
CFSAN

New Methodologies: Application in Food Safety and International Trade. European examples

José V. Tarazona, DVM, PhD

Research Professor on Environmental Health Risk Assessment Science

Spanish National Environmental Health Centre
Instituto de Salud Carlos III
Ministry of Science and Innovation, Spain

- **Over 80% of current toxicological research is based on alternative methods, including *in vitro* approaches and omics**

- **… but this innovative knowledge is scarcely integrated in regulatory risk assessments**

Challenges for using NAMs in regulatory assessments

21st Century Toxicology

Experience

- Lack of guidance blocks use
- Need of experience for developing guidance

Guidance

High innovation limits traditional standardisation/harmonisation

Key elements for chemical food safety

- Built on science, implemented in regulatory provisions

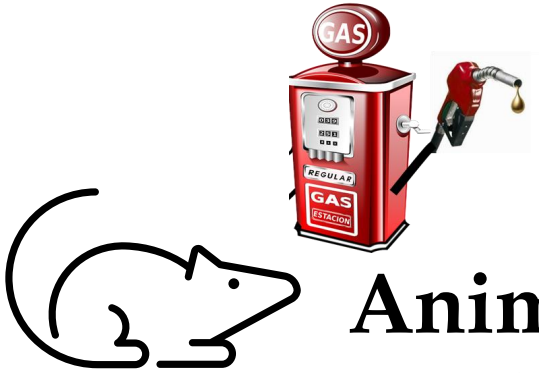
- Based on risk (hazard and exposure), but…
  - Exposure depends on diets
  - The EU has also implemented hazard based regulations

- Premarketing assessments are based on regulatory information requirements and regulatory guidance, <u>using all available information improves the assessment</u>

Additional elements for international trade

- Based on regulatory provisions supported by science based concerns
- Mostly hazard based
  - Exposure depends on diets and scenarios
- Ideally based on internationally agreed guidelines
- Requires confidence between jurisdictions

Toxicological models

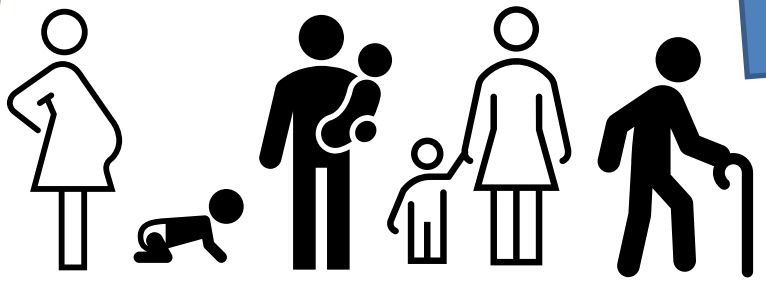


Animal models

Human *in vitro* models

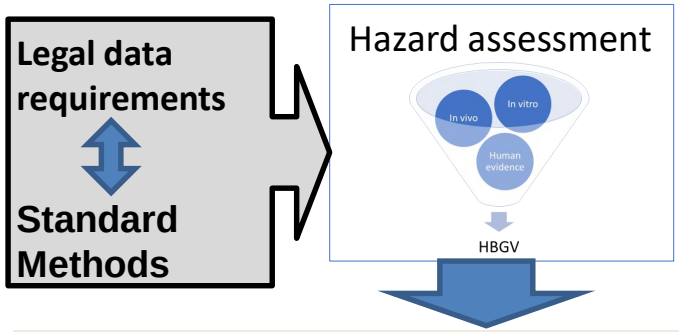
Inter species extrapolation

***In vitro* to *in vivo* extrapolation**



The current paradigm

20th Century paradigm



Guidance & experience

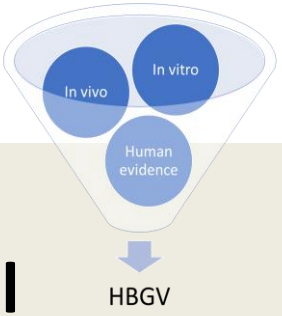
70 years of experience and legal certainty for applicants

- **Agreed methodology**
- **Sectoral guidance**
- **Trained risk assessors**
- **Trained risk managers**

- **Evidence based on animal models**
  - **Available information**
- **Providing predictability**
  - **Expert judgement**

Hazard assessment

20th Century paradigm



Apical endpoints
No Adverse Effect Level
Animal to human extrapolation

21st Century Toxicology

Pathways for adversity

No Adverse Effect Level / 100

≠

Intermediate endpoints
Mechanistic connectors

- Over 80% of current toxicological research is based on alternative methods, including *in vitro* approaches and omics
- … but this innovative knowledge is scarcely integrated in regulatory risk assessments

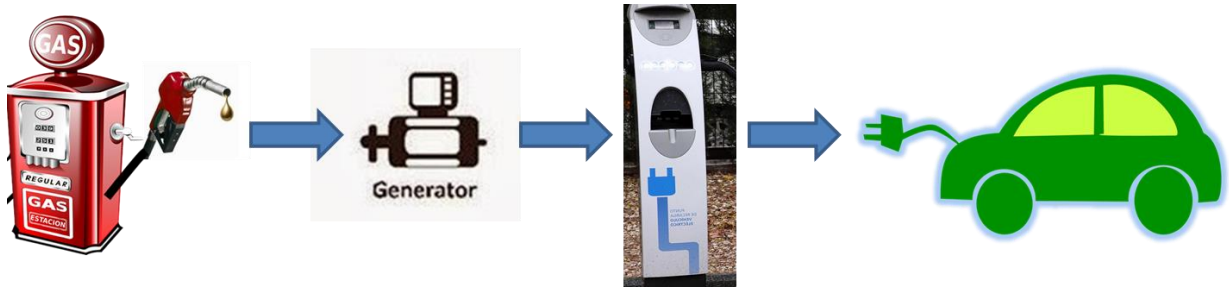
- **One exception: Consolidated path for Genotoxicity**

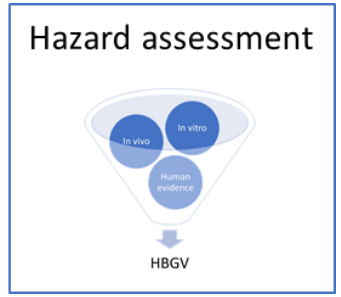
- **Independent <u>qualitative</u> hazard endpoint**
- **Based on <u>mechanistic</u> information**
- **Complexity increases in a tiered approach**
- **International guidelines are available… but non-guideline methods are usually accepted**

How? Evolution *versus* revolution

Paradigm evolution

Using alternative methods for setting <u>THE</u> Guidance Value





Paradigm revolution

Developing new paradigms for safety assessments based on mechanistic understanding

Assess
SAFETY
… like for genotoxicity

Ready for the revolution?

In vitro to *in vivo* extrapolation

Pesticides

Food additives

General chemicals (REACH)

Feed additives

Nutrients

Novel foods

GMOs

Food contaminants

Trends in Food Science & Technology 133 (2023) 277–290

Contents lists available at ScienceDirect

Trends in Food Science & Technology

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

Implementing New Approach Methodologies (NAMs) in food safety assessments: Strategic objectives and actions taken by the European Food Safety Authority

Irene Cattaneo *, Maria Chiara Astuto, Marco Binaglia, Yann Devos, Jean Lou C.M. Dorne, Ana Fernandez Agudo [1], Antonio Fernandez Dumont, Pilar Garcia-Vello, George E.N. Kass, Anna Lanzoni, A.K. Djien Liem, Martina Panzarea, Konstantinos Paraskevopulos, Juan Manuel Parra Morte, Jose V. Tarazona [2], Andrea Terron

European Food Safety Authority (EFSA), Via Carlo Magno 1/A, 43126, Parma, Italy

https://doi.org/10.1016/j.tifs.2023.02.006

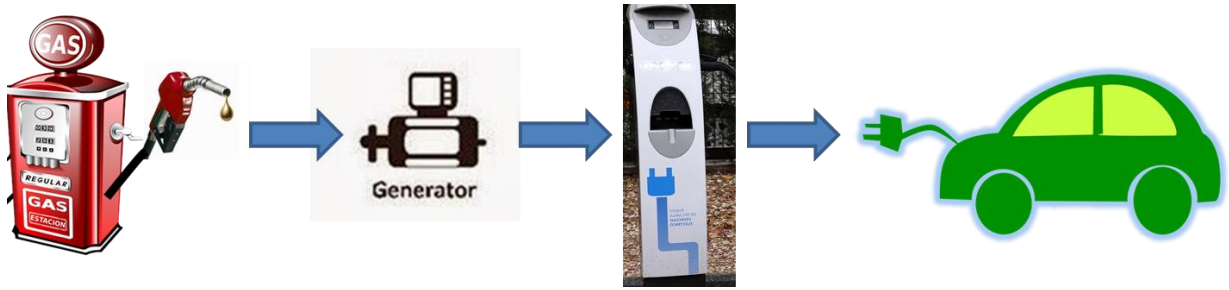
Table 1
EU regulatory framework for data requirements.

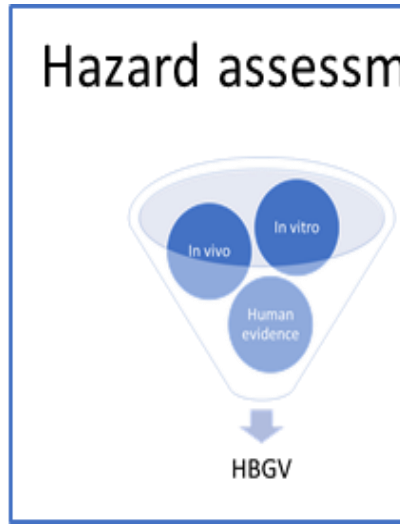
	Are data requirements fixed by regulation or by guidance?	Are data requirements drafted in a way that *in vivo* data are mandatory?	Is it possible to conclude safety based on NAMs?	May external partners submit additional studies during the RA process?
General chemicals: REACH	REACH Regulation Annexes VII-X.	Yes, unless exceptions.	Yes, for read-across but not based on *in vitro* data only.	Only for some REACH processes.
General chemicals: CLP	No data requirements, based on existing information.	Not formally, but current criteria are based on information extracted from animal studies.	Not applicable, there is no classification in case of lack of information.	Yes, for harmonised classification, during the RAC process.
Pesticides	Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market.	Yes, but methods are updated on regular basis.	No.	Yes, systematic literature review is a data requirement. Data can be submitted to the Rapporteur MS and also during EFSA consultation on the Draft Assessment.
Food additives	Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives. Commission Regulation (EU) No 257/2010 of 25 March 2010 setting up a programme for the re-evaluation of approved food additives in accordance with Regulation (EC) No 1333/2008 of the European Parliament and of the Council on food additives.	No, the regulation only specifies that 'Food additives must be safe when used'. No, the regulation stipulates that the information should be as comprehensive as possible to allow EFSA the re-evaluation and should be submitted following to the extent possible the applicable guidance on submissions for food additive evaluations.	No, minimum requirement includes a 90-day study.	Yes, if triggered by EFSA; the stop-the-clock procedure is in place to allow for additional data to be submitted.
Feed additives	COMMISSION REGULATION (EC) No 429/2008, complemented with EFSA guidance.[a]	Yes, for tolerance studies and for safety assessments.	No, minimum requirement includes a 90-day study; there are exceptions based on no exposure or substances already approved in foodstuff.	Yes, if triggered by EFSA; the, stop-the-clock procedure is in place to allow for additional data to be submitted.
Nutrients	EFSA guidance.[b]	No, human information is the most relevant source. If information is insufficient, requirements for animal studies are linked to novel foods and food additives.	Yes, human data can be complemented with mechanistic understanding using NAMs.	Yes, if triggered by call for data or stop-the-clock procedures in case of applications.
Novel foods	Regulation (EU) 2015/2283 of the European Parliament and of the Council of 25 November 2015 on novel foods, amending Regulation (EU) No 1169/2011 of the European Parliament and of the Council and repealing Regulation (EC) No 258/97 of the European Parliament and of the Council and Commission Regulation (EC) No 1852/2001, complemented with EFSA guidance.[c]	No, the regulation only specifies that 'the food does not, on the basis of the scientific evidence available, pose a safety risk to human health.'	In principle, No, minimum requirement includes a 90-day study, and triggers may lead to additional studies. However, considerations on history of safe use can be made.	If triggered by EFSA, stop-the-clock procedure in place to allow for additional data to be submitted.
GMOs	Commission Implementing Regulation (EU) No 503/2013 of 3 April 2013 on applications for authorisation of genetically modified food and feed in accordance with Regulation (EC) No 1829/2003 of the European Parliament and of the Council and amending Commission Regulations (EC) No 641/2004 and (EC) No 1981/2006complemented with EFSA guidance.[d]	Yes, but only for studies on the whole food and feed in rodents (single events).	Yes, in some areas (molecular characterisation; toxicity and allergenicity of newly expressed proteins).	Yes. if triggered by EFSA, the stop-the-clock procedure is in place to allow for additional data to be submitted.
Food contaminants	Council Regulation (EEC) No 315/93 of 8 February 1993 laying down Community procedures for contaminants in food. Commission Regulation (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs.	No.	Yes, in principle.	Yes.

Comparison of EU general chemicals framework with legislations on chemical risk assessments in the food and feed area.

[a] See this link for details: https://www.efsa.europa.eu/en/applications/feedadditives/regulationsandguidance.
[b] See this link for details: https://www.efsa.europa.eu/en/applications/nutrition/regulationsandguidance.
[c] See this link for details: https://www.efsa.europa.eu/en/applications/novel-food-traditional-food/regulationsandguidance.
[d] See this link for details: https://www.efsa.europa.eu/en/applications/gmo/regulationsandguidance.

Paradigm evolution

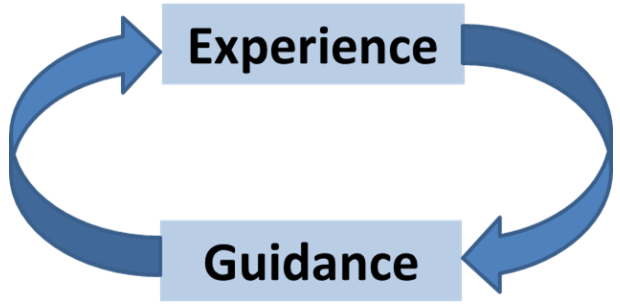




Integrative approaches for setting THE Guidance Value

Existing information	New information	Integration
	• *In vitro* • Read-across	To support/challenge the guidance value

- Are all NAM effects covered by *in vivo* observations?
- Are population groups with expected high susceptibility?
- Are interactions of specific concern?



Centro Nacional de Sanidad Ambiental

Instituto de Salud Carlos III

TECHNICAL REPORT

APPROVED: 15 October 2020

doi:10.2903/sp.efsa.2022.e200502

Theme (Concept) Paper - New Approach Methodologies

European Food Safety Authority (EFSA), Jose Tarazona, George Kass, Jean-Lou Dorne, Djien Liem, Konstantinos Paraskevopoulos, Juliane Kleiner, Claudia Heppner, Marta Hugas

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 Kie Victoria de Leeuw[3], Rosmarie Reuss[4], Katrina-Magdalena Lindemann[4], Susanne Hougaard Benr

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

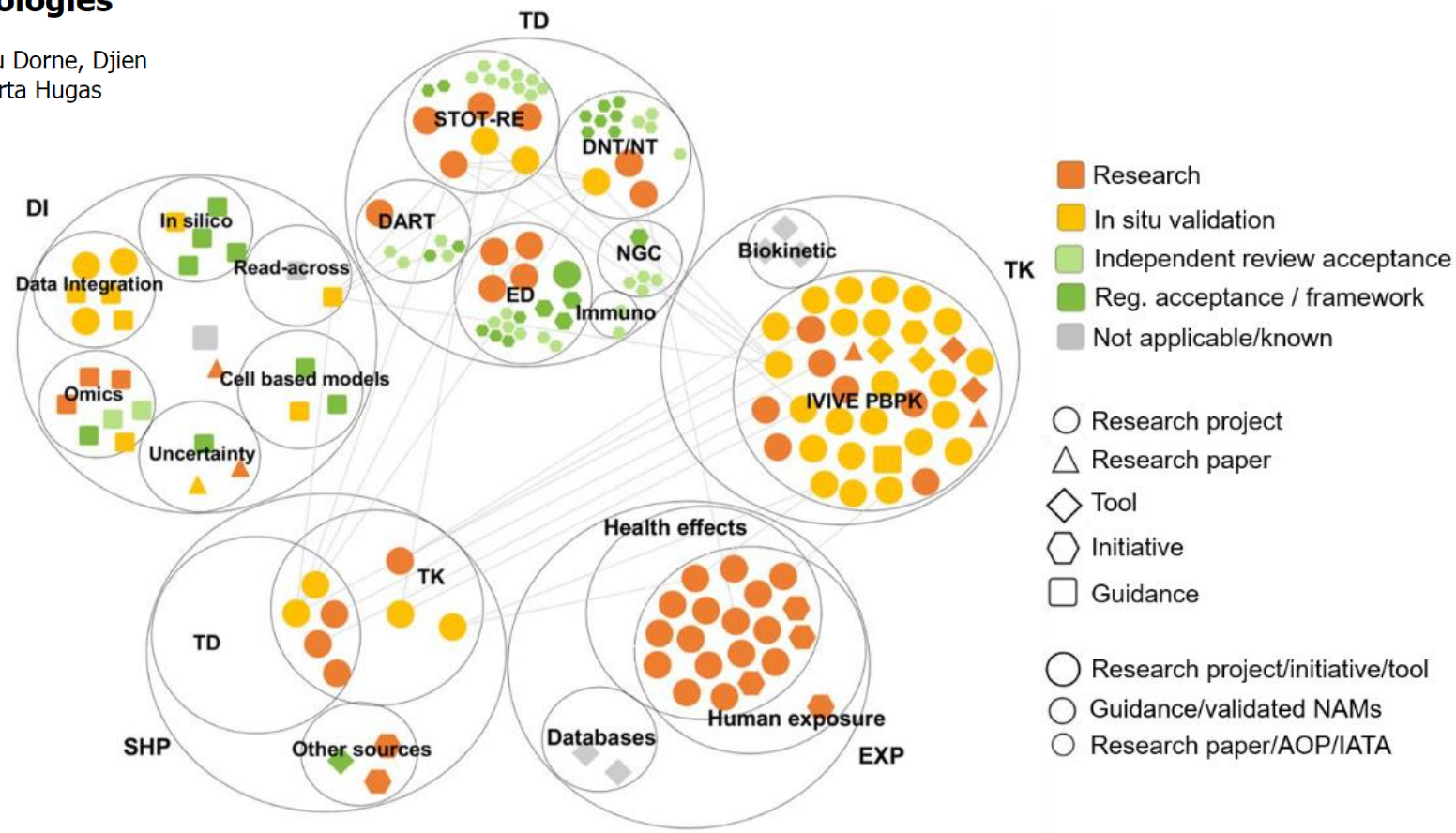
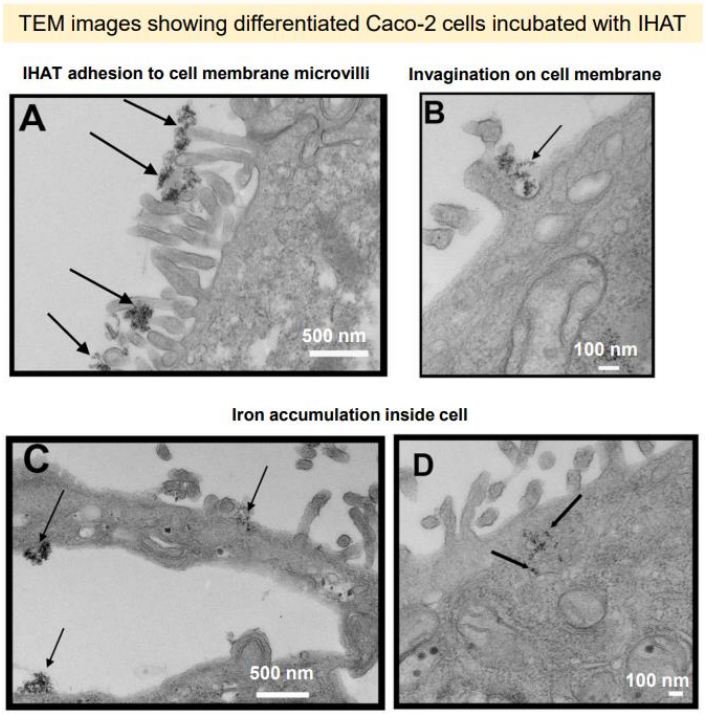


Figure 20: Regulatory readiness of individual activities defined per sub discipline and research areas. More information on the separate activities can be found in the previous sections of each research area. Colours indicate regulatory readiness, shape shows activity type and the size of the activity represents proportions between different activities as stated in the legend.

Centro Nacional de Sanidad Ambiental

First food safety example: novel foods

Nano-formulated organic iron and absorption mechanism



The Applicant followed the EFSA Nano-Guidance and included *in vitro* information, detailing the mechanisms for:

- **Uptake by enterocytes**
- **Accumulation in enterocytes**
- **Transfer to blood**
- **Homeostatic control**

SCIENTIFIC OPINION

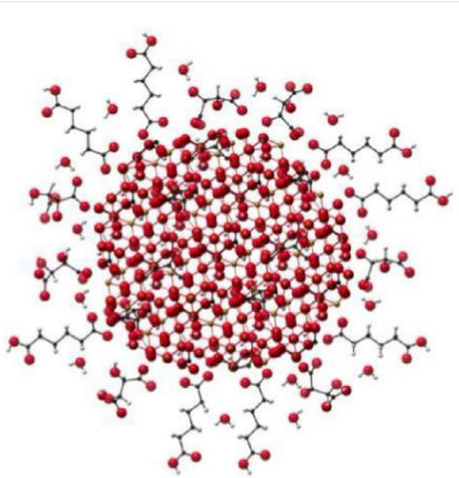
EFSA Journal

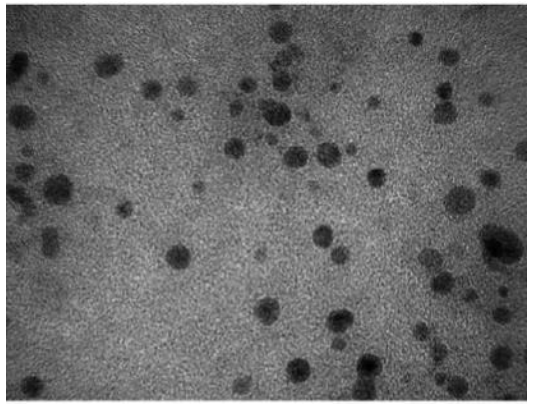
ADOPTED: 27 October 2021

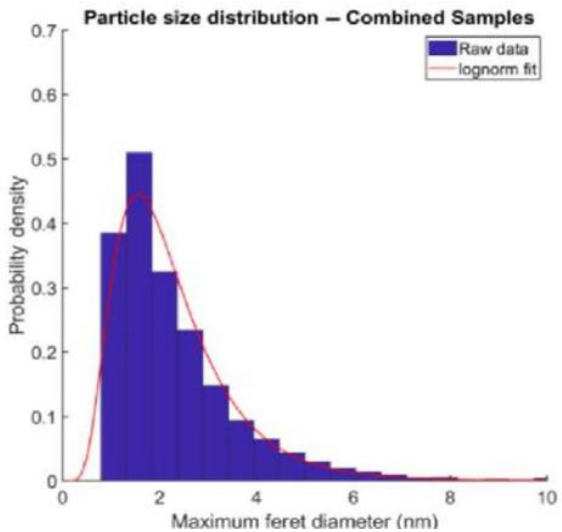
doi: 10.2903/j.efsa.2021.6935

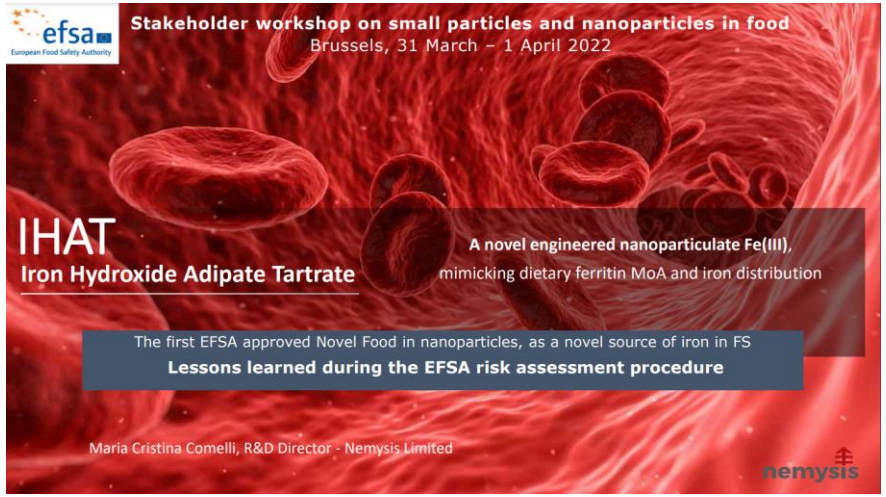
Safety of iron hydroxide adipate tartrate as a novel food pursuant to Regulation (EU) 2015/2283 and as a source of iron in the context of Directive 2002/46/EC

EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA), Dominique Turck, Torsten Bohn, Jacqueline Castenmiller, Stefaan De Henauw, Karen Ildico Hirsch-Ernst, Alexandre Maciuk, Inge Mangelsdorf, Harry J McArdle, Androniki Naska, Carmen Pelaez, Kristina Pentieva, Alfonso Siani, Frank Thies, Sophia Tsabouri, Marco Vinceti, Francesco Cubadda, Thomas Frenzel, Marina Heinonen, Miguel Prieto Maradona, Rosangela Marchelli, Monika Neuhäuser-Berthold, Morten Poulsen, Josef Rudolf Schlatter, Henk van Loveren, Andrea Germini and Helle Katrine Knutsen









https://www.efsa.europa.eu/en/events/stakeholder-workshop-small-particles-and-nanoparticles-food#

Take-home message from first example

Nanotoxicology & NAMs are an ideal combination

NAM-based mechanistic information reduce uncertainties

Trends in Food Science & Technology 134 (2023) 98–111

Contents lists available at ScienceDirect

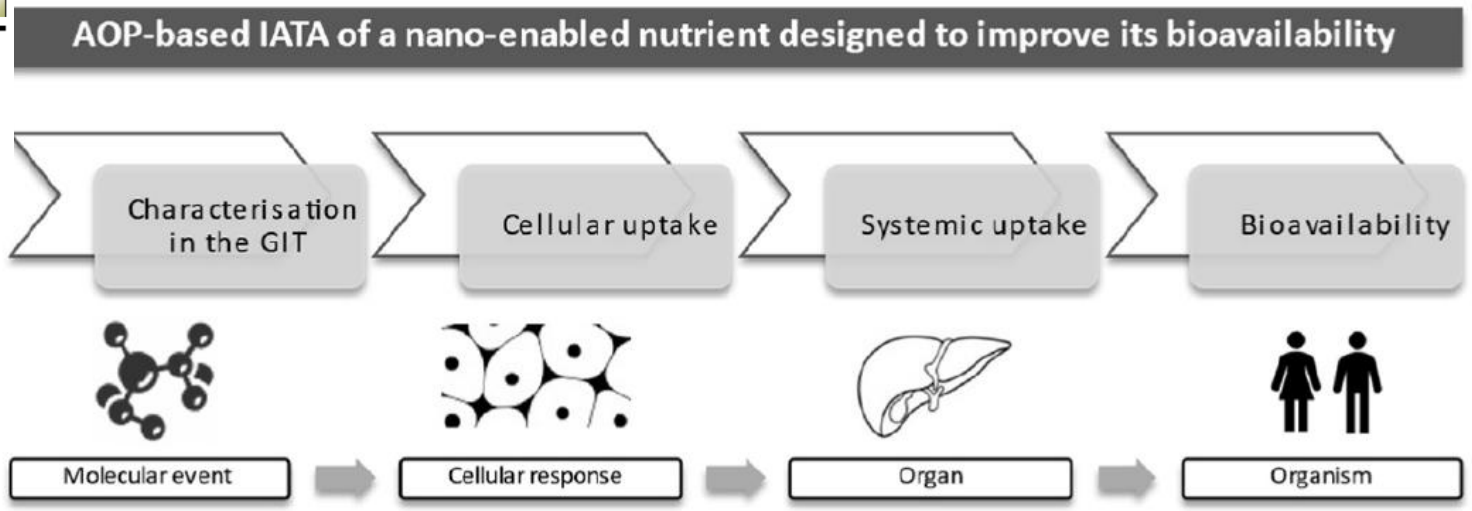
Trends in Food Science & Technology

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

Regulatory safety assessment of nanoparticles for the food chain in Europe

Reinhilde Schoonjans [a,*], Jacqueline Castenmiller [b], Qasim Chaudhry [c], Francesco Cubadda [d], Takis Daskaleros [e], Roland Franz [f], David Gott [g], Jan Mast [h], Alicja Mortensen [i], Agnes G. Oomen [j,m], Hubert Rauscher [k], Stefan Weigel [l], Maria Chiara Astuto [a], Irene Cattaneo [a], Eric Barthelemy [a], Ana Rincon [a], José Tarazona [a,1]

https://doi.org/10.1016/j.tifs.2023.01.017



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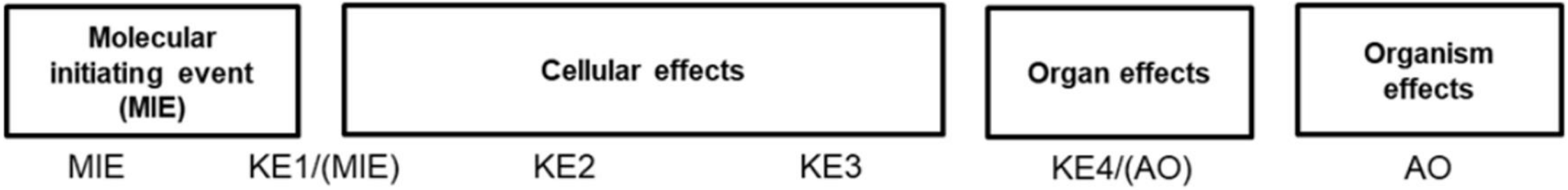
Second food safety example: pesticides

Neurotoxicity (Parkinsonian motor deficiencies)

Adverse Outcome Pathways

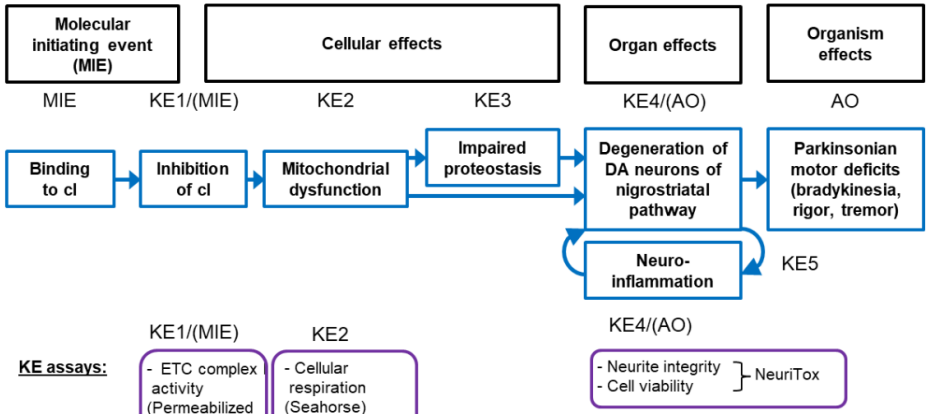


APPROVED: 23 November 2022
doi:10.2903/sp.efsa.2023.EN-7794

EFSA Pilot Project on New Approach Methodologies (NAMs) for Tebufenpyrad Risk Assessment. Part 2. Hazard characterisation and identification of the Reference Point

Mahshid Alimohammadi, Birthe Meyburg, Anna-Katharina Ückert, Anna-Katharina Holzer, Marcel Leist

University of Konstanz, UKN – University of Konstanz, Universitätsstr. 10, 78464 Konstanz



Endpoint	Point of Departure [nM]	
	Glucose	Galactose
(KE4/(AO): Viability)	39000	660
KE4/(AO): Neurite area	34000	**8**
KE2: ATP levels	36000	6
KE2: MMP assay	48000	6
KE2: Mitochondrial respiration inhibition	45	
KE1/(MIE): Complex I inhibition	40	

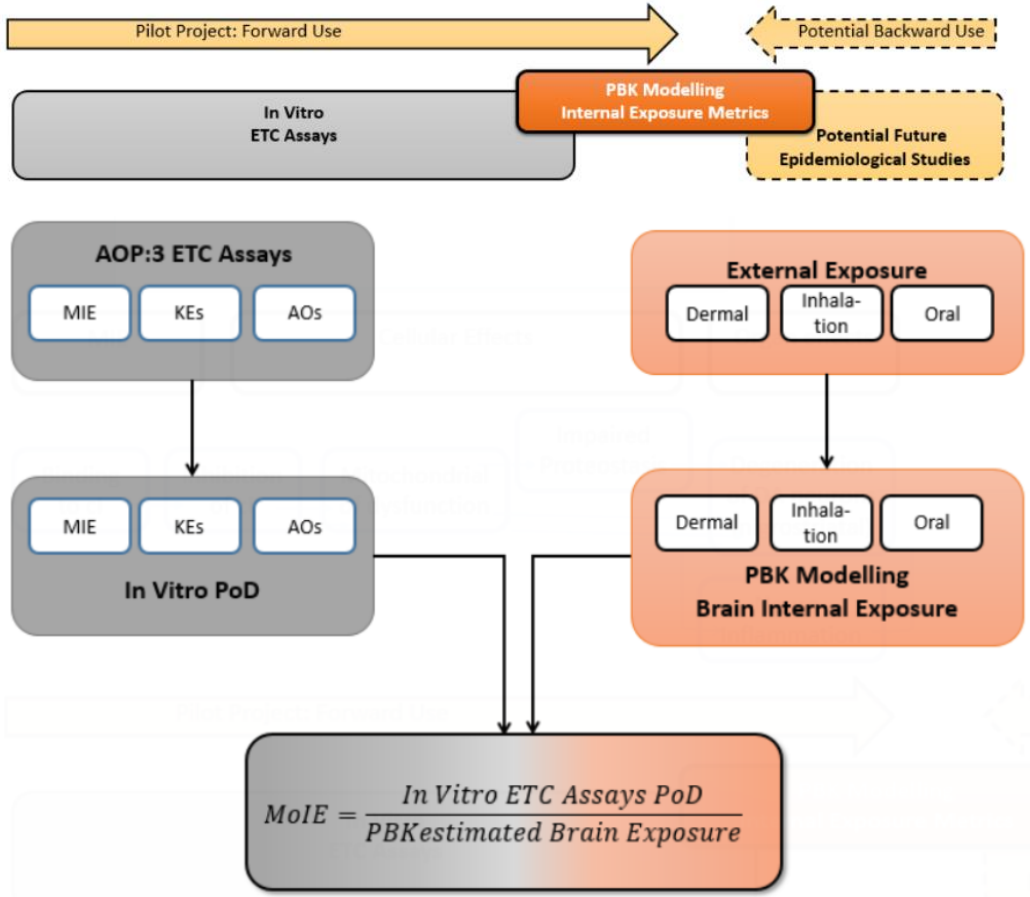
APPROVED: 29 November 2022
doi:10.2903/sp.efsa.2023.EN-7793

EFSA Pilot Project on New Approach Methodologies (NAMs) for Tebufenpyrad Risk Assessment. Part 1. Development of Physiologically-Based Kinetic (PBK) Model Coupled With Pulmonary and Dermal Exposure

Jérôme HENRI[1], Ludovic LEHEGARAT[1], Adeline CAVELIER[2], Bertrand DESPREZ[2]

French Agency for Food, Environmental and Occupational Health & Safety (ANSES)

[1]ANSES Fougères Laboratory, 10 rue Claude Bourgelat-Javené CS 40608 F-35306 Fougères Cedex



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Take-home message from second example

NAMs may provide the solution when the animal model is insensitive or has low relevance

PBPK modelling can support the extrapolation, uncertainties should be always considered

Third example: endocrine disruption

ECHA EUROPEAN CHEMICALS AGENCY

GUIDANCE

efsa European Food Safety Authority

ADOPTED (ECHA): 5 June 2018
ADOPTED (EFSA): 5 June 2018

doi: 10.2903/j.efsa.2018.5311

Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009

European Chemical Agency (ECHA) and European Food Safety Authority (EFSA) with the technical support of the Joint Research Centre (JRC)

Niklas Andersson, Maria Arena, Domenica Auteri, Stefania Barmaz, Elise Grignard, Aude Kienzler, Peter Lepper, Alfonso Maria Lostia, Sharon Munn, Juan Manuel Parra Morte, Francesca Pellizzato, Jose Tarazona, Andrea Terron and Sander Van der Linden

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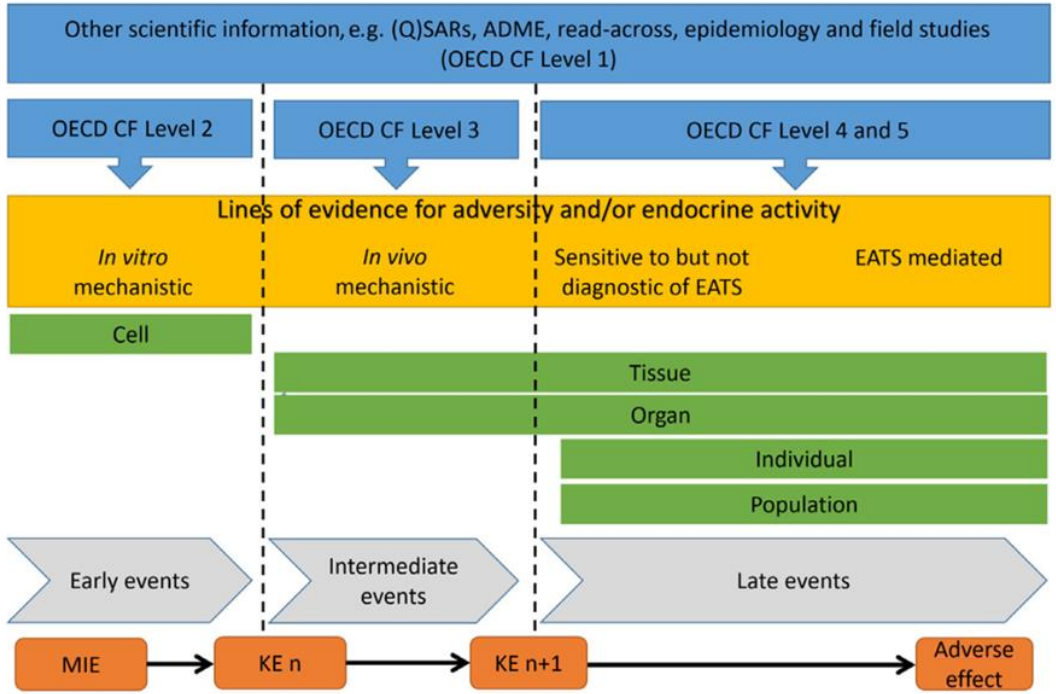

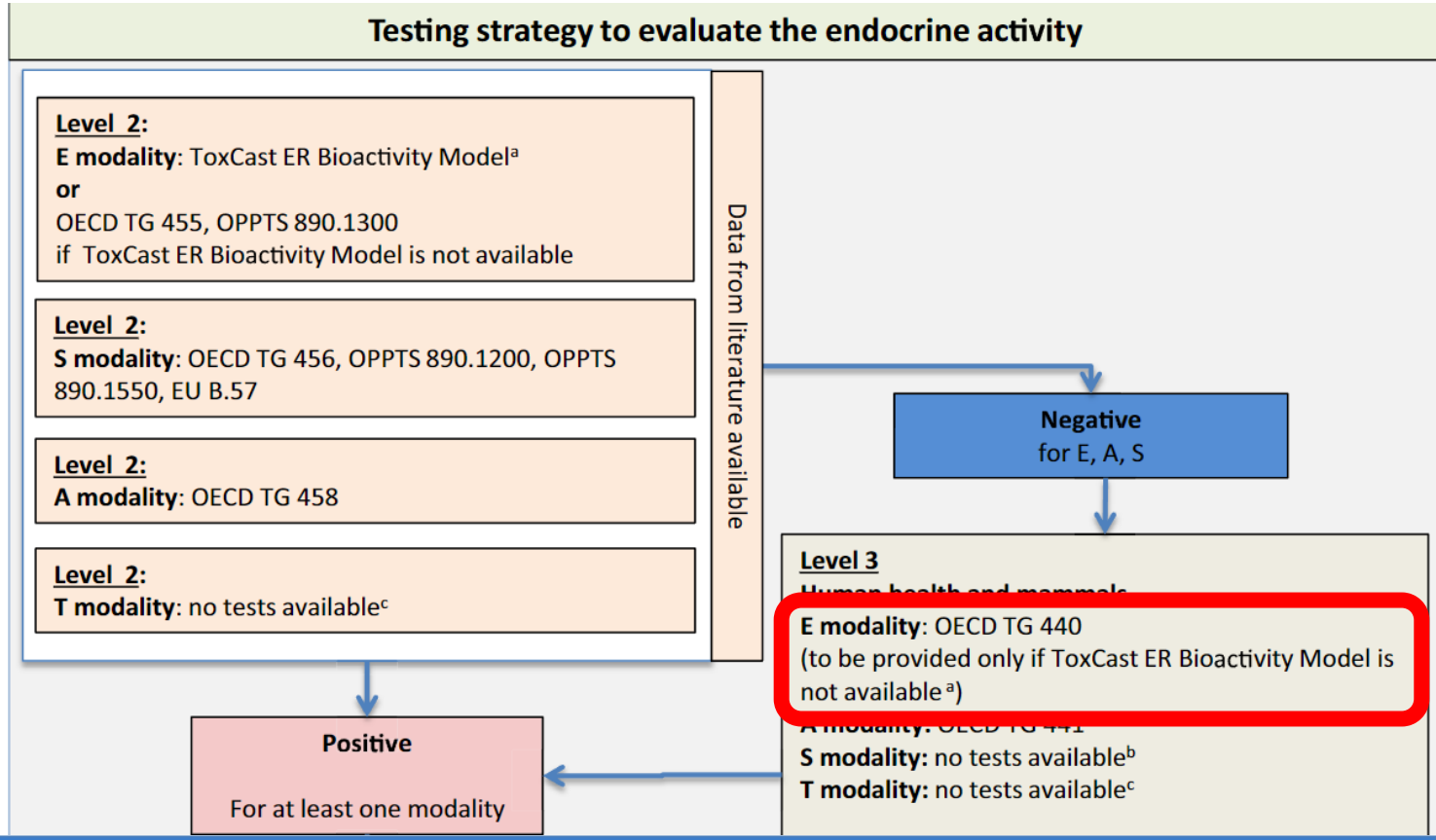

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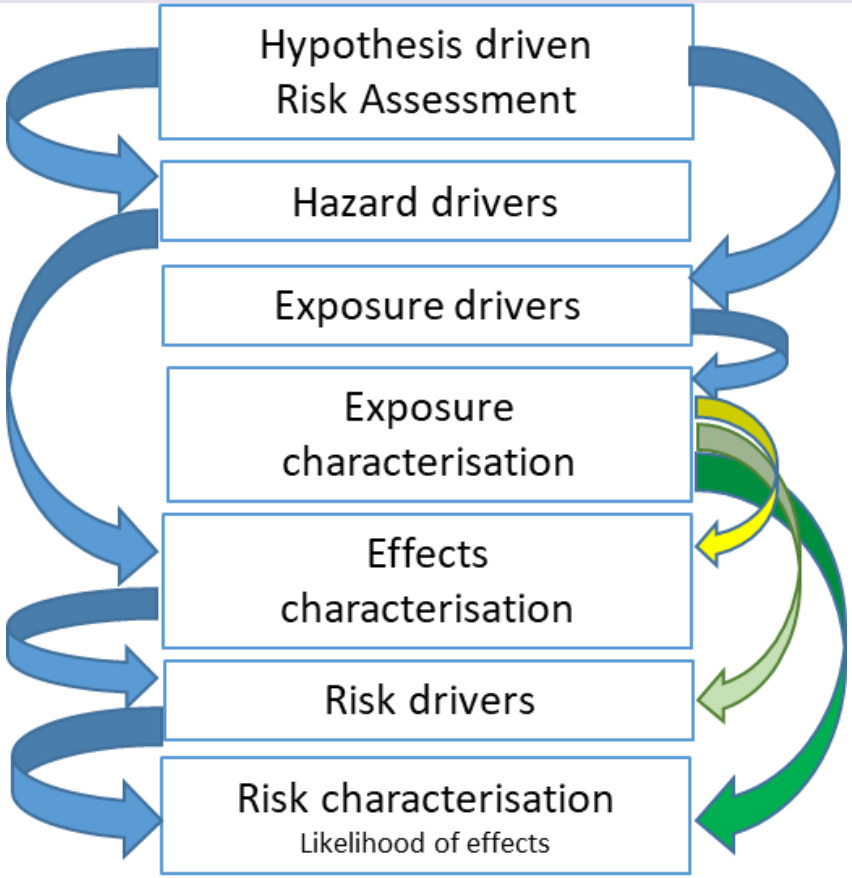
Take-home message from third example

For hazard-based assessments, NAMs already provide the required information without the need for animal studies

Closer to the future: Paradigm revolution

Hypothesis driven Next Generation Risk Assessment Methods



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Some EU contributions for regulatory science

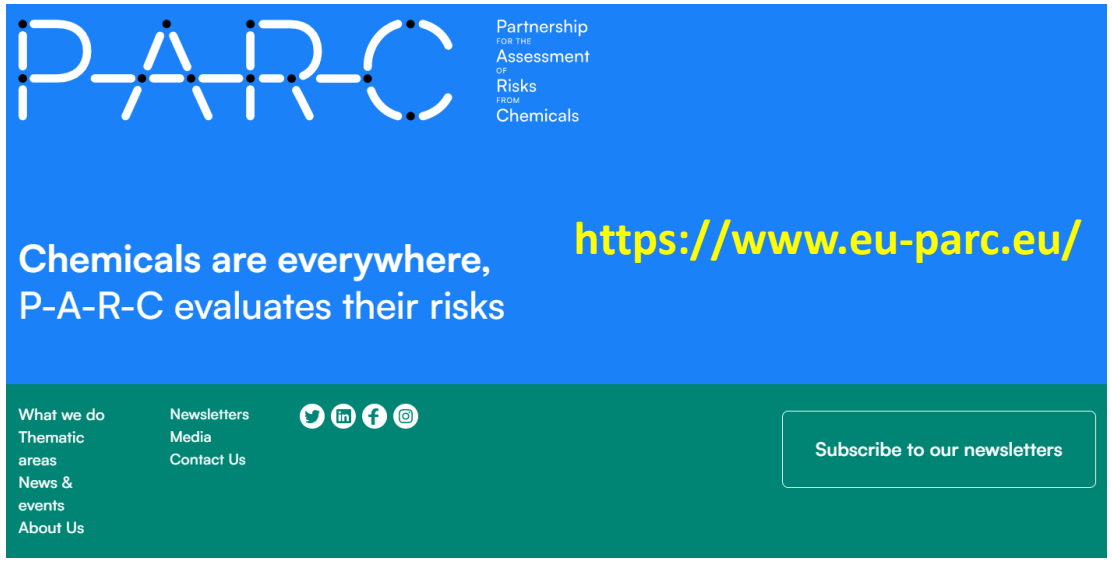
Archives of Toxicology (2021) 95:1867–1897
https://doi.org/10.1007/s00204-021-03034-y

REVIEW ARTICLE

Check for updates

Current EU regulatory requirements for the assessment of chemicals and cosmetic products: challenges and opportunities for introducing new approach methodologies

Francesca Pistollato[1] · Federica Madia[1] · Raffaella Corvi[1] · Sharon Munn[1] · Elise Grignard[1] · Alicia Paini[1] · Andrew Worth[1] · Anna Bal-Price[1] · Pilar Prieto[1] · Silvia Casati[1] · Elisabet Berggren[1] · Stephanie K Bopp[1] · Valérie Zuang[1]



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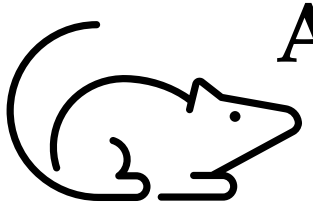
NAM-based Integrated Approaches to Testing and Assessment (NAM-IATA)

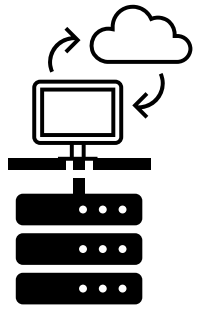


Available animal data

+

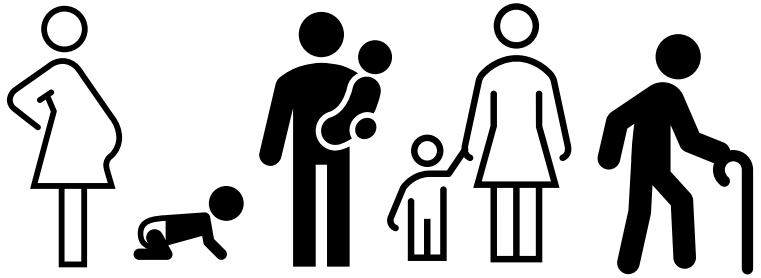
Human *in vitro* models

+



***In silico* & AI-supported evidence assessment**

Lines of evidence extrapolation



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Final take-home messages

Science-based and verifiable NAM results can be used now.

Advance is evident in many areas.

We need new and international agreed paradigms for speeding the advance of NAMs and improve our safety assessments.

Thank you!

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Email: jtarazona@isciii.es

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International Association for Food Protection® WEBINAR

May 31 , 2023	Matrix Additions to Rapid Pathogen Detection Methods- Part 1: Assuring the Right Fit
June 05, 2023	Work Smarter, Not Harder - discussing the challenges and opportunities to improve support specific to small processors
June 07, 2023	WHO Global Strategy for Food Safety 2022-2030
June 14, 2023	Dry Cleaning: Is Water Friend or Foe in Food Safety and Sanitation?
June 15, 2023	Tech-Enabled Traceability: Get Ready For FSMA 204 With GS1 Standards
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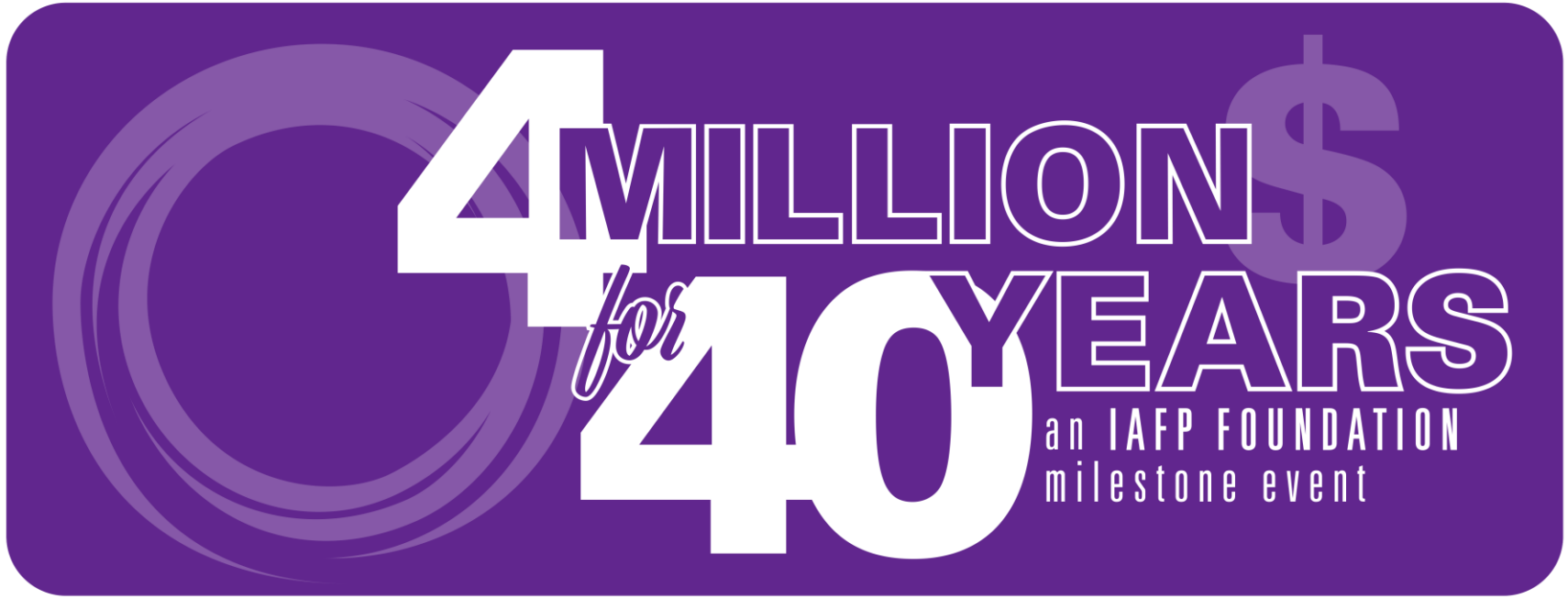

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